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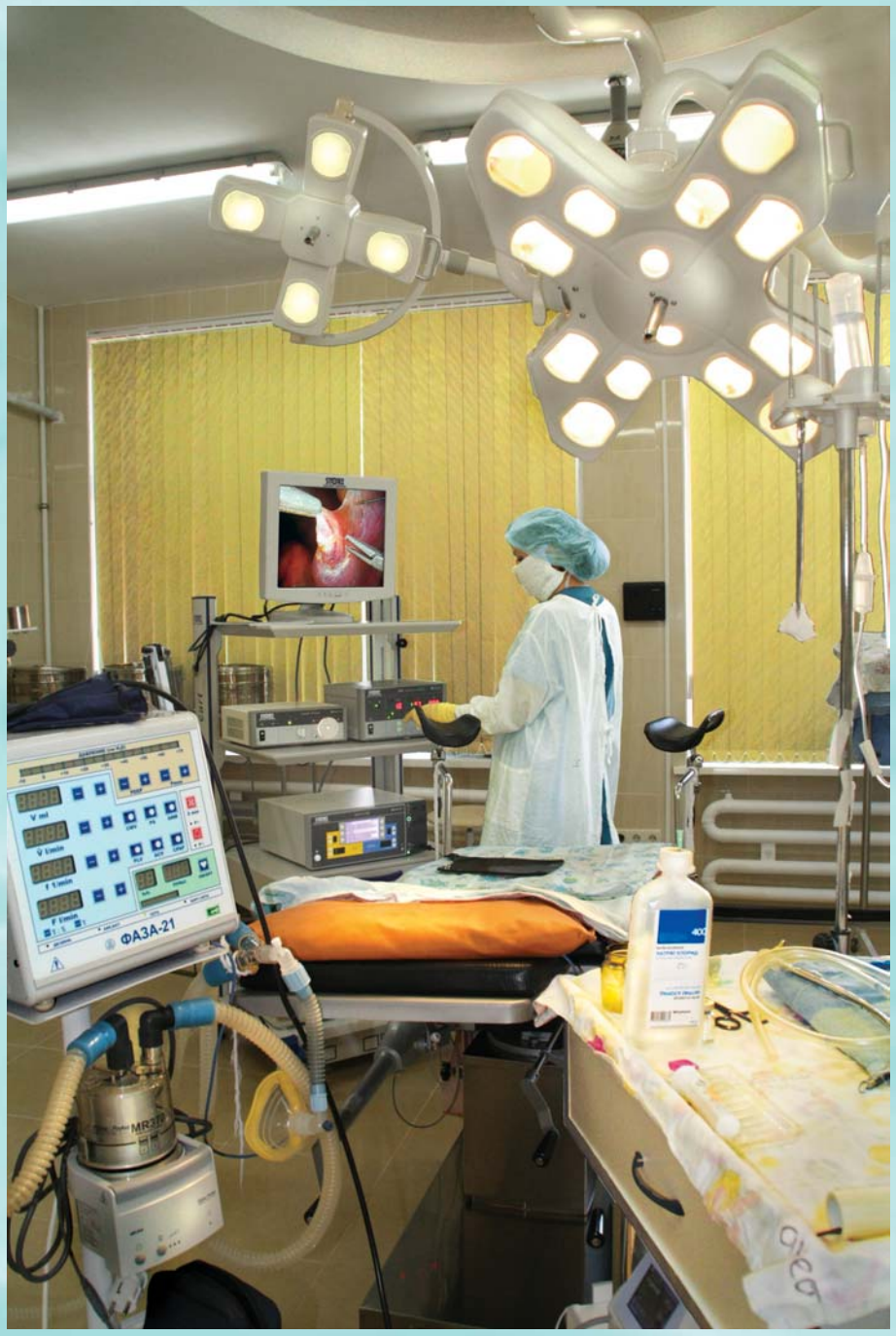

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ЩОДО ПРОБЛЕМ ЕНДОСКОПІЇ
ABOUT ENDOSCOPY PROBLEMS

Цей номер журналу присвячено проблемам ендоскопії — перспективного напряму медицини, який сьогодні розвивається швидкими темпами. Саме ці проблеми обговорювалися у Києві на нещодавньому IV Всесвітньому конгресі лікарів-ендоскопістів, на якому головували головний редактор нашого журналу академік НАМН України, президент Української асоціації малоінвазивної та лазерної хірургії В. М. Запорожан і президент Всесвітньої асоціації лікарів-ендоскопістів професор Янгде Жанг (Китай).

У номері опубліковано статті, надіслані до журналу учасниками конгресу.

This Journal's issue is dedicated to problems of endoscopy — a perspective trend of medicine, which develops quickly nowadays. These problems were discussed in Kiev at the IV World Endoscopy Doctors Congress, which was headed by the editor-in-chief of our Journal academician of NAMS of Ukraine, president of the Ukrainian Association of Minimally Invasive and Laser Surgery V. M. Zaporozhan and chairman of the IV World Endoscopy Doctors Association professor Yang-de Zhang.

The articles for publication in this issue were sent by the Congress participants.

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УВАГА!

Змінено правила підготовки статей до «Одеського медичного журналу». Статті, прийняті до друку за попередніми правилами, будуть опубліковані. Нові статті приймаються за новими правилами, які вміщено наприкінці цього номера, друкуватимуться у наступних номерах, а також на сайтах Одеського національного медичного університету odmu.edu.ua та «Одеського медичного журналу» journal.odmu.edu.ua

До відома авторів! Постановами президії ВАК України № 1-05/2 від 27 травня 2009 р. та № 1-05/5 від 31 травня 2011 р. «Одеський медичний журнал» включено до переліку видань, у яких можуть публікуватися основні результати дисертаційних робіт з медицини, біології та фармації.

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К ЧИТАТЕЛЯМ
TO READERS

Дорогие друзья!

Рад приветствовать читателей специального номера «Одесского медицинского журнала», посвященного IV Всемирному конгрессу врачей-эндоскопистов. Конгресс прошел в начале октября в столице Украины Киеве под эгидой Министерства здравоохранения Украины, Национальной академии медицинских наук Украины, Ассоциации акушеров-гинекологов Украины, Украинской ассоциации малоинвазивной и лазерной хирургии, Всемирной ассоциации врачей-эндоскопистов и Одесского национального медицинского университета. Это первая украино-китайская встреча на высшем уровне специалистов в области эндоскопии.

Киев известен во всем мире как центр политической, финансовой активности, образования, науки и средств массовой информации. Он стал идеальным местом для проведения конгресса, который, несомненно, будет иметь большое значение для развития не только медицинского и научного, но также культурного сотрудничества между двумя странами. Стратегическими целями и задачами этого конгресса являются содействие освоению новейших инновационных технологий в эндоскопической хирургии на международном уровне, выработке международных стандартов и сертификации специалистов.

Вот почему во время конгресса была предоставлена возможность свободного обмена мнениями, сообщений в виде видео- и постерных докладов. Один день конгресса полностью посвящен «живой хирургии» с трансляцией из клиник Одесского национального медицинского университета. Во время конгресса состоялись выставки эндоскопических инструментов. Представители компаний, производящих медицинское оборудование, участвовали в конгрессе и представили наиболее важные технические нововведения.

В данном журнале опубликованы статьи, посвященные возможностям, преимуществам и научным доказательствам эффективности эндоскопических методов, представленные международными экспертами в этой области. Мы очень надеемся, что изложенные в нем материалы помогут нашим читателям проникнуться духом Всемирного конгресса врачей-эндоскопистов.

В. Н. ЗАПОРОЖАН,
председатель IV Всемирного конгресса врачей-эндоскопистов, академик НАМН Украины, президент Украинской ассоциации малоинвазивной и лазерной хирургии, главный редактор «Одесского медицинского журнала»

Dear friends!

I am glad to welcome the readers of the special issue of the Odessa Medical Journal dedicated to the IV World Endoscopy Doctors Congress. This Congress took place at the start of October in the capital of Ukraine Kiev, under the aegis of the Ministry of Health of Ukraine, National Academy of Medical Science of Ukraine, Association of Obstetricians and Gynecologists of Ukraine, Ukrainian Association of Miniinvasive and Lazer Surgery, the World Endoscopy Doctors Association and the Odessa National Medical University. It is the first Ukraine-China meeting for endoscopy specialists at the highest level.

Kiev is world known as a global metropolis influential in politics, finance, education, science and media, and thus is the perfect location for the Congress, which has great importance for development of not only medical and scientific but also cultural collaboration between the two countries. Strategic aims and tasks of this Congress are assistance in realization of the most modern innovation technologies in endoscopy at the international level, elaboration of international standards and sertification of specialists.

At the Congress all colleagues had a possibility for free communication, posters and video-reports. One of the Congress day was fully dedicated to “live surgery” with telecast from the Odessa Medical University’s clinics. Medical instrument industry representatives participated in the Congress presenting their important technical innovations.

This Journal’s number presents the articles dedicated to possibilities, advantages and scientific proofs of efficacy of endoscopic methods, represented by international experts in this field. We hope that the publications in this Journal will aid our readers to enter into the spirit of the World Endoscopy Doctors Congress.

V. N. ZAPOROZHAN,
Chairman of the IV World Endoscopy Doctors Congress, academician of NAMS of Ukraine, president of the Ukrainian Association of Minimally Invasive and Laser Surgery, editor-in-chief of “The Odessa Medical Journal”

РАД НАШЕЙ ВСТРЕЧЕ
I AM GLAD TO MEET YOU

Дорогие друзья и коллеги!

От имени Всемирной ассоциации врачей-эндоскопистов имею удовольствие и честь приветствовать читателей «Одесского медицинского журнала» — издания, приверженность которого пропаганде передовых медицинских технологий известна далеко за пределами Украины.

Не случайно и нынешний номер журнала посвящен эндоскопии — одной из перспективных и быстро развивающихся отраслей медицины. Особенно приятно, что он приурочен к IV Всемирному конгрессу врачей-эндоскопистов, который состоялся недавно в Киеве — столице Украины. Это мероприятие организовано совместно с Министерством здравоохранения Украины, Национальной академией медицинских наук Украины, Одесским национальным медицинским университетом и Всемирной ассоциацией врачей-эндоскопистов (WEDA).

Минимальная травма, быстрое восстановление, минимум лекарств и кратковременная госпитализация — вот явные преимущества эндоскопической хирургии. Основанная в 2009 году, Всемирная ассоциация врачей-эндоскопистов (WEDA) является международной федерацией медицинских технологий и науки. Она призвана изучить вопрос создания единых норм в эндоскопической практике, способствовать интеграции различных направлений науки, техники и медицины, разработке оценки и экспертизы стандартов такой высокотехнологичной медицинской специальности, как эндоскопия. IV Всемирный конгресс врачей-эндоскопистов, тема которого «Создание международных стандартов эндоскопии и лапароскопии, обучение и сертификация по малоинвазивной хирургии», стал важным шагом на пути к международному медицинскому сообществу.

Мы уверены, что это событие станет важной вехой в деле развития эндоскопии и лапароскопии, а публикации в нынешнем номере «Одесского медицинского журнала» — значительным вкладом в достижение прогресса в медицине.

С уважением,

Янгде ЖАНГ,
председатель IV Всемирного конгресса врачей-эндоскопистов,
президент Всемирной ассоциации врачей-эндоскопистов,
директор Национального исследовательского центра гепатобилиарной хирургии Министерства здравоохранения КНР,
профессор Центрального Южного университета провинции Хунань (КНР)

Dear friends and colleagues!

On behalf of the World Endoscopy Doctors Association, it is great pleasure and honor to greet the readers of “The Odessa Medical Journal” — the journal which is well known outside Ukraine for popularization of advanced medical technologies.

It is no coinsidence that this issue of the Journal is dedicated to endoscopy — one of perspective and fast developing fields of medicine. The fact that it is timed to the IV World Endoscopy Doctors Congress which took place in the capital of Ukraine Kiev, is of special pleasure. This meeting was organized in cooperation with the Ministry of Health of Ukraine, the National Academy of Medical Sciences of Ukraine, the Odessa National Medical University and the World Endoscopy Doctors Association (WEDA).

Smaller trauma, quicker recovery, less medication and shorter hospitalization are the bright advantages of endoscopic surgery. Founded in 2009, WEDA is the international federation of medical technology and science. It is aimed to explore the establishment of unified global norms in endoscopy, provide integration of different directions of science, technique and medicine, and the building of assessment and examination of standards for such high-tech medical technology as endoscopy. The IV World Endoscopy Doctors Congress, the theme of which was “Establishing International Standards for Endoscopy and Laparoscopy Procedures, Training and Certification of Minimally Invasive Surgery” became an important step to the international medical association.

We are certain that this event will be a milestone for endoscopy and laparoscopy development and the publications in the present issue of “The Odessa Medical Journal” will contribute greatly to medicine progress.

Yours sincerely,

Yang-de ZHANG,
Chairman of the IV World Endoscopy Doctors Congress,
President of the World Endoscopy Doctors Association,
Chairman of the National Hepabiliary Surgery Research Center of Ministry of Health of China,
professor of the Central South University, Hunan Province (China)

UDC 617-089-072.1(477.74-25)(091)

V. M. Zaporozhan[1], I. Z. Gladchuk, N. M. Rozhkovska, V. G. Marichereda, A. G. Volyanska

RETROSPECTIVE ANALYSIS, CURRENT STATE AND CHALLENGES OF ENDOSCOPIC AND MINIINVASIVE SURGERY IN THE ODESSA NATIONAL MEDICAL UNIVERSITY (1975–2012)

The Odessa National Medical University, Odessa, Ukraine

УДК 617-089-072.1(477.74-25)(091)

В. Н. Запорожан, И. З. Гладчук, Н. Н. Рожковская, В. Г. Маричереда, А. Г. Волянская

РЕТРОСПЕКТИВНЫЙ АНАЛИЗ, СОСТОЯНИЕ И РАЗВИТИЕ ЭНДОСКОПИЧЕСКОЙ И МАЛОИНВАЗИВНОЙ ХИРУРГИИ В ОДЕССКОМ НАЦИОНАЛЬНОМ МЕДИЦИНСКОМ УНИВЕРСИТЕТЕ (1975–2012)

Одесский национальный медицинский университет, Одесса, Украина

Эндоскопия является приоритетным направлением научной и лечебной деятельности Одесского национального медицинского университета — ведущего центра эндоскопической хирургии Украины. Первые эндоскопические операции в Одессе были выполнены в гинекологической клинике в конце 70-х годов прошлого века, видеоэндоскопические — в 1992 г. За 35-летний период становления и развития эндоскопической гинекологической хирургии в Одесском национальном медицинском университете проанализировано более 20 000 гинекологических эндоскопических и малоинвазивных вмешательств. Увеличение количества операций и снижение числа осложнений связаны как с усовершенствованием оборудования, так и с повышением квалификации хирургов. Этому в значительной мере способствовали создание учебного и тренировочного центра эндоскопической и малоинвазивной хирургии в 2001 г., проведение конференций, мастер-классов, сотрудничество с ведущими эндоскопическими центрами мира.

Ключевые слова: эндоскопическая и малоинвазивная хирургия, анализ, Одесский национальный медицинский университет.

UDC 617-089-072.1(477.74-25)(091)

V. M. Zaporozhan, I. Z. Gladchuk, N. M. Rozhkovska, V. G. Marichereda, A. G. Volyanska

RETROSPECTIVE ANALYSIS, CURRENT STATE AND CHALLENGES OF ENDOSCOPIC AND MINIINVASIVE SURGERY IN THE ODESSA NATIONAL MEDICAL UNIVERSITY (1975–2012)

The Odessa National Medical University, Odessa, Ukraine

Endoscopy is an exclusive tool of modern medicine and a priority direction of scientific and medical activity of the Obstetrics and Gynecology Department of the Odessa National Medical University, the leading recognized center of endoscopic surgery of Ukraine. The first endoscopic operations in Odessa gynecologic clinics were implemented at the end of 70th years last century, videoendoscopic — since 1992. Alongside with cryosurgical techniques, we have started operative endoscopy interventions using high-frequency currents, laser energy, and other newest mechanical tools and manipulations. We have analyzed more than 35-year period of formation and development of endoscopic gynecologic surgery at the Odessa National Medical University. We have studied more than 20,000 gynecologic endoscopic interventions, considering indications to operations, analyzed their types during a certain period, and specific complications of video-endoscopic interventions, that were executed in gynecologic clinics of Odessa. The retrospective analysis of endoscopic interventions of more than 35 years' period shows stable dynamics of increase in number of endoscopic interventions, especially during last ten years. Substantially it is connected with improvement of endoscopic operational equipment, introduction of modern operative endoscopic techniques, improvement of qualification and accumulation of experience of gynecologic endoscopic surgeons. Complications rate during operative laparoscopy was near 1%. The gained experience in the field of endoscopic surgery in gynecology was the background for foundation of the Educating and Training Center since 2001, organization of conferences and master-classes, cooperation with the leading centers of endoscopic surgery, cooperation with the world leading centers of endoscopic surgery.

Key words: endoscopic and miniinvasive surgery, analysis, the Odessa National Medical University.

Endoscopy is an exclusive tool of modern medicine. It is a priority direction of scientific and medical activity of Obstetrics and Gynecology Department of the Odessa National Medical University, the leading recognized center of endoscopic surgery of Ukraine. Hysteroscopic treatment of hyperplastic processes of endometrium and myometrium was conducted for the first time in the ONMedU by the end of 70's last century [1–3]. We have managed to verify clinical and morphological aspects of intrauterine pathology due to these operations, via domestic

[1] Rector of ONMedU, academician of National Academy of Medical Science of Ukraine, President of Ukrainian Gynecologic Endoscopic Association, Head of Obstetric & Gynecology Department N 1 ONMedU.

equipment "LOMO", "Krasnogvardeets" and German "Carl Zeiss". The fundamental background of mini-invasive method's medical effect was shown according to the results of cryo-hysteroscopy implementation [1; 15; 16]. Practical results of the research in cryo-endoscopic surgery promoted developing of unique cryo-endoscopic device (CED-1), using liquid nitrogen [14; 17].

Videoendoscopy have been implemented in gynecologic clinics of Odessa since 1992. Alongside with cryosurgical techniques, we have started operative endoscopy interventions using high-frequency currents, laser energy and other newest mechanical tools and manipulators. We have gradually mastered various legation techniques, ultrasonic scalpel, etc. [3–5; 12; 13]. Professional skills of the gynecologists specializing in endoscopic surgery, is constantly increasing, as like as number of the doctors, obtaining endoscopic surgery skills. The number of endoscopic operations in our clinic has three times increased comparing to 1998 and reached about 2000 in 2012. The list of endoscopic operations has considerably extended and their parameters have changed.

At modern stage, the treatment of more than 90% benign gynecologic pathology, requiring surgical intervention, are carried out by means of endoscopic surgery [6–11; 13]. At the same time, the problems connected with a laparoscopy and surgical methods, which arise at many gynecologic laparoscopic manipulations, demand the detailed analysis. Thus, we have analyzed more than a 35-year period of formation and development of endoscopic gynecologic surgery at the Odessa National Medical University. We have studied more than 20,000 gynecologic endoscopic interventions, considering indications to operations, analyzed their types during certain period, and specific complications of video-endoscopic interventions, that were executed in gynecologic clinics of Odessa.

All the operations are being conducted by application of modern video-endoscopic equipment of Karl Storz (Germany), Olympus (Japan), Martin (Germany), Circon Acmi (USA), Everest Medical (USA) and others. Firms "Martin" (Germany), bipolar cutting nippers BICOAG "Everest Medical" (USA), medical laser system Medilas 4060 of MVV (Germany), ultrasonic (harmonious) scalpel of "Olympus" (Japan), stepplers of "Ethicon Endo-Surgery" (USA), Ukrainian cryosurgical equipment, generators of a high frequency current. Hysteroscopy is maintained by application of flexible and rigid hysteroscopes. The cryo-endoscopic techniques and various mechanical tools are used while operative hysteroscopy, Nd YAG laser and resectoscopy techniques were introduced in 1993–1994.

Preoperative preparation of patients for laparosroscopic operations is similar to laparotomic interventions, and has not changed essentially at the expired period. Anesthesia is carried out by means of endotracheal narcosis. Intravenous anesthesia is used at hysteroscopic operations, and spinal/peridural anesthesia — at vaginal operations [2].

We conduct only gas laparoscopy with carboxiperitoneum. At suspicion of presence of widespread intraperitoneal adhesions, we prefer an open Hasson method (1989) with pneumoperitoneum. We try to preserve a level of intra-abdominal pressure within the limits of 9–16 mm Hg during operation. The quantity of laparoscopic ports is defined by clinical situation, but in overwhelming majority of cases, we use three punctures, one of that is intended for optics, and two others — for manipulators. Evacuation of macropreparations of solid structure, which do not exceed 3–4 cm diameters, is done through punctures for manipulators. Solid masses of greater sizes are removed through posterior colpotomy aperture or by means of tissue morcellator. Abdominal cavity drainage is applied under indications [1].

The analysis of structure of indications for laparoscopy, diagnostic or medical, shows certain differences. It is notable, that less than 3% of laparoscopies were diagnostic. The most part of indications was infertility, endometriosis and chronic pelvic pain, benign gynecologic pathologies (95%). Other indications for laparoscopy were the control of hysteroscopic procedures (1.5%) and suspected müllerian duct anomaly (0.5%).

Operative hysteroscopy was used because of the polyps (29%) and hyperplastic process of endometrium (27%), submucous fibroids of uterus (17%). Less often indications to operative hysteroscopy were resection of intrauterine septa (11%), fallopian tube occlusions in the proximal part (5%), uterine synechias in fertility disorders (5%) and retention of a small fragment of IUD (1%), retention of product of conception parts (4 %).

Introduction of new operative techniques promoted increasing of endoscopic operations and expansion of their list [14]. During last five years, quantity of endoscopic interventions due to uterine and ovarian pathology have noticeably increased, just as laparoscopic surgery of endometriosis, its severe form, in most of cases (74%). On a background of increase of total number of endoscopic interventions, the quantity of laparoscopic salpingostomy and tubal sterilization remained unchanged [5; 8].

The remote results of the operations of various factors of infertility testify to correctly chosen management and an adequate professional level of surgery, 41% pregnancy has come within 1.5–2 years after operation; more than 700 infertile patients in the period 1998–2012 had ART.

In 1994 we have started laparoscopic-assisted vaginal hysterectomy (LAVH) [6], in 1996 — mastered the technique of laparoscopic supracervical hysterectomy (LSH), in 1997 — total laparoscopic hysterectomy (LH). Laparoscopic access is more actively applied at combined gynecologic and simultaneous operations, urgent conditions in gynecology, pelvic inflammatory diseases, in urological gynecology and oncological gynecology.

The method of endosurgical staging in patients with clinical stage I of endometrial cancer became popular during last decade. This approach means a combination of laparoscopic assisted vaginal radical or total laparoscopic hysterectomy with bilateral salpingoophorectomy and laparoscopic bilateral pelvic lymphadenectomy. Pelvic lymphadenectomy only, or in a complex with paraaortal lymphadenectomy, plays the important role in surgical staging of endometrial cancer, and shows more precise prognostic information. The therapeutic role of lymphadenectomy, its ability to change adjuvant therapy, is studied less, and available publications have inconsistent character.

Our experience includes 86 patients with clinical stage I of endometrial cancer [1; 7]. At 64 patients, laparoscopic procedure included full survey of abdominal cavity, peritoneal lavage and radical laparoscopic assisted or total laparoscopic hysterectomy. During laparoscopy pelvic and aortic lymphatic nodes samplings was carried out at all patients with G2 or G3, the same as for patients with the first stage of damage in which depth of myometrial invasion was more, than 1/2 on the frozen section, or those with more aggressive type of cancer (adenoacantoma, papillary serous or clear-cell carcinoma) were found. Laparoscopy revealed the later stage of endometrial carcinoma in 7 patients, therefore we performed laparotomy with omentectomy. The received results testify to reduction of duration of operation in comparison with laparotomic access ((150.4± ±10.2) min) and ((115.3±9.2) min) ($p<0.05$), duration of stay in hospital (2.9±0.5 and 6.3±1.4), of complications rate (1.7% and 10.5%). All patients are alive within 5 years [7].

A high-level operative endoscopic technique of simultaneous laparoscopic operations, which we have started since 1995, was revealed during this research. The multidisciplinary operative interventions that we perform are laparoscopic hysterectomy in combination with laparoscopic cholecystectomy (57 cases), laparoscopic supracervical hysterectomy and laparoscopic holecystectomy (17 cases) and others [15].

The annual quantity of hysteroscopic operation during noted period also constantly increased. It was promoted by introduction of laser and electro-surgical operative technics with endometrial ablation and submucous fibroid resection.

Frequency of complications at carrying out operative laparoscopy was near 1%. The most frequent complication happened during introduction of Veress needle and trocar (67%). Less often complications took place during an operative stage of laparoscopy. Only 3 cases have been classified, as severe among all the complications. They were puncture of intestines (n=1), damage of the bladder (n=1) and thermal damage of the urether (n=1). Frequency of complications at hysterectomy was 1.4%. There are three cases of uterine punching among them. All three complications have occurred at the stage of dilatation of the uterine cervix. Late complications included uterine bleedings (n=13).

During the last years, gynecologic endoscopy has reached a new level because of technical progress. The retrospective analysis of endoscopic interventions of more than 35 years' period shows stable dynamics of increase in quantity of endoscopic interventions, especially during last ten years. Substantially it is connected with improvement of endoscopic operational equipment, introduction of modern operative endoscopic techniques, improvement of qualification and accumulation of experience of gynecologic endoscopic surgeons.

The most significant increase concerns operative endoscopic interventions, both laparoscopic, and hysteroscopic. It was promoted by expansion of a spectrum of operations, like laparoscopic surgery of ovarian and fallopian tubes pathology, hysterectomy, laparoscopic treatment of severe forms of endometriosis and simultaneous endoscopic operation. Development of technology of endoscopic equipments stimulated expansion of indications for laparoscopic surgery and increasing in quantity of patients year after year. Similar succession of events could lead to the justified increase in complications during or after laparoscopic interventions. However, increasing of number of more complex endoscopic operations has not led to uphold the frequency of surgical complications. Both at laparoscopy, and hysteroscopy, their frequency during last five years, remained stable and corresponded to data of the other authors. There were no complications connected with surgical wound of blood vessels. Evidence distinction between the quantity of the complications, which have arisen after endoscopic and laparotomic operations at similar pathology, has not been established. We aspire to improvement of skills in laparoscopic surgery and optimization of usage of endoscopic tools for the greatest possible reduction of complications further. Careful research of the complications, which may increase due to increase in number of endoscopic interventions in our clinics, allows developing

strategy of their prevention and optimum conducting.

Nowadays almost all the operative interventions at the gynecologic clinics of the ONMedU are carried out via endoscopic access, for example, surgery of benign and malignant tumors of ovaries, extrauterine pregnancy, tumor-like formations of the uterine appendages, plastic surgery of fallopian tubes pathology, inflammatory diseases of uterine appendages, conservative myomectomy, hysterectomy of vaginal prolapse, stress incontinence, correction of all types of developmental anomalies of genitals, endometriosis involving intestines and excretory tract, malignant lesions of uterus and uterine cervix combined with lymphadenectomy, etc. Our experience testifies, that endoscopy may and should be accepted in obstetrics, in extragenital pathology, demanding operative intervention, such as ovarian tumors, postnatal endometritis and complications of operative delivery, like haematoma, bleeding, and pelvic abscesses. Endoscopic access allows reducing essentially postoperative period, and thus frequency of postoperative complications makes 0.36 per cent. Operative treatment in our center is carried out not only to inhabitants of Odessa and regions of Ukraine, but also from near and far abroad.

More than 2,000 operations were done per year 2012, among them 1,100 laparoscopies, 250 hysteroscopies, 135 combined interventions (laparoscopy + hysteroscopy), 355 vaginal operations, 210 laparotomic ones. Total amount of endoscopic operations have increased by 123% comparing with 1998, 4.7 times as much laparoscopies, and 2.9 as much hysteroscopies, comparing with 1998.

The acquired experience in the field of endoscopic surgery in gynecology was a background for foundation of the Training Center based on Department of Mini-Invasive Technologies of the ONMedU in 2001, organization of conferences and masterclasses. We realized that physicians in regional hospitals do not use most of the advances in endoscopic surgery promoted in the University clinic. Leading surgeons and professors, recognized for their surgical skills, are heading the training courses.

The cadets master complex laparoscopic manipulations during the courses. Still, despite of increase in quantity of complex operative interventions with participation of cadets, the level of complications remains stable. Training in the center of gynecologic endoscopy improves a professional level of cadets, without being reflected on quality of medical aid to patients of our clinic. The received professional experience allows introducing modern endoscopic techniques in the hospitals of trained doctors, and, thus, raising the quality of the gynecologic aid for patients across the whole Ukraine.

Integral and significant part of our activity is research. We conduct research in the field of genetics, morphology, immunology, biochemical aspects of endometriosis and rare internal genital abnormalities [16; 17]. Innovative techniques of treatment of mentioned pathology are being developed and modified. New pathogenesis mechanisms of infertility, endometriosis, chronic pelvic pain syndrome are established. The scientific basis of new medical and diagnostic techniques is being worked out too.

The clinic is proud of cooperation with the leading centers of endoscopic surgery in Europe (Poland, Germany, France, Italy, Russia), Asia (China) in which members of our staff train every year. Owing to this cooperation, we organize the international scientifically practical conferences. During the conferences, in a mode of a “live surgery”, the latest achievements in endoscopic surgery are demonstrated from different clinic outside Ukraine. Conferences stimulate free exchange of experience that, undoubtedly, promotes our professional growth.

The analysis of introduction and development of endoscopic surgery in gynecologic practice in the Odessa National Medical University clinic shows that positive dynamics of an annual gain of quantity of endoscopic operations, expansion of indications for them, corresponds to world tendencies. Modern endoscopy means the universal access, allowing carrying out both diagnostic and surgical treatment within the adequate limit, and postoperative monitoring. The conventional advantages of endoscopy such as minimal operative trauma, fast rehabilitation of patients and excellent cosmetic effect comprise high quality and patient-oriented treatment and, thereof, high quality of life of gynecologic patients. Modern endoscopic technologies allow replacing many gynecologic laparotomic operations; however, alternative methods of surgical treatment in gynecology, oncology, gynecology, and urologic gynecology should also be actively developed.

Along with low-invasive endoscopic surgery, other methods of innovative gynecological surgery are introduced at the University clinics. The technique of retropubic urethropexy by TVT/TVT-O is used in the treatment of genuine urinary stress incontinence in women since 2002–2003. According to our data, both methods are highly effective (over 85%) under the adequate selection of patients. Lower risk of complications for the application of TVT-O promotes more frequent using of this method. Treatment of vaginal prolapse is performed by transvaginal sacrospinous colposuspension using the Miya hook, since 2003. This method significantly improves the results of vaginal reconstructive surgery of total uterine prolapse complicated by vaginal eversion (enterocele). Nevertheless, a revolutionary approach to

prolapse surgery is undoubtedly technique using polypropylene mesh. We used Prolift System (Anterior, Posterior, Total) since 2003, just as our own construction — polypropylene allotransplantate. From our point of view, these innovative methods undoubtedly improve results and reduce the frequency of relapses to the minimum level. However, operative technique is currently quite complex and demands perfect anatomical dissection to avoid intra- and postoperative complications. There were 2 complications in 90 operations: intraoperative injury of the bladder — 1, mesh erosion — 1. No recurrences were observed within 1–5 years.

We believe that endoscopic and mini-invasive innovative technologies will be widely implicated in the integrated complex of diagnostics, treatment and monitoring of gynecologic pathology, and in prospective research in the nearest future.

REFERENCES

1. *Запорожан В. М.* Ендоскопічна хірургія в гінекології / В. М. Запорожан // Вісник Академії медичних наук України. – 1998. – № 4. – С. 25–31.

2. *Запорожан В. М.* Ендохірургія в гінекології: тенденції та перспективи / В. М. Запорожан // Одеський медичний журнал. – 1998. – № 3. – С. 3–7.

3. *Запорожан В. М.* Становлення і здобутки Одеської школи гінекологічної ендоскопії / В. М. Запорожан // Одеський медичний журнал. – 2003. – № 4 (78). – С. 9–12.

4. *Запорожан В. М.* Лапароскопічне, комбіноване і повторне лапароскопічне лікування у безплідних хворих із тяжким ендометріозом / В. М. Запорожан, І. З. Гладчук, А. Г. Волянська // Одеський медичний журнал. – 1998. – № 4. – С. 28–30.

5. *Запорожан В. М.* Досвід лапароскопічного лікування раку ендометрія / В. М. Запорожан, І. З. Гладчук, Н. М. Рожковська // Зб. наук. праць Асоціації акушеров-гінекологів України. – К. : Інтермед, 2004. – С.182–185.

6. *Запорожан В. М.* Комбінована з лапароскопічним етапом гістеректомія у лікуванні жінок з опущенням і випадінням внутрішніх статевих органів / В. М. Запорожан, В. В. Стежковий, І. З. Гладчук // ПАГ. – 1995. – № 6. – С. 61–63.

7. *Запорожан В. Н.* Видеоэндоскопические операции в хирургии и гинекологии / В. Н. Запорожан, В. В. Грубник, В. Ф. Саенко. – К. : Здоров'я, 1999. – 301 с.

8. *Запорожан В. Н.* Лазеры в эндоскопии / В. Н. Запорожан, В. В. Грубник, Б. К. Поддубный. – К. : Здоров'я, 1998. – 206 с.

9. *Endoscopic* Surgery for Gynecologists / ed. by C. Sutton, M. Diamond. – L. : W. B. Saunders, 1993. – 416 p.

10. *Gallinat A.* Gynecologic Laparoscopy and Hysteroscopy in Day Clinic: Trends and Perspectives / A. Gallinat, W. Nugent, R. Lueken // The Journal of the American Assotiation of Gynecologic Laparoscopists. – 1994. – N 2 (1). – P. 103–111.

11. *Zaporozhan V.* Intratissue Laser Thermotherapy in Treatment of Uterine Myoma / V. Zaporozhan // The Journal of the American Assotiation of Gynecologic Laparoscopists. – 1996. – N 4 (3). – P. 310–311.

12. *Zaporozhan V.* Electrosurgical and Nd:YAG Lasers to Treat Infertile Women with Severe Endometriosis / V. Zaporozhan, I. Gladchuk // The Journal of the American Assotiation of Gynecologic Laparoscopists. – 1997. – N 4 (4). – P. 40–41.

13. *Simultaneous* laparoscopic Surgery: First Results / V. Zaporozhan, I. Gladchuk, E. Kononenko, M. Kashtalian // Proceedings of the World Congress of Gynecologic Endoscopy. – Rome, 1997. – P. 160–165.

14. *Zaporozhan V.* Combined Laparoscopic Cryosurgery in the Treatment of Polycystic Ovarian Disease / V. Zaporozhan // The Journal of the American Assotiation of Gynecologic Laparoscopists. – 1994. – N 4 (1). – P. 40–47.

15. *Zaporozhan V. N.* Conservative Myomectomy / V. N. Zaporozhan, I. I. Gladchuk, N. N. Rozhkovska // Zaawansowane techniki laparoskopowe w ginekologii. – Lodz, 2005. – P.127–129.

16. *Zaporozhan V. N.* Regenerative medicine: state in Ukraine / V. N. Zaporozhan, V. Kordium, O. Kholodkova // Regenerative medicine. – 2007. – N 5 (2). – P. 715.

17. *Zaporozhan V. N.* Cryoendoscopy in the Treatment of Some Forms of Tubal Infertility, Polyps, and Endometrial Hyperplasia / V. N. Zaporozhan, O. V. Khait // Proceedings of the World Congress of Gynecologic Endoscopy 20th Annual Meeting of the AAGL. — Chicago, Illinois, 1991. – P. 211–215.

REFERENCES

1. Zaporozhan V.N. Endoscopic surgery in gynecology. Visnyk Academii medychnykh nauk Ukrainy 1998; 4:25-31.

2. Zaporozhan V.N. Endosurgery in gynecology: trends end perspectives Odesky medychny zhurnal 1998;3:3-7.

3. Zaporozhan V.N. Formation and achievements of the Odessa School of gynecological endoscopy. Odesky medychny zhurnal 2003;4(78):9-12.

4. Zaporozhan V.N., Gladchuk I.Z., Volyanska A.G. Laparoscopic, combined and second-look laparoscopic treatment in infertility patients with severe endometriosis. Odesky medychny zhurnal 1998;4:28-30.

5. Zaporozhan V.N., Gladchuk I.Z., Rozhkovska N.M. Experience of laparoscopic treatment of endometrial carcinoma. Zbyrnik naukovykh prats Asociacii akusheriv-ginecologiv Ukrainy. Kyiv: Intermed;2004:82-185.

6. Zaporozhan V.M., Stezhkovyi V.V., Gladchuk I.Z Combined with laparoscopy part hysterectomy in treatment genital organ prolapses in women. PAG 1995;6:61-63.

7. Zaporozhan V.N., Grubnik V.V., Saenko V.F. Videoendoscopic operations in surgery and gynecology. Kyiv, Zdorovya, 1999:301.

8. Zaporozhan V.N., Grubnik V.V., Poddubny B.K. Lasers in endoscopy Kyiv, Zdorovya;1998:206.

9. Endoscopic Surgery for Gynecologists. Edited by C. Sutton, M. Diamond, London, W.B.Saunders;1993: 416.

10. Gallinat A., Nugent W., Lueken R. Gynecologic Laparoscopy and Hysteroscopy in Day Clinic: Trends and Perspectives. The Journal of the American Assotiation of Gynecologic Laparoscopists. 1994;2(1):103-111.

11. Zaporozhan V. Intratissue Laser Thermotherapy in Treatment of Uterine Myomata. The Journal of the American Assotiation of Gynecologic Laparoscopists 1996;4(3):310-311.

12. Zaporozhan V., Gladchuk I. Electrosurgical and Nd:YAG Lasers to Treat Infertile Women with Severe Endometriosis. The Journal of the American Assotiation of Gynecologic Laparoscopists 1997;4(4):40-41.

13. Zaporozhan V., Gladchuk I., Kononenko E., Kashtalian M.. Simultaneous laparoscopic Surgery: First Results (Proceedings of the World Congress of Gynecologic Endoscopy), Rome,1997:160-165.

14. Zaporozhan V., Gladchuk I., Khait O. Combined Laparoscopic Cryosurgery in the Treatment of Polycystic Ovarian Disease. The Journal of the American Assotiation of Gynecologic Laparoscopists 1994;4(1):40-47.

15. Zaporozhan V.N., Gladchuk I.I., Rozhkovska N. Conservative Myomectomy. Zaawansowane techniki laparoskopowe w ginekologii. Lodz, 2005: 127-129.

16. Zaporozhan V.N., Kordium V., Kholodkova O. Regenerative medicine:state in Ukraine. Regenerative medicine, 2007;5(2):715.

17. Zaporozhan V.N., Khait O.V. Cryoendoscopy in the Treatment of Some Forms of Tubal Infertility, Polyps, and Endometrial Hyperplasia // Proceedings of the World Congress of Gynecologic Endoscopy 20th Annual Meeting of the AAGL. Chicago, Illinois, 1991:211-215.

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EXPRESSION OF NY-ESO-1 GENE IN HUMAN HEPATOCELLULAR CARCINOMA

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Human NY-ESO-1 gene encodes for an antigen belonging to cancer/testis (CT) protein. NY-ESO-1 gene is expressed in many human cancers with various histological types, but not in normal tissues except testis. The NY-ESO-1 antigen is a potential target for cancer immunotherapy. We investigated the expression of gene NY-ESO-1 in the samples of hepatocellular carcinoma (HCC) tissues and adjacent liver tissues by RT-PCR. 56 of 124 tumor tissues from HCC patients were NY-ESO-1 positive (45.2%). In contrast, NY-ESO-1 mRNA was not detected in any of the adjacent tissues. A cDNA fragment of 329bp was amplified by RT-PCR from each of the 56 positive samples and sequenced. Four samples were found to have point mutations at 2 sites resulting in a substitution of one amino acid residue. Such substitution is predicted to have a profound effect on the protein structure and hence on the functional motif in the protein. To distinguish whether the substitution is a point mutation or a polymorphism present in normal population, the genomic DNA fragment has been amplified from 10 samples of the peripheral blood mononuclear cells (PBMCs) of healthy donors and sequenced. All the tested samples displayed the same sequence as that had been reported. Thus, the base pair change occurred in HCCs is maybe a point mutation. In HCCs, the expression of NY-ESO-1 has no correlation with other parameters tested, such as tumor markers (aFP, AFU), metastasis, recurrence, and tumor diameter ($P<0.05$). The relatively high rate of NY-ESO-1 gene expression in HCCs indicates that NY-ESO-1 protein may be a vaccine candidate to be developed as immunotherapy for HCC patients.

Key words: NY-ESO-1, RT-PCR, hepatocellular carcinoma, gene expression, immunotherapy.

Introduction

A number of human tumor antigens which are recognized by CD4/CD8 T cells or autologous antibodies have been increasingly identified by various approaches for the last decade [1]. Of the more than ten genes or gene families coding for CT antigens, NY-ESO-1 was identified from esophageal cancer by a serological approach (SEREX), which is based on the screening of recombinant tumor cDNA expression libraries for specified interactions with autologous serum antibodies [2]. A large-scale serologic survey of over 700 tumor patients' sera showed that anti-NY-ESO-1 antibody(Ab) was often present in patients with NY-ESO-1$^+$ tumors, with 30% to 50% of those patients in the study having detectable NY-ESO-1 Ab [3]. In comparison, Ab responses to other CT antigens were found to be much lower. More importantly, the NY-ESO-1 protein contains both B cell epitope and T cell epitope capable of simultaneously inducing both humoral and cellular immune response in vivo and in vitro [4; 5]. It is further confirmed by the identification of a 10-mer antigenic peptide in NY-ESO-1 protein capable of presenting HLA-A31 molecule to induce specific CTL response [6]. Furthermore, recent report has demonstrated that fucoidin enhances the cross-presentation of NY-ESO-1 to T cells, resulting in an increase of T-cell cytotoxicity against NY-ESO-1 expressing human cancer cells [7]. NY-ESO-1 has been reported to be frequently expressed in melanoma [2; 8], breast cancer [9; 10], neuroblastoma [11], esophageal squamous cell carcinoma [2], prostate cancer [12; 13], transitional cell carcinoma [14; 15], and lung cancer [16]. There have been so far several reports describing a moderate rate of NY-ESO-1 expression in HCC samples [17–20]. We extended this study to investigate NY-ESO-1 cDNA expression in 124 human HCC tumor tissues and their respective adjacent liver tissues.

Materials and Methods

Patients

All 124 HCC patients aged 24 to 70 years old were admitted for surgery at Xiangya Hospital of Central South University from May 2005 to January 2009. The clinicopathological data, including gender, stage of disease, tumor invasion, TNM classification, etc. are listed in table 1. Normal controls of PBMCs were collected from healthy donors at the age of 20 to 24 years old to detect NY-ESO-1 genomic DNA.

Cell Lines

The melanoma cell line SK-MEL-37, which expresses NY-ESO-1 mRNA, were kindly provided by Xiangya Hospital of Central South University for Cancer Research.

Tissue Samples

Samples of HCCs and liver tissues were collected from pa-

Table 1

The Relationship between the Expression of NY-ESO-1 Gene and the Clinicopathological Parameters

Clinicopathological parameters	Expression of NY-ESO-1 gene				
	Positive	Negative	Positive rate, %	χ^2	p
Total	56	68	45.2	—	—
Sex					
male	46	53	46.5	0.5617	0.45
female	10	15	40.0%		
Age					
< 40 yr	17	21	44.7	0.9497	0.33
> 40 yr	39	47	45.3		
Tumor diameter					
< 5 cm	10	15	40.0	0.5617	0.45
> 5 cm	46	53	46.5		
Tumor embolism of portal vein					
yes	7	10	41.2	0.7223	0.40
no	49	58	45.8		
Tumor capsule					
integrity	25	42	37.3	0.0569	0.81
incompletion	31	26	54.4		
Tumor number					
single	43	47	47.8	0.3408	0.56
multiple	13	21	38.2		
HBV infection					
yes	49	61	44.5	0.6993	0.40
no	7	7	50.0		
HCV infection					
yes	9	5	64.3	0.1268	0.72
no	47	63	42.7		
Cirrhosis					
none/light	27	32	45.8	0.8980	0.34
middle/heavy	29	36	44.6		
AFP					
normal (< 20 ng/l)	16	25	39.0	0.3345	0.56
high	40	43	48.2		
AFP mRNA					
positive	46	54	46.0	0.7017	0.40
negative	10	14	41.7		
AFU					
normal (<198 nKat)	5	14	26.3	0.0728	0.79
high	51	54	48.6		
Survival time					
< 2 years	34	37	47.9	0.4802	0.49
> 2 years	22	31	41.5		
Metastasis and recurrence					
< 1 year	23	16	59.0	0.0363	0.85
> 1 year	33	52	38.8		

tients who were undergoing routine hepatic surgery at Xiangya Hospital (n=204). Among them, 124 patients suffered form HCC, 37 were cirrhosis without HCC, and the remaining 43 were non-cirrhotic liver diseases. HCC tissues and the adjacent tissues (5 cm away from the tumor margin) were collected from patients undergoing HCC resection. Written informed consent was obtained from each patient. The resected tissues were stored in liquid nitrogen after snap frozen until being used for RNA extraction.

Isolation of RNA

Total RNA was extracted from liver tissue samples, using RNeasy mini kit and QIAshredder (QIAGEN). Tissue samples were homogenized in liquid nitrogen and lysed in TRIZOL (1 ml / 50-100 mg tissue, GIBCOL BRL). Total RNA was isolated by phenol/chloroform extraction, precipitated with isopropanol, washed with 75% EtOH, and finally dissolved in RNase-free dH_2O. RNA concentration was assessed using UV spectrophotometry at OD_{260}. The ratio of $OD_{260/280}$ was 1.78-1.82. The RNA samples were analyzed in 2% agarose gel electrophoresis to determine the RNA integrity.

Synthesis of cDNA

RNA samples (5 ug) were mixed with oligo-dT15 (0.5 ug/ul, Promega, USA) and random hexamers (0.5 ug/ul, Promega, USA), and added with RNase-free dH_20 to 12 ml. The mixture was heated to 70°C for 10 minutes and quickly chilled on ice. The contents in the tube were collected by brief centrifugation, and then added with the following reagents: 4 ml 5× reverse transcriptase buffer (250 mM Tris-HCL [pH 8.3 at room temperature], 375 mM KCL, 15 mM $MgCL_2$), 2 ml 0.1 M DTT and 1ml 10 mM dNTP Mix (10 mM for each dATP, dGTP, dCTP and dTTP at neutral pH). The contents were mixed gently and in-

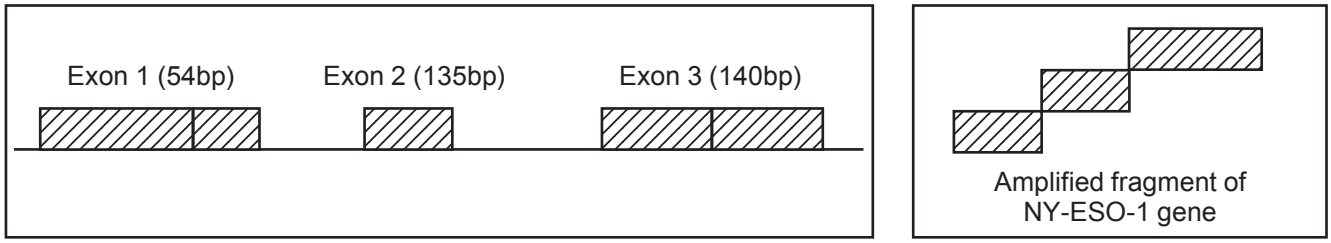

Fig. 1. The structure of NY-ESO-1gene (329bp).
Note. There are three exons in NY-ESO-1 gene; underlined frame indicates the amplified fragments

cubated at 42°C for 2 minutes, and then added with 200 U of superscript II reverse transcriptase (GIBCO BRL, USA), 20 U RNase inhibitor (RNAsin, Promega), and RNase-free dH_2O to a total volume of 20 ml. cDNA synthesis was performed at 42°C for 50 minutes. The RT enzyme was heat-inactivated at 70°C for 15 minutes.

PCR Amplification of G3PDH cDNA

To assess the integrity of the cDNA, amplification reactions (50 ml) were performed with the following reagents: 1 ml cDNA, 10 mM glyceraldehyde-3-phosphate dehydrogenase (G3PDH) primers (sense: 5'- ACC ACA GTC CAT GCC ATC AC-3'; antisense: 5'- TCC ACC ACC CTG TTG CTG TA-3'), PCR buffer (20 mM Tris-HCL [pH 8.4], 50 mM KCl), dNTP (1 ul, 10 mM, Promega) and 2.5 U Taq polymerase (GIBCO BRL, USA), and by Thermal Cycler (Perkin-Elmer 9700, USA) under the following conditions: 94°C for 20 seconds, 65°C for 40 seconds, and 72 °C for 40 seconds (35 cycles, followed by a final extension at 37°C for 7 minutes.

PCR Amplification of NY-ESO-1 cDNA

The amplification reactions (50 ml) contained 1ml cDNA, 10 mM NY-ESO-1 primers (sense: 5'-ATG GAT GCT GCA GAT GCG G-3'; antisense: 5'- GGC TTA GCG CCT CTG CCC TG-3' (Fig. 1), 5 ml 10 × PCR, 3 ml 25 mM $MgCl_2$, 1 ml 10 mM dNTP Mix (10 mM for each dATP, dGTP, dCTP and dTTP at neutral pH), 2.5 ml DMSO, 1.5 U Tag DNA polymerase(GIBCO BRL, USA) and PCR H_2O. The samples were denaturation at 94°C for 2 minutes, and the amplifications were performed under the following conditions: 94°C for 40 seconds, 60°C for 40 seconds, and 72°C for 30 seconds (35 cycles), followed by a final extension at 72 °C for 7 minutes. The amplified cDNAs were run in 1.5% agarose gel with a NY-ESO-1 band of 329 bp.

Southern Blot Analysis

The RT-PCR products were fractionated by electrophoresis in 2% agarose gels and transferred to nitrocellulose membranes at 4°C for 16 hours. A NY-ESO-1 cDNA fragment (25 ng) of 329 bp, derived from RT-PCR products and confirmed by DNA sequencing, was labeled with [^{32}P]dCTP (HIGH PRIME kit, Boehringer Mannheim GmbH, Germany) and used as probe. The cDNAs immobilized on the membranes were prehybridized with 6 × SSC, 2 × Denhardts, 0.1% SDS, and 100 mg/ml denatured fragmented salmon sperm DNA at 68°C for 16 hours, and then hybridized with the probe at 68°C for 8 hours. After hybridization, the membranes were sequentially washed twice at 68°C in 2 × SSC and 0.1% SDS, 30 minutes each, and twice at 68°C in 0.1 × SSC and 0.1% SDS, 1 hour each. The membranes were exposed to X-ray film at -70°C with intensified screens to obtain an autoradiogram.

Cloning and Sequencing of NY-ESO-1 cDNA

The purified NY-ESO-1 cDNAs obtained from PCR amplification were cloned into a pGEM-T vector (Promega) by T4 DNA ligase and amplified in E. coli, DH5a. The positive colonies were selected with EcoR1 digestion of miniprep DNA. The putative NY-ESO-1 cDNA samples were sequenced with T7 and M13 sequencing primers using an automatic gene sequencer (Visible Genetics Inc., Canada).

Analysis of NY-ESO-1 Gene Sequence in Genomic DNA

To determine polymorphism or point mutation of NY-ESO-1 variants, human genomic DNA was extracted from PBMCs obtained from 10 healthy donors using Trizol Reagent (GIBCO BRL). The human genomic DNA samples were boiled for 10 minutes and purified through Sephadex G-50 column. The primers (sense, 5'-ACC TCG CCA TGC CTT TCG -3'; antisense, 5'-GTC GGA TAG TCA GTA TGT TGC C-3') were designed according to the sequence of the second exon harbouring the mutated site (Fig. 2). The amplifica-

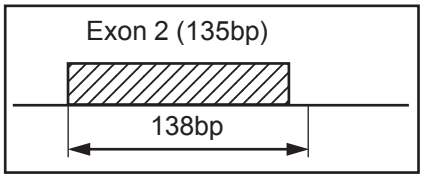

Fig. 2. The amplified fragment of Exon 2
Note. The length of Exon 2 is 135bp; the arrows indicate the amplified fragment.

tion reactions (50 ml) contained 5 ml 10 × PCR buffer, 3 ml 25 mM $MgCl_2$, 1 ml 10 mM dNTP Mix (10 mM for each dATP, dGTP, dCTP and dTTP at neutral pH), 1.5 U Tag DNA polymerase, 0.5 ml of each primer, 35 ml PCR water and 1 ml genomic DNA template. The amplified DNAs were run in 2.0% agarose gel with a positive band of 138bp (Fig. 3). The positive PCR products were ligated to a pGEM-T Easy vector and sequenced as described above. The putative NY-ESO-1 genomic cDNA samples were sequenced with T7 and M13 sequencing primers using an automatic gene sequencer (Visible Genetics Inc., Canada).

aFP mRNA detection

The total RNAs was extracted from PBMCs and reverse transcribed into cDNAs. The aFP mRNA was detected by amplification using nested RT-RCR.

Results

Expression of NY-ESO-1 in HCC

After the amplification by RT-PCR with the designed primers, a 329 bp product that the expected size of NY-ESO-1 cDNA was amplified from the NY-ESO-1 positive cell lines SK-MEL-37. Of the 124 HCC samples, 56 (45.2%) were found to express NY-ESO-1 mRNA, shown as a single band of 329 bp in the RT-PCR product, and each gave a strong and specific signal of the same size in Southern blot hybridization. In contrast, none of the adjacent liver tissues was NY-ESO-1 positive by RT-PCR (Fig. 4), nor in Southern blot hybridization (Fig. 5). Furthermore, all the 80 samples of liver tissues from non-cirrhotic (n=43) and cirrhotic patients (n=37) were NY-ESO-1 negative by RT-PCR.

NY-ESO-1 variants in HCC

All of the 56 NY-ESO-1-positive PCR products were cloned into the pGEM-T vector and transfected into DH5a. Three clones from each individual PCR product were picked up for DNA sequencing. The data were compared with GenBank database. The sequences of 156 clones from 52 samples were identical to the second exon of NY-ESO-1 cDNA. However, the sequences of 9 clones from 3 samples (H2, H28, H29) were shown to have point mutations at 2 sites (A347T, A432G, Fig. 6); the A347T mutation did not affect the coding amino acids, whereas the A432G mutation resulted in a substitution of threonine to alanine at position 127. Another sample (H10) exhibited only one point mutation as A432G. Notably, the A432G mutation in NY-ESO-1 cDNA was identified in each of the four samples, resulting in an identical substitution of amino acids. As it was independently confirmed by experiments, in which 3 clones were picked up and sequenced for each sample, this point mutation was unlikely to be caused by PCR artifacts.

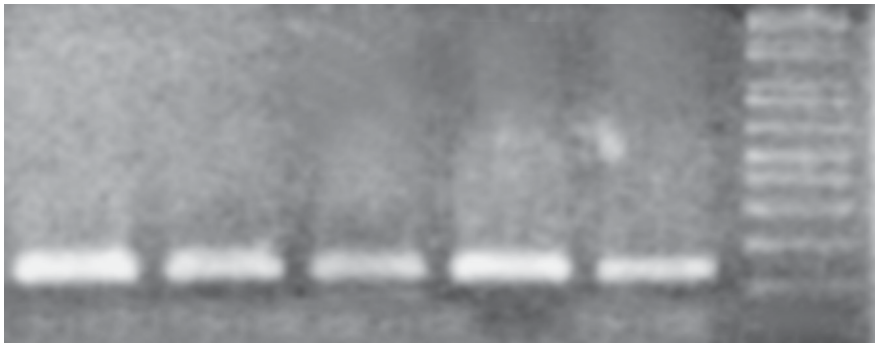

Fig. 3. The PCR results of genomic DNA

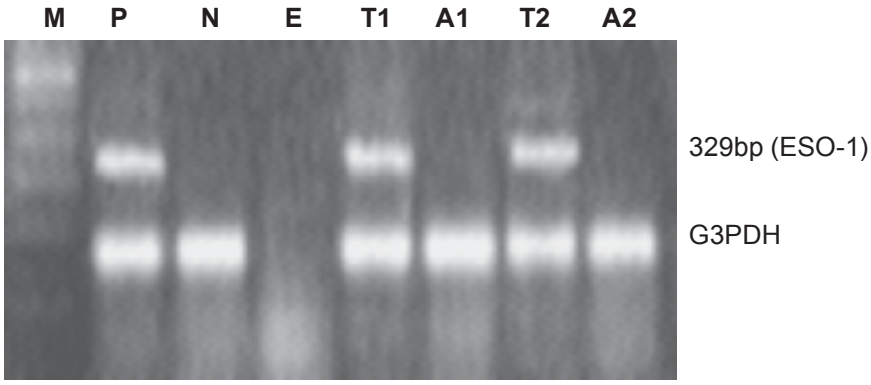

Fig. 4. The RT-PCR results of NY-ESO-1

Note. M, marker; P, positive control; N, negative control; E, empty control; T, tumor tissue; A, adjacent non-tumor tissue.

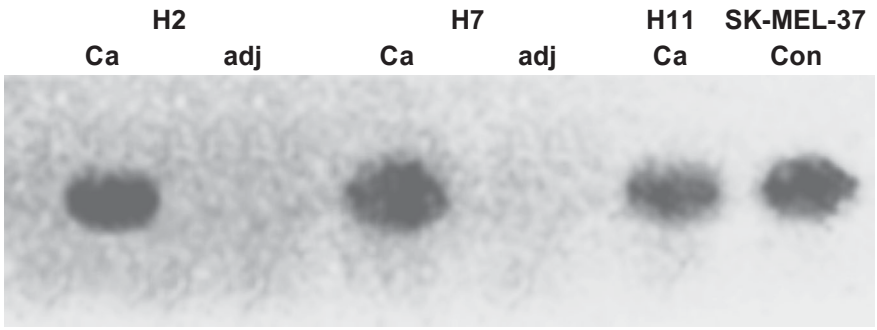

Fig. 5. The Southern Blot results of NY-ESO-1

The Relationship between NY-ESO-1 Expression and Clinicopathological Parameters

The expression of NY-ESO-1 mRNA was not correlated with other clinicopathological parameters, such as the tumor marker aFP tested at both protein and mRNA levels, AFU, metastasis, recurrence, tumor diameter, etc. (see Table 1).

Discussion

To accurately estimate the frequency of NY-ESO-1 expression in the HCCs of Chinese patients, the possibility that the RNA samples were contaminated with genomic DNA was excluded by control assay, in which no target band was detected in the PCR products amplified from RNA samples without prior reverse transcription. Our results showed that NY-ESO-1 was expressed in 45.2% (56/124) of the Chinese HCCs. In contrast, NY-ESO-1 mRNA was detected in none of the 124 adjacent tissues samples. To ensure the results' reliability, all positive PCR products were subjected to DNA sequencing and confirmed to be NY-ESO-1 cDNA fragments.

A total of 168 clones from 56 samples of the NY-ESO-1 positive RT-PCR products have been sequenced (3 clones were picked up from each positive RT-PCR product). The sequences of 156 clones from 52 samples were identical to the corresponding region of NY-ESO-1 cDNA in Genbank database. However, 3 samples (H2, H28, H29) were shown to have point mutations at 2 sites (A347T, A432G) in exon 2. The first point mutation of A347T did not lead to a change of amino acid residue, whereas the second point mutation (A432G) resulted in a substitution of one amino acid residue (Thr127Ala). In addition, one sample (H10) was shown to have only one point mutation of A432G, resulting in the substitution of threonine to alanine. To exclude any errors caused by PCR amplification, three clones from each individual positive PCR product of the four samples

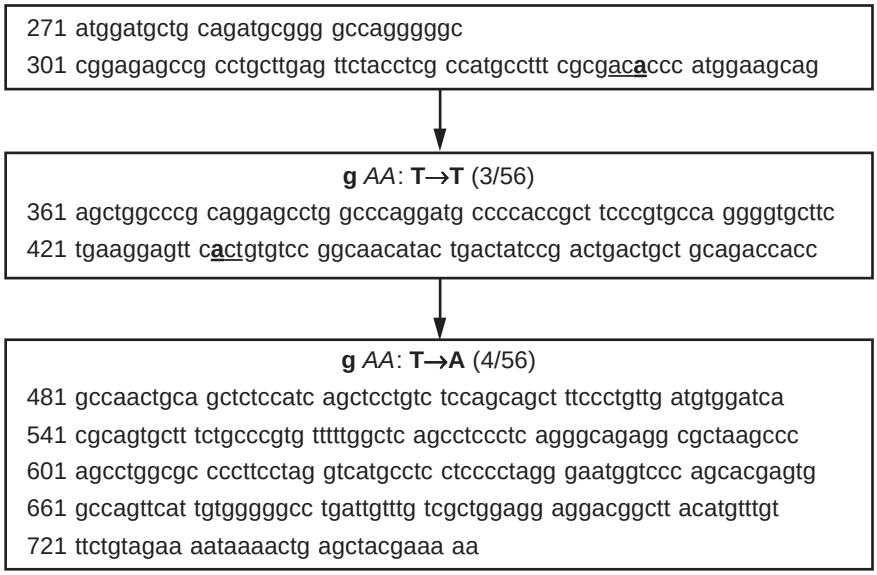

Fig. 6. The mutation positions of NY-ESO-1 gene
Note. A was replaced by T at position 347 (3/14), with no change of amino acids; A was replaced by G at position 432 (4/14), and the amino acid changed from Threonine to Alanine. Both of the two sites simultaneously mutated in three samples.

were randomly picked up for DNA sequencing, and all gave the same results. Besides, Taq plus DNA polymerase was used in PCR to minimize mismatches of base pairs during the amplification cycles. Thus, the base pair changes are unlikely to be PCR artifacts. More studies are needed to determine whether this cDNA sequence pattern reflects a gene polymorphism or should be attributed to point mutation occurred in HCC.

The substitution of threonine to alanine at position 127 may have implications in the biological properties of the protein. Based on the analysis of the linear and 2-demensional structure by Gene Runner (Fig. 7), it shows no change in protein hydrophilia;

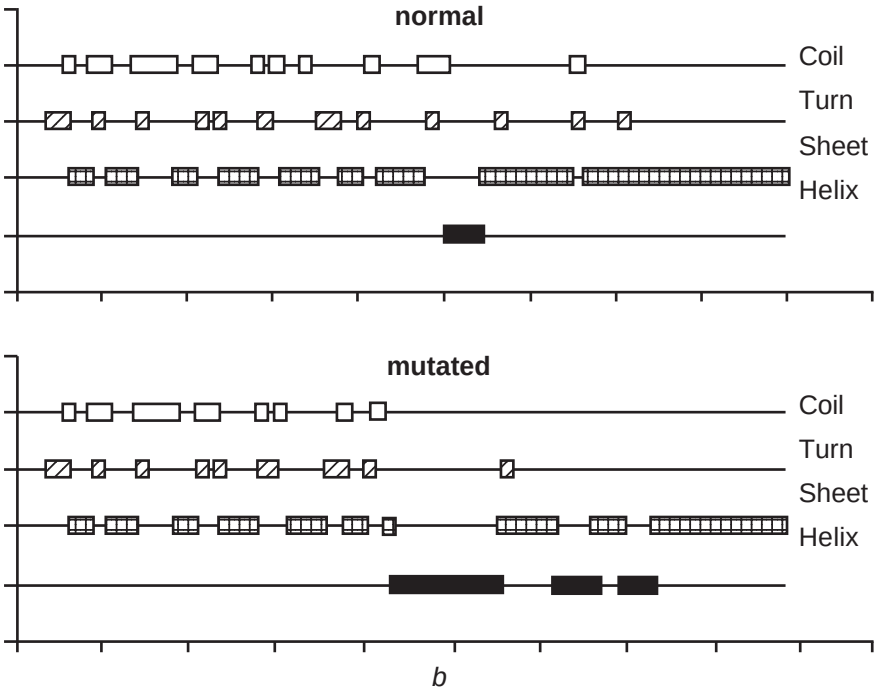

Fig. 7. The analyses of the linear and 2-demensional structures of the normal and mutated NY-ESO-1 genes by Gene Runner

however, the α-helix and β-sheet in the secondary structure of the variant NY-ESO-1 protein is predicted to be changed. These changes in the secondary structure may lead to an alternation in the tertiary structure, and hence, affect the exposure of antigenic epitopes or form new ones.

Currently, the clinical HCC diagnosis is based on disease history, liverish background, AFP, and CT scan. It is reported that NY-ESO-1 specific antibodies were detected in the serum of a part of patients whose NY-ESO-1 expression was positive, while the antibodies were not detected in the patients whose NY-ESO-1 expression were negative. Though the biological function of NY-ESO-1 protein has not been fully understood yet, the expression of NY-ESO-1 mRNA in liver tissues is indicative of hepatoma. Detection of NY-ESO-1 expression, therefore, adds a new parameter for the diagnosis of HCC. It is reported that HLA-A2-restricted T cells from HCC patients target NY-ESO-1, but exist in an exhausted state that might require additional activation to restore function [21], and currently, there are several ongoing cancer vaccine trials based on NY-ESO-1 that are showing promising results [22–24]. NY-ESO-1 may be a good candidate for vaccine development in the immunotherapy for HCC patients.

REFERENCES

1. Lee SY, Obata Y, Yoshida M, Stockert E, Williamson B, Jungbluth AA, Chen YT, Old LJ, Scanlan MJ. Immunomic analysis of human sarcoma. Proc Natl Acad Sci USA. 2003 Mar 4;100(5):2651-6.

2. Chen YT, Scanlan MJ, Sahin U, Türeci O, Gure AO, Tsang S, Williamson B, Stockert E, Pfreundschuh M, Old LJ. A testicular antigen aberrantly expressed in human cancers detected by autologous antibody screening. Proc Natl Acad Sci USA. 1997 Mar 4;94(5):1914-8.

3. Stockert E, Jäger E, Chen YT, Scanlan MJ, Gout I, Karbach J, Arand M, Knuth A, Old LJ. A survey of the humoral immune response of cancer patients to a panel of human tumor antigens. J Exp Med. 1998 Apr 20;187(8):1349-54.

4. Jäger E, Stockert E, Zidianakis Z, Chen YT, Karbach J, Jäger D, Arand M, Ritter G, Old LJ, Knuth A. Humoral immune responses of cancer patients against "Cancer-Testis" antigen NY-ESO-1: correlation with clinical events. Int J Cancer. 1999 Oct 22;84(5):506-10.

5. Jäger E, Nagata Y, Gnjatic S, Wada H, Stockert E, Karbach J, Dunbar PR, Lee SY, Jungbluth A, Jäger D, Arand M, Ritter G, Cerundolo V, Dupont B, Chen YT, Old LJ, Knuth A. Monitoring CD8 T cell responses to NY-ESO-1: correlation of humoral and cellular immune responses. Proc Natl Acad Sci USA. 2000 Apr 25;97(9):4760-5.

6. Wang RF, Johnston SL, Zeng G, Topalian SL, Schwartzentruber DJ, Rosenberg SA. A breast and melanoma-shared tumor antigen: T cell responses to antigenic peptides translated from different open reading frames. J Immunol. 1998 Oct 1;161(7):3598-606.

7. Hu Y, Cheng SC, Chan KT, Ke Y, Xue B, Sin FW, Zeng C, Xie Y. Fucoidin enhances dendritic cell-mediated T-cell cytotoxicity against NY-ESO-1 expressing human cancer cells. Biochem Biophys Res Commun. 2010 Jan 11.

8. Vourc'h-Jourdain M, Volteau C, Nguyen JM, Khammari A, Dreno B. Melanoma gene expression and clinical course. Arch Dermatol Res. 2009 Oct;301(9):673-9.

9. Grigoriadis A, Caballero OL, Hoek KS, da Silva L, Chen YT, Shin SJ, Jungbluth AA, Miller LD, Clouston D, Cebon J, Old LJ, Lakhani SR, Simpson AJ, Neville AM. CT-X antigen expression in human breast cancer. Proc Natl Acad Sci USA. 2009 Aug 11;106(32):13493-8.

10. Sugita Y, Wada H, Fujita S, Nakata T, Sato S, Noguchi Y, Jungbluth AA, Yamaguchi M, Chen YT, Stockert E, Gnjatic S, Williamson B, Scanlan MJ, Ono T, Sakita I, Yasui M, Miyoshi Y, Tamaki Y, Matsuura N, Noguchi S, Old LJ, Nakayama E, Monden M. NY-ESO-1 expression and immunogenicity in malignant and benign breast tumors. Cancer Res. 2004 Mar 15;64(6):2199-204.

11. Söling A, Schurr P, Berthold F. Expression and clinical relevance of NY-ESO-1, MAGE-1 and MAGE-3 in neuroblastoma. Anticancer Res. 1999 May-Jun;19(3B):2205-9.

12. Nakada T, Noguchi Y, Satoh S, Ono T, Saika T, Kurashige T, Gnjatic S, Ritter G, Chen YT, Stockert E, Nasu Y, Tsushima T, Kumon H, Old LJ, Nakayama E. NY-ESO-1 mRNA expression and immunogenicity in advanced prostate cancer. Cancer Immun. 2003 Jul 31;3:10.

13. Alsøe L, Stacy JE, Fosse A, Funderud S, Brekke OH, Gaudernack G. Identification of prostate cancer antigens by automated high-throughput filter immunoscreening. J Immunol Methods. 2008 Jan 31;330(1-2): 12-23.

14. Sharma P, Gnjatic S, Jungbluth AA, Williamson B, Herr H, Stockert E, Dalbagni G, Donat SM, Reuter VE, Santiago D, Chen YT, Bajorin DF, Old LJ. Frequency of NY-ESO-1 and LAGE-1 expression in bladder cancer and evidence of a new NY-ESO-1 T-cell epitope in a patient with bladder cancer. Cancer Immun. 2003 Dec 18;3:19.

15. Kurashige T, Noguchi Y, Saika T, Ono T, Nagata Y, Jungbluth A, Ritter G, Chen YT, Stockert E, Tsushima T, Kumon H, Old LJ, Nakayama E. NY-ESO-1 expression and immunogenicity associated with transitional cell carcinoma: correlation with tumor grade. Cancer Res. 2001 Jun 15;61(12):4671-4.

16. Chapman CJ, Murray A, McElveen JE, Sahin U, Luxemburger U, Tьreci O, Wiewrodt R, Barnes AC, Robertson JF. Autoantibodies in lung cancer: possibilities for early detection and subsequent cure. Thorax. 2008 Mar;63(3):228-33.

17. Nakamura S, Nouso K, Noguchi Y, Higashi T, Ono T, Jungbluth A, Chen YT, Old LJ, Nakayama E, Shiratori Y.J Expression and immunogenicity of NY-ESO-1 in hepatocellular carcinoma. Gastroenterol Hepatol. 2006 Aug;21(8):1281-5.

18. Wang XY, Chen HS, Luo S, Zhang HH, Fei R, Cai J. Comparisons for detecting NY-ESO-1 mRNA expression levels in hepatocellular carcinoma tissues. Oncol Rep. 2009 Mar;21(3):713-9.

19. Peng JR, Chen HS, Mou DC, Cao J, Cong X, Qin LL, Wei L, Leng XS, Wang Y, Chen WF. Expression of cancer/testis (CT) antigens in Chinese hepatocellular carcinoma and its correlation with clinical parameters. Cancer Lett. 2005 Mar 10;219(2):223-32.

20. Chen CH, Chen GJ, Lee HS, Huang GT, Yang PM, Tsai LJ, Chen DS, Sheu JC. Expressions of cancer-testis antigens in human hepatocellular carcinomas. Cancer Lett. 2001 Mar 26;164(2):189-95.

21. Gehring AJ, Ho ZZ, Tan AT, Aung MO, Lee KH, Tan KC, Lim SG, Bertoletti A. Profile of tumor antigen-specific CD8 T cells in patients with hepatitis B virus-related hepatocellular carcinoma. Gastroenterology. 2009 Aug;137(2):682-90.

22. Caballero OL, Chen YT. Cancer/testis (CT) antigens: potential targets for immunotherapy. Cancer Sci. 2009 Nov;100(11):2014-21.

23. Nicholaou T, Ebert LM, Davis ID, McArthur GA, Jackson H, Dimopoulos N, Tan B, Maraskovsky E, Miloradovic L, Hopkins W, Pan L, Venhaus R, Hoffman EW, Chen W, Cebon J. Regulatory T-cell-mediated attenuation of T-cell responses to the NY-ESO-1 ISCOMATRIX vaccine in patients with advanced malignant melanoma. Clin Cancer Res. 2009 Mar 15;15(6):2166-73.

24. Gnjatic S, Altorki NK, Tang DN, Tu SM, Kundra V, Ritter G, Old LJ, Logothetis CJ, Sharma P. NY-ESO-1 DNA vaccine induces T-cell responses that are suppressed by regulatory T cells. Clin Cancer Res. 2009 Mar 15;15(6):2130-9.

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IMPROVING THE METHODS OF SPONTANEOUS PNEUMOTHORAX TREATMENT BY VIDEOTHORACOSCOPIC OPERATIONS

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УДК 616.25-003.219-089-072.1
В. В. Грубник[1], В. А. Мартынюк[1], П. П. Шипулин, В. В. Байдан[2]
СОВЕРШЕНСТВОВАНИЕ МЕТОДОВ ЛЕЧЕНИЯ СПОНТАННОГО ПНЕВМОТОРАКСА С ПОМОЩЬЮ ВИДЕОТОРАКОСКОПИЧЕСКИХ ОПЕРАЦИЙ
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В статье обобщен 15-летний опыт применения видеоторакоскопических операций при лечении 616 больных со спонтанным пневмотораксом. Описаны методики различных видеоторакоскопических операций в зависимости от объема и локализации патологического процесса в легочной ткани. Рассмотрены этапы развития методик эндоскопического хирургического лечения спонтанного пневмоторакса. Проведен анализ выполненных видеоторакоскопических операций при этом заболевании. Рецидивы заболевания при использовании данного метода хирургического лечения составили 3,6 %. Летальных исходов не было.
Ключевые слова: спонтанный пневмоторакс, видеоторакоскопические операции, плевродез.

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IMPROVING THE METHODS OF SPONTANEOUS PNEUMOTHORAX TREATMENT BY VIDEOTHORACOSCOPIC OPERATIONS
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[2] The Odessa Regional Hospital, Odessa, Ukraine
Introduction. The evolution of treatment of spontaneous pneumothorax (SP) has gone from conservative and punctures treatments to the use of modern videothoracoscopic technologies. Proposed in 1910 by Jacobeus thoracoscopy has been actively used for SP treatment in 70-s of XX century.

Objective. To show the possibility of videothoracoscopic operations in the treatment of patients with spontaneous pneumothorax at the example of the Odessa Regional Hospital.

Materials and methods. In our clinic over the past 15 years (1997–2011) videothoracoscopic operations at SP were conducted in 616 patients. Among them 532 men and 84 women. The average age of patients was 39 years and ranged from 18 to 80 years. All VTO lung resection should be divided into closed VTO lung resection (CVTLR) and videoassisted lung resection (VALR), when the operations are complemented by minithoracotomy (4–5 cm) access.

Discussion. CVTRL and VARL were performed at sufficiently massive defeat of lung tissue by bullas with a defect of the latter. The absence of visible perforation, isolated small bullas were an indication for other method of treatment: ligation, laser or electrocoagulation, pleurodesis. Conversion at the VTO was absent. Terms of drains removing after surgery ranged from 4–5 days at the VTO with resection of lung to 7–8 days — with coagulation or laser pleurodesis. Bed-day at the VTO totaled (5.2±0.2) days. Relapses of the disease using this method of surgical treatment were 3.6%. There were no lethal outcomes for all run-time of the VTO at SP in our hospital.

Conclusions. Videothoracoscopic operations are more effective than standard open surgery. The number of recurrences of spontaneous pneumothorax after videothoracoscopic operations were 3.6%, and after open surgery — 2.6%. Method of choice for surgical treatment of spontaneous pneumothorax is videothoracoscopic operations. Videoassisted operations are more efficient and allow to perform low-impact operations using multiple-cross-linking domestic vehicles apparatuses.
Key words: spontaneous pneumothorax, videothoracoscopic operations, videoassisted operations, pleurodesis.

Introduction

The evolution of treatment of spontaneous pneumothorax (SP) has gone from conservative and punctures treatments to the use of modern videothoracoscopic technologies. Proposed in 1910 by Jacobeus thoracoscopy has been actively used for the treatment of SP in 70-s of XX century [1; 3]. At the same time, the technical capabilities of this method were not allowed to perform endoscopic resection of bullous lung sections. Only the appearance of videothoracoscopic operations and endoscopic suturing devices allowed implementing a methodology to lung resection SP in clinical practice, which has become an alternative to conventional resection [10]. However, the high cost of equipment hampered the development of this method in our country, which led to a certain lag domestic sur-

geons from world standards. Experience in our clinic of modern methods of minimally invasive treatment of SP [4; 5; 8] allowed them in this work.

Materials and Methods

In our clinic over the past 15 years (1997–2011) videothoracoscopic operations (VTO) at SP were made in 616 patients. Among them 532 men, 84 women. The average age of patients was 39 years and ranged from 18 to 80 years.

Varieties of the VTO, held at SP, are shown in table 1. Their diversity is associated with both improved endoscopic equipment and techniques, and different amounts of damage to lung tissue. 61% of them performed under local anesthesia and 39% — under general anesthesia.

All operations at SP can be divided into two groups: radical and suspended palliative. By radical operations at SP can be attributed VTO and videoassisted lung resection, the technique of which was described in previous publications [2; 6; 9–11].

All VTO lung resection should be divided into closed VTO lung resection (CVTLR) and videoassisted lung resection (VALR), when the operations are complemented by minithoracotomy (4–5 cm) access. Implementation of both types of interventions required general anesthesia with one-lung ventilation and breathing off of the operated lung. At CVTRL the installation of three 10–12 mm thoracic ports (TP) was required in the form of a triangle on a "face-to-purpose" than to remove the effect of "fencing" of the endoscopic instruments. With this method of operation after a visual inspection was carried out the seizure of land bullous by endoscopic clips and then stitching it endostaplers Endopath Echelon-60 or Endopath Flex-45, introduced through the wound of one of the extended TP. To perform a radical resection is usually required from one to four cartridges. Resected portion of lung was easily extracted through the wound of one of the TP.

At VARL resection of the pathological area was carried out using the apparatus UO-40 and US-30. At the same suturing device, or immersed into a miniaccess or the area of lung output through its chest wall, where it made its resection.

All kinds of endoscopic resection to prevent recurrence of the disease ended in the creation of pleurodesis by electrocoagulation of the parietal pleura spot and process it with a solution of iodine.

To the respect of palliative operations which do not eliminate the pathological focus, include the following: endoscopic ligation of individual bulls and electro- or laser coagulation of bullae and pathological lung area with the creation of pleurodesis. With regard of palliative operations, these are called conditional because they are not satisfied with lung resection, however, this amount is enough for a small lesion of the lung tissue. At the ligation bullas performing, TP were installed in standard locations. Then bullas localized and under endoscopic control imposed on them Roeder loop. The latest delay endoscopically and tie. In this bull may remain or be cut off ligated [4; 5]. Surgeries using electro- and laser pleurodesis performed using electrocoagulators various capacities and designs, as well as using lasers: neodymium-YAG laser, "Raduga-1" with a wavelength of 1.064 nm and a power of 30–40 W, the energy of radiation 5000–7000 J and CO2 laser "Scalpel-3". At the same time visceral and parietal pleurodesis was running to form a crust of gray colour. All surgical interventions, regardless of the amount must come to an end thoracostomy drains by two large-diameter connecting them to a system of active aspiration. The final stage of operations is the creation of additional parietal physical and chemical pleurodesis to prevent recurrence of the disease [4; 8]. Chemical pleurodesis is performed with a solution of 5% iodine, and in exceptional cases — suspension of tetracycline.

Table 1

Types of Endoscopic Operations for Spontaneous Pneumothorax

Type of endoscopic operation	Number
Videothoracoscopic closed lung resection	180 (29.2%)
Videoassisted lung resection	58 (9.4%)
Videothoracoscopy + bullas electrocoagulation	118 (19.2%)
Videothoracoscopy + laser bullas coagulation	42 (6.8%)
Videothoracoscopic revision, drainage	216 (35.1%)
Ligation of bullas	2 (0.3%)
Total	**616 (100%)**

Results and Discussion

VTO at SP are continuously improved and are the method of choice for this pathology. The main advantages of endoscopic surgery to open interventions are low invasiveness and good cosmetic effect. But we should not think that this is the only method of surgical intervention at SP, and all the other forgotten and do not apply. Open interventions at SP also have the right to life, not less effective, but evidence for them is limited [5; 7].

CVTRL and VARL were performed at sufficiently massive defeat of lung tissue by bullas with a defect of the latter. The absence of visible perforation, isolated small bullas were an indication for other methods of treatment: ligation, laser or electrocoagulation, pleurodesis.

Contraindications to the VTO at SP consider severe comorbidity, did not allow for general anesthesia, polycystic lung with the presence of large bullas and cysts in various parts of the lung.

It would like to mention a certain evolution in the algorithm and the approach to the VTO that has occurred over the past 15 years. It can be divided into two periods: mostly conservative and operative. During the first period from 1997 to 2005, the management was as follows: when you receive a patient with SP in emergency procedure was performed videothoracoscopy (VTS) and the detection of small defects in lung bullas and perform them electro- or laser coagulation with subsequent drainage of the pleural cavity. Upon detection of large-diameter bullas finishing operation by draining the pleural cavity. After a diagnostic VTS open lung resection under general anesthesia were performed at 35% of patients [4; 7]. The second period (2006–2011) is characterized by more frequent use of primary lung resections even with a small lesion of the lung tissue. All patients with SP were performed on admission diagnostic VTS, in which the detected size of bullas and areas of lung destruction, which is subsequently determined the amount of resection and the use of necessary equipment. Patients, even with a small lung lesion the endoscopic resection of the latter by means of devices Endopath ETS Flex-45 and Echelon EC-60 Ethicon considered more radical method of surgical treatment. As cross-linking devices are quite expensive to the patient and cost savings at the same time preserve the principles of low-impact intervention techniques have been developed VARL, described above [2; 6; 9; 11].

Conversion at the VTO was absent. Terms of drains removing after surgery ranged from 4–5 days at the VTO with resection of lung to 7–8 days — with coagulation or laser pleurodesis. Bed-day at the VTO totaled (5.2±0.2) days.

Among the complications are the following: residual cavity — 18 (3.0%), abscesses at the TP injection site — 12 (2.0%), pleural empyema — 3 (0.5%) cases. Recurrence of disease was 3.6% (22 patients). 17 cases required additional drainage of the pleural cavity, 3 cases — with the drainage of the pleural cavity readjustment antiseptic solutions, 2 — lobectomy.

For all run-time of the VTO at SP in our hospital deaths were not observed.

We don't want to create impression that the VTO at SP is the panacea, and solves all questions of surgical treatment of this pathology. Open surgery keeps its place and value. Moreover, it is necessary to remember that endoscopic intervention can be performed only in specialized centers with the necessary equipment. We should not exaggerate the indications for endoscopic surgery. Such enthusiasm can lead to adverse consequences for the patient and the discrediting of this surgical technique. Under no circumstances should one try by all means no matter what the operation endoscopically, in the event of technical difficulties, you must immediately go to the open intervention of the (conversion), following the economical thoracotomy and removing them. Conversion in any case is not an error and does not detract from the merits of a specialist performing surgery. Attempts at any cost to complete the operation endoscopically can cost a patient's life or contribute to serious complications in the postoperative period, which will be commensurate with the excessive use of minimally invasive surgery.

Conclusions

1. Videothoracoscopic operations are more effective as standard open surgery. The number of recurrences of spontaneous pneumothorax after videothoracoscopic operations was 3.6%, and after open surgery — 2.6%.

2. Method of choice for surgical treatment of spontaneous pneumothorax is videothoracoscopic operations.

3. Videoassisted operations are more efficient and allow to perform low-impact operations using multiple-cross-linking domestic vehicles apparates.

REFERENCES

1. *Авилова О. М.* Торакоскопия в неотложной грудной хирургии / О. М. Авилова, В. Г. Гетьман, А. В. Макаров. – К. : Здоров'я, 1986. – 128 с.

2. *Видеоторакоскопические* операции в лечении спонтанного пневмоторакса / П. П. Шипулин, В. В. Байдан, А. А. Кирилюк [и др.] // Український журнал малоінвазивної та ендоскопічної хірургії. – 2012. – Т. 16, № 1. – С. 31–34.

3. *Гетьман В. Г.* Клиническая торакоскопия / В. Г. Гетьман. – К. : Здоров'я, 1999. – 207 с.

4. *Грубник В. В.* Хирургическое лечение спонтанного пневмоторакса / В. В. Грубник, П. П. Шипулин, В. А. Мартынюк // Український журнал малоівазивної та ендоскопічної хірургії. – 1999. – Т. 3, № 4. – С. 26–28.

5. *Мартинюк В. А.* Застосування відеоторакоскопічних операцій при спонтанному пневмотораксі : автореф. дис. … канд. мед. наук. – К., 2001. – 18 с.

6. *Опыт* применения видеоторакоскопических и видеоассистированных атипичных резекций легкого / П. П. Шипулин, В. В. Байдан, В. И. Байдан [и др.] // Харківська хірургічна школа. – 2010. – № 6 (45). – С. 82–84.

7. *Хирургическая* тактика при спонтанном пневмотораксе / Л. Н. Бисенков, А. В. Гриднев, М. З. Кобак [и др.] // Хирургия. – 1996. – № 2. – С. 74–77.

8. *Шипулин П. П.* Торакоскопическая хирургия спонтанного пневмоторакса / П. П. Шипулин, В. А. Мартынюк // Грудная и сердечно-сосудистая хирургия. – 1999. – № 2. – С. 49–53.

9. *Ясногорский О. О.* Видеоторакоскопические и видеоассистированные вмешательства в коррекции спонтанного пневмоторакса / О. О. Ясногорский, А. М. Шулутко, Н. А. Саакян // Эндоскопическая хирургия. – 2000. – № 5. – С. 16–19.

10. *Thoracoscopic* stapled resection for spontaneous pneumothorax

/ S. R. Hazelrigg, R. J. Landreneau, M. Mack [et al.] // J. Thorac. Cardiovasc. Surg. – 1993. – Vol. 105, N 3. – P. 389–393.

11. *Video*-assisted thoracoscopic surgery (VATS) of the lung / L. Solanini, F. Pruscioano, P. Bagioni [et al.] // Surg. Endosc. – 2008. – Vol. 22. – P. 298–310.

REFERENCES

1. Avilova O.M., Getman V.G., Makarov A.V. Torakoskopiya v neotlozhnoy grudnoy hirurgii [Thoracoscopy in urgent chest surgery]. Kiev, Zdorov'ya, 1986:128.

2. Shipulin P.P., Baydan V.V., Kirilyuk A.A. VATS surgery in the treatment of spontaneous pneumothorax. Ukrayinskiy zhurnal maloivazivnoyi ta endoskopichnoyi hirurgiyi. 2012;16(1): 31-34.

3. Getman V.G. Klinicheskaya torakoskopiya [Clinical thoracoscopy]. Kiev, Zdorov'ya;1999:207.

4. Grubnik V.V., Shipulin P.P., Martyinyuk V.A. Surgical treatment of spontaneous pneumothorax. Ukrayinskiy zhurnal maloivazivnoyi ta endoskopichnoyi hirurgiyi. 1999;3(4):26-28.

5. Martyinyuk V.A. Zastosuvannya videotorakoskopichnih operatsiy pri spontannomu pnevmotoraksi [The use of video-operations for spontaneous pneumothorax]. Abstract of dissertation for candidate of medical sciences. Kiev 2001:18.

6. Shipulin P.P., Baydan V.V., Baydan V.I. Experience of using video- and videoassistirovannyh atypical lung resections. Harkivska hirurgichna shkola 2010;6(45):82-84.

7. Bisenkov L.N., Gridnev A.V., Kobak M.Z. Surgical management of spontaneous pneumothorax. Hirurgiya. 1996;2:74-77.

8. Shipulin P.P., Martyinyuk V.A. Thoracoscopic surgery for spontaneous pneumothorax. Grudnaya i serdechno-sosudistaya hirurgiya. 1999; 2:49-53.

9. Yasnogorskiy O.O., Shulutko A.M., Saakyan N.A. VATS and videoassisted interventions in the correction of spontaneous pneumothorax. Endoskopicheskaya hirurgiya. 2000; 5:16-19.

10. Hazelrigg S.R., Landreneau R.J., Mack M. Thoracoscopic stapled resection for spontaneous pneumothorax. J Thorac Cardiovasc Surg. 1993: 105(3):389-393.

11. Solanini L., Pruscioano F., Bagioni P. Video-assisted thoracoscopic surgery (VATS) of the lung. Surg Endosc. 2008:22:298-310.

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DETERMINATION OF ORGANOCHLORINE PESTICIDES RESIDUES IN BROKEN RICE FOR PHARMACEUTICAL GLUCOSE BY GC

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Objective. To examine rice organochlorine pesticides in several districts in Hunan so as to provide security reference for production of pharmaceutical glucose which was made with broken rice and a reasonable range for the application of organic pesticides.

Method. A modified method of Chinese Pharmacopoeia was used to extract and prepare the samples which were analyzed by gas chromatography equipped with SE-54 fused silica capillary column (3.0 m × 0.25 mm × 0.32 mm) and electronic capture detector, the nine organic chlorine pesticides were separated by column temperature program and their contents could be measured and calculated by external standard method.

Result. The results showed that the nine organic chlorine pesticides could be accurately determined by the proposed method. The content of organic chlorine conformed to Chinese Government Standards for rice.

Conclusion. The proposed method was so fast, simple and accurate that it could be used to determine organic chlorine pesticide in rice. The rice in these districts can be used for rice glucose production.

Key words: organic chlorine pesticides, residue, rice, gas chromatography.

1. Introduction

Some organochlorine pesticides (HCH and DDT) have been prohibited to produce and use as early as 1983 in China [1], but they are still widely and globally used today, because of their lower market prices coupled with strong effects in the control of pests and diseases. In addition, the structural stability of organic chlorine makes it difficult to degrade, so there are different levels of residues in the soil, animals and plants, causing great harm to the organism itself and future generations [2]. The damage caused by pesticides mainly present in three forms: acute intoxication, chronic injury and mutagenesis, carcinogenesis or teratogenesis [3]. BHC, DDT and other organochlorine pesticides enter the body through food, and mainly accumulate in fat, followed in liver, kidney, spleen and brain, what is worse, they can affect the fetus' health through mothers' milk [4]. Therefore, in order to ensure food safety and protection of human health, it is critical to determinate organochlorine pesticides residues in broken rice.

The method was reference to the Chinese Pharmacopoeia (2010 version) and the relevant literatures, through collecting broken rice from several areas in Hunan province and determining organochlorine pesticides residues by GC, we could know the conditions of organochlorine pesticides residues in Hunan Province. The determination provided security for production of regular pharmaceutical glucose and a reasonable reference for the intelligent use of organic pesticides.

2. Material and Methods

2.1. Reagents

α-BHC(GBW(E)080725), β-BHC(GBW(E)080727), γ-BHC (GBW(E)0807229), δ-BHC (GBW(E)080731), PP'-DDE (GBW(E)080735), OP'-DDT (GBW(E)080739), PP'-DDD (GBW(E)080733), PP'-DDT (GBW(E)080737), PCNB(GBW (E)060617). All of these were purchased from National Research Center for Certified Reference Materials.

2.2. Apparatus

Gas chromatography (Shimadzu GC-2010) was equipped with a SE-54 fused silica capillary column (3.0 m × 0.25 mm × × 0.32 mm), and an electron capture detector. Universal high-speed micro-mill was purchased from Tianjin Taisite Instrument Co., Ltd., KQ-250B ultrasonic cleaner was a product of Kunshan Ultrasonic Instrument Co., Ltd., RE-5250 Vacuum rotary evaporator was from Shenzhen Sanli Chemical Co., Ltd., TDC-40B Centrifuge , N-EVAPTM112 Nitrogen analyzer were made in USA.

2.3. Sample Collection

The broken rice was taken from six areas (Changde, Changsha, Yueyang, Zhuzhou, Chenzhou, Yiyang) in Hunan using random sampling method, nine samples for each region.

2.4. Method

2.4.1. Preparation of Standard Solution

It was weighed BHC(α-BHC, β-BHC, γ-BHC, δ-BHC), DDT (DDT) (PP'-DDE, PP'-DDD, OP'-DDT, PP'-DDT) and pentachloronitrobenzene (PCNB) pesticides standard solution respectively, then diluted to each milliliter containing 4–5 μg pesticides with petroleum ether (60–90°C). It was taken precisely amount of reference stock solution 0.5 mL into a 10 mL volumetric flask, petroleum ether (69–90°C) diluted to the mark, shook. It was taken precisely amount of reference mixed stock solution and diluted petroleum ether (69–90°C) to each liter contains 0 μg, 1 μg, 5 μg, 10 μg, 50 μg, 100 μg, 250 μg pesticides respectively.

2.4.2. Preparation of Sample Solution

It was taken 2.0000 g broken rice powder extracted by water (20 mL) for 30 min ultrasonic extraction, added acetone 40 mL and weighed, ultrasonic treatment 30 min, let it cool, used acetone to supply losing weight after weighing, add 6 g sodium chloride and 30 mL dichloromethane, weighed, then 15 min ultrasonic treatment, used dichloromethane to supply losing weight after weighing again, put it aside (stratification), moved the organic phase into a 100 mL flask with anhydrous sodium sulfate rapidly, placed 4 hours. It was taken 35 mL extracted solution and dried in the water bath at 40°C on a rotary evaporator, concentrated to nearly dry, addded a small amount of petroleum ether (60–90°C), repeated at least three times until dichloromethane and acetone were eliminated, dissolved with petroleum ether (60–90°C) in a 10 mL centrifuge tube and diluted to 5 mL, added sulfuric acid 1 mL carefully, shake 1 min and centrifuged (3000 r/min) 10 minutes. It was taken 2 mL supernatant into a test tube, concentrated with Nitrogen analyzer and diluted to 1 mL.

2.4.3. Chromatographic Conditions

Operating conditions were as follows: initial temperature 120°C (6 min), increased at a rate of 5°C min^{-1} to 220°C, held for 10 min, then increased at a rate of 8°C min^{-1} to 250°C and finally held at 250°C for 15 min; injector temperature: 260°C ; carrier gas: N_2(99.999%); column flow-rate: 1 mL/min; detector temperature: 300°C injection volume: 1 uL; External standard quantitative method.

3. Results and Discussion

3.1. System Suitability

The mixed standard stock solution was injected into chromatograph under the chromatographic conditions mentioned above. The results showed that, adjacent peaks' efficiency of separation was greater than 1.5 [5], number of theoretical plates was higher than 1×10^6 calculated ac-

cording to α-BHC, and made sure the retention time (RT) of nine organochlorine pesticides (Table 1).

3.2. Reproducibility

Took 2.0 g broken rice powders from Changde for 9 groups and treated the powder by the same method according to sample preparation. Then determined each sample solution continuously according to the above chromatograph condition took the peak area into the regression equation and then calculated the pesticides content. The results show that, PCNB was detected only and RSD value was 0.97% the best is less than 1% [6], the method repeatability was good.

3.3. Stability

Took the sample solution (Yueyang) and inject to the chromatograph for four times during a single day (0 h, 2 h, 4 h, and 6 h) according to the above chromatographic condition. The α-BHC, β-BHC, γ-BHC, δ-BHC, PP'-DDE, PP'-DDD were detected and RSD value were 0.8%, 0.5%, 1.1%, 0.3%, 0.6%, 0.8% respectively (less than 5%), indicating that the preparation of the sample was stable within 6 hours.

3.4. Limit of Detection (LOD)

The mixed standard stock solution were injected into chromatograph respectively under the chromatographic conditions mentioned above, then calculated the instrument limit of detection (IDL) (three times the value of the instrument background signal) and the method limit of detection (MDL). The results showed that the IDL of nine organochlorine pesticides were all lower than 1 μg/L, indicating that the sensitivity was good (Table 2).

3.5. Linearity

1 μL of the mixed standard solution was injected into the chromatograph respectively, the peak area as the vertical axis and the concentration as the abscissa (μg/L), calculated the regression equation (Table 3). The results showed that all tested components from 0 μg/L to 250 μg/L appeared a good linear relationship between the peak area and concentration.

Table 1

The Retention Time of 9 Organochlorine Pesticides

Species	t(RT)/min
α-BHC	15.56
β-BHC	16.75
γ-BHC	17.02
PCNB	17.24
δ-BHC	18.07
PP'-DDE	25.77
PP'-DDD	27.72
OP'-DDT	27.91
PP'-DDT	29.91

Table 2

The Device Limit Determination and Method Limit Determination of 9 Organochlorine Pesticides

Species	IDL, ng/L	MDL, mg/kg
α-BHC	100	0.00025
β-BHC	128	0.00032
γ-BHC	180	0.00045
PCNB	140	0.00035
δ-BHC	200	0.0005
PP'-DDE	368	0.00092
PP'-DDD	298	0.00075
OP'-DDT	275	0.00069
PP'-DDT	336	0.00084

Table 3

Regression Equation of 9 Organochlorine Pesticides

Standard	T (RT)	Regression equation	R^2
α-BHC	15.56	y = 2228.1x – 8818.3	0.9987
β-BHC	16.75	y = 1299.6x + 4282.3	0.9988
γ-BHC	17.02	y = 2026.6x – 5099	0.9993
PCNB	17.24	y = 2154.1x + 7490	0.9993
δ-BHC	18.07	y = 2256.3x – 9267.9	0.9989
PP'-DDE	25.77	y = 1616.3x – 5766.3	0.9985
PP'-DDD	27.72	y = 1108.3x – 268.92	0.9969
OP'-DDT	27.91	y = 959.9x – 1899.3	0.9996

3.6. Recovery

Took the broken rice powder from Changde into 9 portions, each 2.0 g, precisely weighed, and divided them into three groups. Add 0.1 ml, 0.5 ml, 0.9 ml 250 μg/L mixed standard solutions to each group respectively, and then air. Prepare the test sample solution according to the method of 2.3. Each portion determines 3 times, and calculated the recovery; the results can be seen in Table 4.

From the table above we can learn that under different amount of pesticides, the recovery and RSD of 9 types of organochlorine pesticides meet the requirements of pesticide residues detection.

3.7. Determination of Samples

To weigh accurately broken rice powder from different areas, and prepared the test sample solution according to the method of 2.3, then injected them into the gas chromatograph with the above chromatographic condi-

Table 4

Results of Recovery

Species	The amount of adding		
	25 ng	125 ng RSD/%	225 ng
α-BHC	1.28	0.97	0.65
β-BHC	1.92	0.38	0.87
γ-BHC	1.05	0.97	2.32
PCNB	1.21	0.52	0.30
δ-BHC	0.40	0.85	1.06
PP'-DDE	1.47	1.40	0.59
PP'-DDD	1.26	1.57	0.95
OP'-DDT	1.02	1.63	1.27
PP'-DDT	1.02	1.14	1.44

Table 5

The Organochlorine Determination Results in the Rice Sample (w/mg·Kg^{-1})

	α-BHC	β-BHC	γ-BHC	PCNB	δ-BHC	PP'-DDE	PP'-DDD	OP'-DDT	PP'-DDT
Changde	—	—	—	0.1147	—	—	—	—	—
Yueyang	0.0116	0.0256	0.012	—	0.0272	0.0147	0.0387	—	—
Zhuzhou	—	—	—	—	0.013	—	—	—	—
Yiyang	—	0.002	0.008	—	0.01	0	0.013	—	—
Changsha	—	—	—	—	—	—	0.006	—	—
Chenzhou	—	—	—	—	—	—	0.007	—	—

tions. At last, calculated the content of pesticide residues by peak area through external standard method, the results can be seen in table 5.

According to the Chinese national standard of pesticide residues: the maximum limits of DDT, BHC and PCNB was 0.2 mg/Kg, 0.3 mg/Kg and 0.1 mg/Kg in agricultural products [7]. From the above table, it can be known that only the sample of Changde exceeds the limits, the content of PCNB was 0.1147 mg/Kg slightly greater than the limit of 0.1 mg/Kg. The result can be seen in fig. 1.

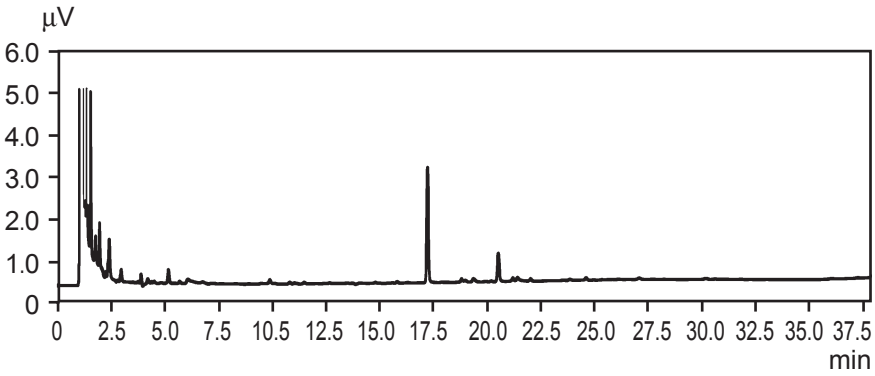

Fig. 1. GC chromatogram of Changde's rice

4. Discussion

It can be seen from the methodology that, firstly, the extraction method we used was modified according to the Pharmacopoeia, for our method was more simple and efficient, time-saving and consuming less reagents than the Pharmacopoeia. Compared to the pre-treatment technology developed in recent years, such as solid-phase extraction, solid phase micro-extraction, supercritical fluid extraction, microwave-assisted extraction, accelerated solvent extraction, gel permeation extraction and so on [8–11], our method was simple and low cost. Secondly, the retention time of nine kinds of organic chlorine, through gas chromatography we established, was shorter than Zeming Guan's [12] literature reported by nearly half. So it can not only saved a lot of time, but also reduced the loss of the instruments. Finally, after the methodological verification, it can be seen that this method had high recovery, good reproducibility, high sensitivity, and can be used to test large quantities of samples. It provides a reliable the method to detection the residues of organochlorine pesticide.

From the results we can find that there were more types of organochlorine pesticide residues in Yiyang and Yueyang, mainly BHC and DDT, but not exceeded. So we can learn BHC and DDT were over used in these two places, and strict controls should be implemented on the amount, otherwise it will have serious consequences beyond the safe limits. Although the rice sample of Changde had only one type of residues-PCNB, it exceeds the safe range. So the pesticides that farmers used were relatively simple, but the amount was large, or abusive. The results of Zhuzhou, Chenzhou and Changsha was good, only have one kind of trace pesticide residues. And the pesticide residues of broken rice in Yiyang have many types but the amount was small. In summary, different places use different pesticides, but generally speaking BHC and DDT were still used frequently. So the government should strengthen restrictions on the two types of pesticides to ensure food security.

REFERENCES

1. Qi YM, Sun JY, Yang X. Determination of organic chlorine pesticides [N], Life Science Instruments, 2011(9): 48-52.

2. Li HB, Sun WZ, Fang Y, et al. The analysis of organochlorine pesticide contamination in food [J]. Chinese Journal of Public Health engineering, 2008, 1(4): 220-222.

3. Zhao SH. Plant Chemical Protection [M]. 3rd ed. Beijing: Agriculture Publishing House. 2003, 6-18, 431-484.

4. Robert S. Murphy, Fredrick W. Kutzt, Sandra C. Strassmant, Selected Pesticide Residues or Metabolites in Blood and Urine Specimens from a General Population Survey [J].1983,48: 81-86.

5. Cha Yue-zhen. Identification of Trace Impurities in Cyhalothrin by HPLC-MS[N]. Journal of Instrumental Analysis, 2009: 23-27

6. John E. ASE of Pesticide Residue in Food Products[J]. GIT laboratory journal, 2008, 4(I): 17-19.

7. Gong| ZJ. The research of the determination of pestcides in rape-

seed by martrix solid-phase disperse and gas chromatography. The Chinese Academy of Agricultural Sciences Institute of Oil Crops, 2010: 37-42.

8. Ji XX, Shi ZH, Cao YZ, Shi LL, Wang N, Pang GF. Determination of 111 Pesticides Residues in Animal Fat by Gel Permeation Chromatography Purification/Liquid Chromatography-Tandem Mass Spectrometry[N]. Journal of Instrumental Analysis, 2009, 28(12): 1433-1439.

9. He XY, Chen SB, Yu XJ, Fan YM, Zhu J, Xie DH. Multiresidue of thiobencard, deltamethrin and 19 organochlorine pesticide in aquatic products by freezing lipid filtration-solid-phase extraction and gas chromatography-mass spectrometry[N]. Journal of Instrumental Analysis, 20009, 28(3): 306-309.

10. Tong L, LI CJ. Determination of Multi-residues of 50 Pesticides in Sulfur-containing Vegetables by Gas Chromatography-Tandem Mass Spectrometry[N]. Journal of Instrumental Analysis, 2008, 27(9): 930-935.

11. Song SL, Li CJ, Ma XD. Study on Clean-up Method for Co-extractions of Multiple Pesticide Residues in Vegetables[N]. Journal of Instrumental Analysis, 2008, 27(8): 795-799.

12. Guan ZM, Guo XL, Liang MH, Luo Y. Determination of organochlorine pesticide residues in Siraitiae Fructus [N]. Journal of Guangdong Pharmaceutical College, 2010, 26(4): 351-354.

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ONE-DAY SURGERY (SHORT TERM DEPARTMENT) IN THE TREATMENT OF PATIENTS SUFFERING FROM CHOLELITHIASIS

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ХИРУРГИЯ ОДНОГО ДНЯ (СТАЦИОНАР КОРОТКОГО ПРЕБЫВАНИЯ) В ЛЕЧЕНИИ БОЛЬНЫХ ЖЕЛЧНОКАМЕННОЙ БОЛЕЗНЬЮ

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В 2006–2011 гг. в нашей клинике выполнено 4533 лапароскопических холецистэктомий. 557 (12,3 %) пациентов находились в стационаре короткого пребывания. Совместно с анестезиологом проводился тщательный отбор пациентов. Выписывали больных при полной уверенности в благополучном течении послеоперационного периода — через 24 ч после поступления с последующим медицинским «сопровождением» в амбулаторных условиях. Из запланированных в стационаре короткого пребывания 678 больных операция и лечение в предполагаемые сроки состоялись у 557. Пациенты наблюдались оперирующим хирургом на протяжении 4–7 дней. При тщательном отборе больных с хроническим калькулезным холециститом возможно их успешное лечение в стационаре короткого пребывания (до 20 %).

Ключевые слова: желчнокаменная болезнь, хронический калькулезный холецистит, стационар короткого пребывания, хирургия одного дня.

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ONE-DAY SURGERY (SHORT TERM DEPARTMENT) IN THE TREATMENT OF PATIENTS SUFFERING FROM CHOLELITHIASIS

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Introduction. Laparoscopic cholecystectomy was recognized as operation of choice in treatment of cholelithiasis. The terms of hospital treatment were maximum decreased with a widespread introduction of laparoscopic technologies in treatment of cholelithiasis. In USA, Japan, European countries the hospitalization after elective laparoscopic cholecystectomy may be no more than 24 hours. From 15 to 30% of laparoscopic cholecystectomies are carried out by “one day surgery” principles.

Materials and methods. In our hospital within the period from 2006 to 2011 there were carried out 4,533 laparoscopic cholecystectomies. There were operated 2,800 (61.8%) patients suffering from chronic cholelithiasis. 557 (12.3%) patients suffering from cholelithiasis were discharged from the hospital in 24 hours.

Results and discussion. There were planned 678 patients with cholelithiasis to be operated by “one day surgery”, but operation and treatment within this term took place in 557 patients. With raising experience the number of patients has grown from 39 (9,9%) in 2006 to 156 (19.5%) in 2011. There were no severe complications. Umbilicitis was formed in 14 patients in periomphalic area, which didn’t require hospital treatment. From 2007 to 2010 in our hospital 102 (2.3%) patients, which were hospitalized with acute cholecystitis, were treated in a short term department.

Conclusions. Laparoscopic cholecystectomy in a "short term department" may be made in 20% of patients suffering from cholelitiasis. Laparoscopic cholecystectomy in "short term department" needs careful selection: non-presence of severe pathology (ASA I-II), absence of technical difficulties during operation, the ability of medical "support" after discharge. Laparoscopic cholecystectomy in "short term department" allows using surgical departments more effectively and requires the further study and development.
Key words: cholelithiasis, chronic calculous cholecystitis, short term department, one day surgery.

Introduction

About 20% of adult population suffer from cholelithiasis [1]. Since the nineties of last century the surgical technique and laparoscopic instruments have been improved. It caused the reduction of operation duration and quantity of postoperative complications. Laparoscopic cholecystectomy was recognized as operation of choice in treatment of cholelithiasis [2]. It has advantages in reduction of intraoperative trauma, and as a consequence the reduction of postoperative rehabilitation period [3]. The duration of hospitalization after laparoscopic cholecystectomy is 2–3 days, after laparotomy is 7–9 days [4]. The terms of hospital treatment were maximum decreased with a widespread introduction of laparoscopic technologies in treatment of cholelithiasis. In USA, Japan, European countries the hospitalization after elective laparoscopic cholecystectomy may be no more than 24 hrs. This direction is successfully introduced in cases of acute appendicitis treatment, hernioplasty of inguinal and umbilical hernias, in cases of GERD surgical treatment, as well as in gynecology practice. From 15% to 30% of laparoscopic cholecystectomies are carried out by principles of "one day surgery" [5].

Materials and Methods

In our hospital in period from 2006 to 2011 there were carried out 4533 laparoscopic cholecystectomies. There were operated 2800 (61.8%) patients suffering from chronic cholelithiasis. 557 (12.3%) patients suffering from cholelithiasis were discharged from the hospital in 24 hours. The most of them were women (87.3%). The average age of patients was 45±2.

3–5 days before hospitalization patients had comprehensive out-patient examination. There were carried out: common blood count, urinalysis, coagulogram, X-ray examination of thorax, ECG, FGDS, ultrasound examination of abdominal organs. According to clinical picture other examinations were performed (CT, MRI, irrigoscopy etc.). As an important requirement was therapeutic examination. Treatment in the "short term department" was proposed to the patients without concomitant pathology (ASA I-II). Patients with suspected choledocholithiasis (jaundice in anamnesis, delatation of common bile duct according to ultrasound examination) and upper middle laparotomy were excluded. The most important principles of selection were social indicators: accommodation in the city, patient's motivation to stay at home in postoperative period, possibility to contact by phone, family's care. Before a planned hospitalization patients were examined by anesthesiologist and in case of absence of contraindications were informed about the possibility of "one day surgery" treatment.

Patients were hospitalized in the morning. Laparoscopic cholecystectomy was performed in 2–4 hours after admission. It was made by standard methods, as usually with using of 3 ports and in 11 cases by "cosmetic" method of cholecystectomy with elements of NOTES-technology, which was developed by our department [6]. For anesthetic induction propofol, esmiron, phentanil were used. Maintenance of anesthesia was performed by propofol, esmiron, phentanil at the same time with oxygen-nitrous mixture. In order to relieve nausea 8 mg of osetron were injected. Last time at the end of operation subdiaphragmatic and subhepatic space were irrigated by anesthetic solution. Bupivacaine was injected around the trocar wounds. Usually the operation was ended by staging a thin drainage to the foramen Winslow. In postoperative period narcotic analgesics were not used. The prevention using of antibiotics was performed by a standard scheme. By indications there were used LMWH. In case of abnormalities identifying or in case of technical difficulties hospitalization was prolonged as much as clinical course required. The previous operations on abdominal organs weren't the absolute contraindication, the last decision was made intraoperative. Our observation shows that intersection of single commissure has no effect on severity of postoperative pain.

Results and Discussion

There were planned 678 patients with cholelithiasis to be operated by "one day surgery", but operation and treatment in these term in 557 patients. With accumulation of experience the quantity of patients has grown from 39 (9,9%) in 2006 to 156 (19.5%) in 2011. The average duration of laparoscopic cholecystectomy was 30–40 min.

The causes of treatment duration increasing were following: painful syndrome, technical difficulties during surgery, which needed closer observation of surgeon, unplanned simultaneous operations and other reasons.

There were no severe complications. Umbilicitis formed in 14 patients in periomphalic area, which didn't require hospital treatment.

With accumulation of experience the indications for staying in "short term department" were expanded. From 2007 to 2010 in

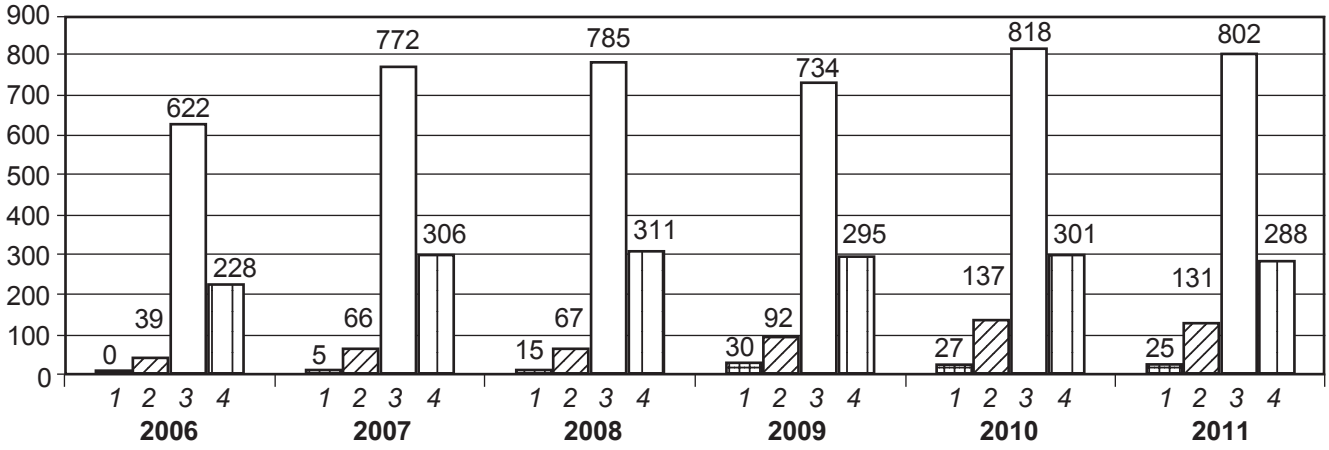

Fig. 1. Quantity of patients with cholelitiasis, which were treated in "short term department" from 2006 to 2011: *1* — one day surgery for acute calculous cholecystitis; *2* — one day surgery for chronic calculous cholecystitis; *3* — laparoscopic cholecystectomy; *4* — laparoscopic cholecystectomy in acute cholecystitis

our hospital 102 (2.3%) patients, which were hospitalized with acute cholecystitis through 3–5 days from the beginning of disease were treated in "short term department" (Fig. 1). Patients were discharged no more than 24 hours if doctors had a complete confidence in the favorable postoperative period. The attention was paid to patient's general health, intensity of postoperative pain and nausea, the quantity and character of discharge by drainage, the individual motivation for discharge. In doubt of successful operation or early postoperative period the terms of being patients in the department were prolonged. Patients were under surgeon's observation during 4–7 days. It was recommended to pass through 1–2 preventive examinations before stitches would be removed.

Conclusions

1. Laparoscopic cholecystectomy in "short term department" may be made in 20% of patients suffering from cholelitiasis.

2. Laparoscopic cholecystectomy in "short term department" needs careful selection: nonpresence of severe pathology (ASA I-II), absence of technical difficulties during operation, the ability of medical "support" after discharge.

3. Laparoscopic cholecystectomy in "short term department" allows using surgical departments more effectively and required the further study and development.

REFERENCES

1. *Stinton Laura M.* Cholesterol Gallstones: from epidemiology to prevention / Laura M. Stinton, Eldon A. Shaffer // Gut Liver. – 2012. – Vol. 6 (2). – P.172–187.

2. *A randomized* controlled study of uncomplicated gallstone disease with a 14-year follow-up showed that operation was the preferred treatment / M. Schmidt, K. Søndenaa, M. Vetrhus [et al.] // Dig Surg. – 2011. – Vol. 28 (4). – P. 270–276.

3. *Keus F.* Systematic review: open, small-incision or laparoscopic cholecystectomy for symptomatic cholecystolithiasis / F. Keus, H. G. Gooszen, C. J. Van Laarhoven // Aliment. Pharmacol. Ther. – 2009. – Vol. 29, N 4. – P. 359–378.

4. *Open* cholecystectomy for all patients in the era of laparoscopic surgery — a prospective cohort study / J. Leo, G. Filipovic, J. Krementsova [et al.] // BMC Surgery. – 2006, Apr 3. – N 6. – 5 p.

5. *Akoh J. A.* Day case laparoscopic cholecystectomy: reducing the admission rate / J. A. Akoh, W. A. Watson, T. P. Bourne // Int J Surg. – 2011. – Vol. 9 (1). – P.63–67.

6. *Каштальян М. А.* Косметический вариант лапароскопической холецистэктомии с элементами NOTES технологий / М. А. Каштальян // Український журнал хірургії. – 2009. – № 4. – С. 72–76.

REFERENCES

1. Laura M. Stinton, Eldon A. Shaffer. Cholesterol Gallstones: from epidemiology to prevention . Gut Liver. 2012: 6(2).172-187.

2. Schmidt M, Søndenaa K, Vetrhus M, Berhane T, Eide GE. A randomized controlled study of uncomplicated gallstone disease with a 14-year follow-up showed that operation was the preferred treatment. Dig Surg. 2011: 28(4):270-6.

3. Keus F, Gooszen HG, Van Laarhoven CJ. Systematic review: open, small-incision or laparoscopic cholecystectomy for symptomatic cholecystolithiasis. Aliment. Pharmacol. Ther. 2009:29, N 4:359-378.

4. Leo J, Filipovic G, Krementsova J, Norblad R, Soderholm M, Nilsson E. Open cholecystectomy for all patients in the era of laparoscopic surgery — a prospective cohort study. BMC Surgery. 2006(Apr 3).6:5

5. Akoh JA, Watson WA, Bourne TP. Day case laparoscopic cholecystectomy: reducing the admission rate. Int J Surg. 2011;9(1):63-67.

6. Kashtalyan MA. Cosmetic version of laparoscopic cholecystectomy with the elements of NOTES technology. Ukr. journ. surgery. 2009;4:72-76.

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TRANSVESICAL SINGLE-PORT LAPAROSCOPIC RADICAL PROSTATECTOMY FOR ORGAN-CONFINED PROSTATE CANCER: TECHNIQUE AND OUTCOMES

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Background. Laparoendoscopic single-site radical prostatectomy (LESS-RP) is obtaining popularity. To improve continence and overcome current limitations, transvesical single-port laparoscopic RP could be applied to LESS. Our experience in performing transvesical single-port laparoscopic RP was analyzed.

Methods. A total of 20 consecutive men with organ-confined prostate cancer underwent transvesical single-port laparoscopic RP between November 2010 and July 2011 by a single surgeon. A novel port (QuadPort®) was used percutaneously into the bladder to establish pneumovesicum through a 4-cm bladder incision. All the operative procedures, including incision of the posterior bladder neck, dissection of the seminal vesicles and vas deferens, ligation of prostatic pedicles, preserving of neurovascular bundles, apical dissection, urethral transection, and urethro-vesical anastomosis with ventral inlay forskin graft, were performed transvesically and laparoscopically.

Results. All of the 20 transvesical single-port laparoscopic RP was successfully performed, and there was no conversion to standard laparoscopic approach or open surgery. Patients were hospitalized for a mean (range) of 14.7 (12–25) days after surgery. The total operative time range was 75–180 min, and the mean operative time was 105 min. The estimated blood loss was 75–500 ml, and no blood transfusion was required. Catheters were removed after a mean (range) of 12.1 (9–16) days. No intraoperative complications occurred. No patient had positive surgical margins. All the cases were continent after removal of the catheter.

Conclusions. Transvesical single-port laparoscopic radical prostatectomy is technically feasible for cases with organ-confined prostate cancer.

Key words: LESS, prostate cancer, radical prostatectomy, transvesical, single port.

Introduction

As laparoscopy becomes a standard approach in many urological procedures, researchers are striving to make minimally invasive surgery less invasive. Laparoendoscopic single-site radical prostatectomy (LESS-RP) is being increasingly used for the surgical treatment of organ-confined prostate cancer and could be regarded as the most recent progression in laparoscopic RP [1–12]. However, some early clinical experiences with LESS-RP have demonstrated several limitations associated with technical constraints, including limited operating space, and lack of triangulation.

Desai et al. [13] first reported an initial feasibility of performing transvesical single-port RP in a cadaver. They suggested that the insufflated bladder might supple with an optimal portal of access to the prostate for RP, by eliminating contact with the peritoneal cavity and its contents, thus providing a direct in-line exposure of the prostate and relevant periprostatic anatomy. The transvesical approach also excludes the need for mobilizing the bladder and dissecting the prevesical space, and could further reduce the dissection injury during RP. However, to our knowledge no study has clinically evaluated the technique in patients with organ-confined prostate cancer.

Herein we report our initial clinical experience of transvesical single-port laparoscopic RP for organ-confined prostate cancer patients. Our aim is to demonstrate the feasibility of the procedure by describing the technique and analyzing early outcomes.

Patients and Methods

Study design

The patient with low risk organ-confined prostate cancer (PSA = 10 ng/ml, Gleason score <7, and clinical stage T1c or T2a) fit for laparoscopic surgery was offered transvesical single-port laparoscopic radical prostatectomy. All data were entered prospectively into an institutional

review board-approved database and queried retrospectively.

Demographic data were accrued including patient age, body mass index, preoperative prostate-specific antigen (PSA) level, the International Index of erectile function 5 (IIEF-5), biopsy Gleason score, Clinical TNM stage, and D'Amico risk classification. The preoperative evaluation included standard history and physical examination, basic laboratory blood work, metastatic staging when required, and further cardiac/pulmonary workup when indicated. Exclusion criteria included previous radiotherapy to the prostate and conventional contraindications to laparoscopic procedures.

Perioperative data including the estimated blood loss, operative time, additional ports or conversion to conventional laparoscopy, intraoperative complications and length of stay were recorded. The patient was checked at 9D postoperatively with fiber cystoscope examination and removed the catheter. Patients were followed at 40D, every 3 mo for 1 yr, and every 6 mo thereafter for continence assessment (pads daily), IIEF-5 and biochemical recurrence (PSA>0.2 ng/ml).

Surgical technique

Port placement

The patient's bladder was instilled with saline water through a catheter and an incision (3–4.5 cm) was created in halfway between the umbilicus and pubic symphysis. The wall of the bladder incision was sutured to the anterior rectus sheath and fixed. An QuadPort® (Olympus Surgical Technologies Europe) was deployed into the bladder through a 4-cm incision (Fig. 1, *a*). The Olympus high-resolution digital 10 mm laparoscope was inserted through a 12 mm inlet; the other two inlets were actually used during the surgery to reduce instruments clashing that is commonly occurred with the single-port approach. There was a separate channel each for insufflation and venting.

Incision of the Posterior Bladder Neck

The initial step consisted of creating a posterior incision along the bladder neck distal to the ureteric orifices (Fig. 1, *b*), which were clearly identified with the transvesical approach. The posterior bladder neck incision was deepened full-thickness to expose the vas deferens and seminal vesicles.

Dissection of Vas Deferens and Deminal Vesicles

The anterior layer of Denonvillier's fascia was incised and the vas deferens and seminal vesicles were completely isolated and incised (Fig. 1, *c*), thereby exposing the fascia of Denonvilliers that is incised for the posterior dissection.

Separation of Denonvilliers' Fascia

Denonvillier's fascia was separated along the posterolateral surface of the prostate in an antegrade direction (Fig. 1, *d*), reaching the prostatic apex, maintaining a completely intrafascial plane.

Lateral Separation of Prostate

The posterior bladder neck incision was extended on both sides to encircle the bladder neck. The bladder neck incision was initially deepened from the 7 o'clock to 11 o'clock position on the left side and the 1 o'clock to 4 o'clock position on the right side (Fig. 1, *e*). This gave exposure to the lateral prostate surface medially and the levator fibres laterally. These incisions were joined in the midline at the 12 o'clock position to expose the anterior surface of the prostate and the dorsal vein complex (Fig. 1, *g*). The lateral prostate pedicles were divided using harmonic scapel and the neurovascular bundles were conserved under surveillance with nerve stimulator (Fig. 1, *f*) [1].

Control the Dosal Vein Complex and Dissection of Urethra

The dorsal vein was controlled with hemostatic forceps and the pubo-prostatic ligaments were incised close to the prostate surface (Fig. 1, *h*), exposing the underlying urethra. The urethra was transected without cautery. The tip of the urethral catheter was withdrawn, and the posterior urethral wall was transected sharply (Fig. 1, *j*). Complete dissection of the prostate apex was accomplished in a retrograde fashion. The completely mobilized prostate was placed within the bladder. The prostate was extracted and examined grossly for adequacy of excision. The catheter balloon was injected with 40 ml of saline water and pulled for oppressing urethra stump and hemostasis.

Vesicourethral Anastomosis by using the Stripe of Free Foreskin Fraft

According to the prostate gland diameter, the isometric stripe of foreskin was prepared and quilted onto the ventral prostatic fossa. Both ends of the free foreskin were anastomosed respectively with margin of the posterior urethra and the posterior bladder neck (Fig. 1, *k, l, m*). A 20F Foley catheter was inserted under vision into the bladder after completion of the anastomosis. A bladder fistula drain was exited via the same skin incision.

Cystograms

Cystogram was performed at day 9 after surgery. The urethral catheter was removed when appropriate.

Results

Demographic data

From Nov 2010 to July 2011, 20 transvesical single-port laparoscopic RPs were scheduled at our institution. Table 1 lists the complete demographic data.

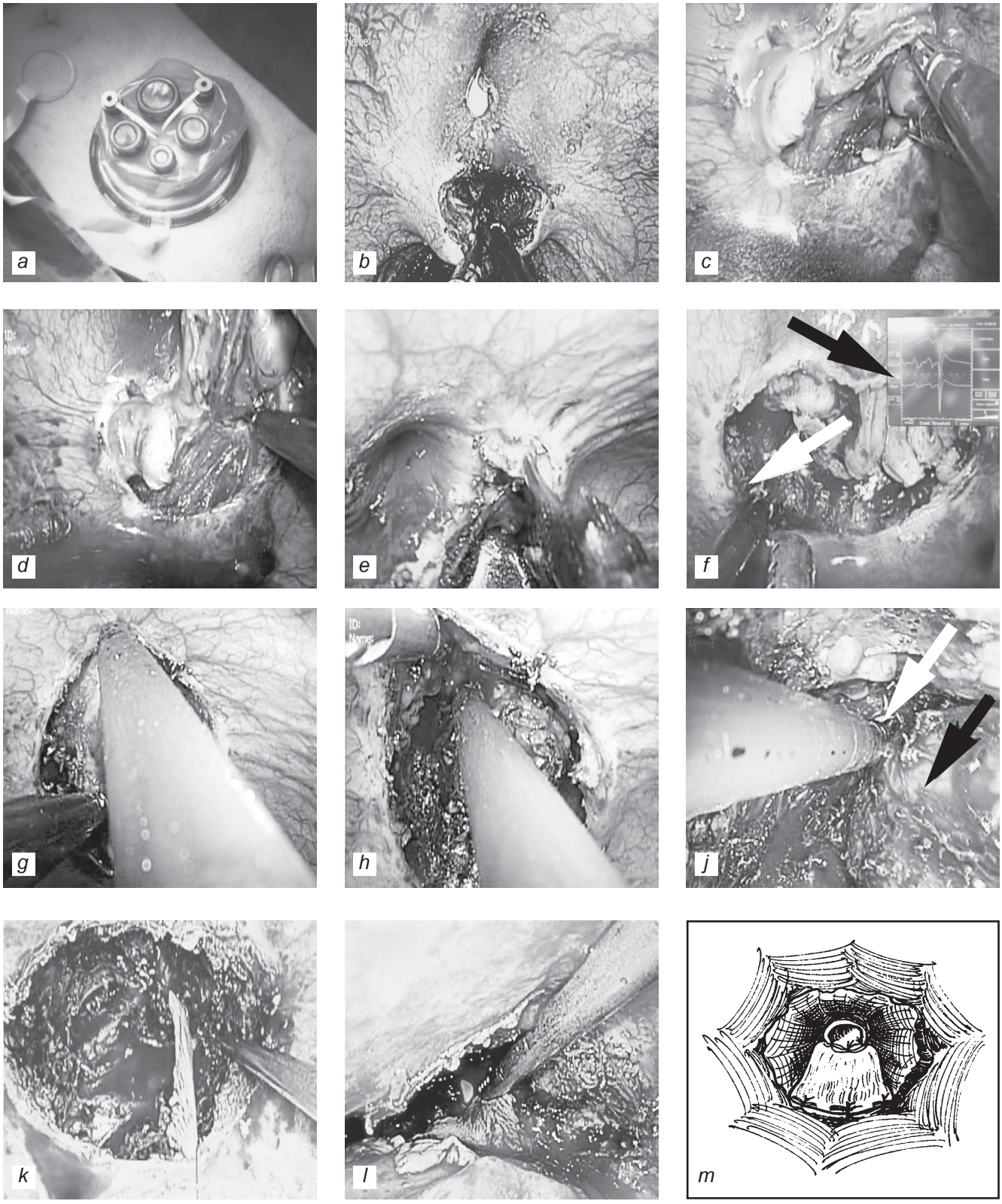

Fig. 1. a — QuadPort® (Olympus Surgical Technologies Europe) was deployed into the bladder through a 4-cm incision; *b* — incision of the posterior bladder neck; *c* — dissection of *Vas deferens* and seminal vesicles; *d* — separation of Denonvilliers' fascia; *e* — lateral separation of prostate; *f* — the neurovascular bundles were under surveillance with nerve stimulator (white arrow: bipolar electrocoagulation as stimulator, black arrow: reflected voltage; *g* — the bladder neck incisions were joined in the midline at the 12 o'clock position; *h* — control the dorsal vein complex; *j* — dissection of urethra (black arrow: prostate, white arrow: urethra); *k* — urethro-vesical anastomosis using the stripe of foreskin; *l* — skin flap was well adhered to the prostate socket; *m* — the model of urethro-vesical anastomosis using the stripe of foreskin

Operative data

The mean operative time was recorded from incision of the bladder to the bladder closure finished by a single surgeon (X.G.). Table 2 details the operative and postoperative data. All of the 20 transvesical single-port laparoscopic RPs were successfully performed, and there was no conversion to standard laparoscopic approach or open surgery. No intraoperative complications occurred. No patient had positive surgical margins.

Postoperative data

The fiber cystoscope examination of epithelial crawling situation and anastomotic healing status was performed on all patients, and catheters were not removed if there was evidence of anastomotic leakage. Seventy percent of patients had their catheters removed 9d postoperatively and 30% after 2 wk. All PSA values postoperatively were less than 0.06 ng/ml as compared with preoperative PSA values (mean: 7.5 ng/ml). All the cases were immediately continent as soon as removal of the catheter. 12 of 20 patients reached satisfactory erection on 6 M postoperatively with IIEF-5 score = 21. No cases demonstrated vesicourethral stricture on 6–15 M follow up postoperatively.

Discussion

Laparoscopic RP has been reported with encouraging results as an alternative to open RP in patients with organ-confined prostate cancer. More recently, the introduction of novel single-port devices has enabled the performance of laparoscopic RP procedures in a virtually scarless fashion through a solitary intraumbilical incision. Although not enough randomized data are available in the literature, it appears as though this technique may have promise compared with its conventional laparoscopic counterpart, in terms of operative outcomes, postoperative pain, and patient-reported convalescence [14–17]. Although promising, it is important to remember the underpinnings of this technique and its inherent difficulties. First and foremost, limited operating space and considerable instrument clashing limits precise tissue handling and retraction. We report our initial experience with transvesical single-port laparoscopic RP for organ-confined prostate cancer performed through a solitary suprapubic incision by way of a single access port inserted directly into the bladder in 20 patients with low risk organ-confined prostate cancer.

There may be several advantages of the single-port transvesical approach for RP. Firstly, with the transvesical approach we do not need to mobilize the bladder or dissect the pre-vesical space, thus the operation is restricted to the area of the deep bony pelvis, which could minimize the dissection injury during RP. Furthermore, recent studies

Table 1

Demographic and Preoperative Data

No. of patients	20
Age, yr, mean (range)	62 (37–74)
BMI, Kg/m^2	22.5 (20–26)
Preoperative PSA, ng/ml, mean (range)	7.5 (3.4–10.0)
IIEF-5, No. ≥21 ≤21	 13 (65.0) 7 (35.0)
Clinical TNM stage, No T1c T2a	 15 (75.0) 5 (25.0)
Biopsy Gleason score, No. (%) 2+2 3+2 3+3	 7/20 (35.0) 11/20 (55.0) 2/20 (10.0)
D'Amico risk stratification, No. (%) Low Intermediate High	 20/20 (100.0) 0/20(0) 0/20(0)

Note. PSA — prostate-specific antigen; IIEF — the International Index of Erectile Function.

Table 2

Perioperative and Postoperative Outcomes

No. of patients	20
Perioperative outcomes	
EBL, ml, mean (range)	129.8 (75–500)
Operative time, min, mean (range)	105.0 (75–180)
Intraoperative complications	0
Conversion to traditional LRP	0
Additional ports	0
Nerve-sparing procedures	20
Postoperative outcomes	
Pathological T stage No. (%) pT2a pT2b pT2c	 7/20 (35.0) 10/20 (50.0) 3/20 (15.0)
Pathologic Gleason score, No. (%) 2+2 3+2 3+3	 3/20 (15.0) 7/20 (35.0) 10/20 (50.0)
Nodes removed, mean (range)	0
Positive nodes, No.	0
Positive margins, No. (%)	0
Follow-up, mo, mean (range)	12.5 (6–15)
Catheterization time, d, mean (range)	12.1 (9–16)
In-hospital stay	14.7 (12–25)
Continent, No. (%)	20 (100.0)
Postoperative Penile Erection	12/20 (60.0)
Biochemical recurrence, No.	0

Note. EBL — estimated blood loss; LRP — laparoscopic radical prostatectomy.

demonstrated that continence-relevant nerves are abundant in the peri-prostatic and prevesical space. There is a wide variety of nerve distribution around the prostate and the continence nerves are much more than previously expected [18; 19]. The transvesical approach for RP excludes the need for mobilizing the bladder and dissecting the prevesical space, and might further reduce the risk of incontinence after surgery, which was in accordant with our results that all 20 cases were with good early functional results. Secondly, there is no need for pneumoperitoneum with transvesical approach. The pneumovesicum confines CO_2 to the bladder and eliminates the need for any bowel retraction, and might also potentially reduce the chance of bowel adhesions and port site complications. Lastly, the gas-insufflated bladder acts as a self-retaining retractor, which may contribute to reduce the number of retracting instruments and trocars required for laparoscopic RP. Herein, the transvesical approach might enable single-port RP to be performed effectively and efficiently [13].

A major challenge arising from this approach is the vesico-urethral anastomosis. Although the oncologic outcome of radical prostatectomy is not compromised, the periprostatic and prevesical fascia adhesion is intact. Tension is present between the bladder neck and urethra when we attempt to peform the vesico-urethral anastomosis. Additionally, recent studies demonstrated that a lot of nerve endings are distributed around periprostatic and prevesical fascia which are relevant to function of continence [20–23]. Thus, the vesico-urethral end to end suturing with tension would impair those nerve endings, compromising postoperative urinary continence. Free dorsal onlay forskin graft was used to repair urethral stricture and patch urethroplasty or augmented anastomotic urethroplasty with foreskin or buccal mucosal graft are considered as good options for the treatment of urethral stricture [22–24]. In the present study, we used the stripe of foreskin to quilt onto ventral fossa of prostate during urethro-vesical anastomosis. The catheter was withdrawn on postoperative day 12. No case in our series had urination difficulty and urethral stricture during a median of 6 months follow-up. A fiber-cystoscope examination showed that the epithelium covered vesico-urethral fossa on postoperative day 40.

What would be emphasized is that transvesical single-port laparoscopic RP is still in its infancy and must be performed by surgeons who have experience in laparoscopic RP. The next step is to conduct randomized controlled trials to compare the oncological and functional results of different approaches for RP, and thus establish evidence-based guidelines.

Conclusions

Transvesical single-port laparoscopic radical prostatectomy is technically feasible for cases with organ-confined prostate cancer. Longer survival and functional data in a larger cohort of patients are necessary to determine the proper place for transvesical single-port laparoscopic RP in patients with low risk organ-confined prostate cancer.

REFERENCES

1. Gettman MT, Box G, Averch T, et al. Consensus statement on natural orifice transluminal endoscopic surgery and single-incision laparoscopic surgery: heralding a new era in urology? Eur Urol 2008;53:1117-20.

2. Raman JD, Bensalah K, Bagrodia A, et al. Laboratory and clinical development of single keyhole umbilical nephrectomy. Urology 2007;70:1039-42.

3. Desai MM, Rao PP, Aron M, et al. Scarless single port transumbilical nephrectomy and pyeloplasty: first clinical report. BJU Int 2008;101:83-8.

4. Kaouk JH, Haber GP, Goel RK, et al. Single-port laparoscopic surgery in urology: initial experience. Urology 2008;71:3-6.

5. Sotelo Noguera RJ, Astigueta JC, Carmona O, et al. Laparoscopic augmentation enterocystoplasty through a single trocar. Urology 2009;73:1371-4.

6. Ponsky LE, Cherullo EE, Sawyer M, et al. Single access site radical nephrectomy: initial clinical experience. J Endourol 2008;22:663-6.

7. Stolzenburg J-U, Kallidonis P, Hellawell G, et al. Technique of laparoscopic-endoscopic single-site surgery radical nephrectomy. Eur Urol 2009;56:644-50.

8. Raman JD, Caddedu JA, Rao P, et al. Single incision laparoscopic surgery: initial urological experience and comparison with naturalorifice transluminal endoscopic surgery. BJU Int 2008;101:1493-6.

9. Rane A, Rao P, Rao P. Single port access nephrectomy and other laparoscopic urologic procedures using a novel laparoscopic port (R-Port). Urology 2008;72:260-3.

10. Msezane LP, Mushtaq I, Gundeti MS. An update on experience with the single instrument port laparoscopic nephrectomy. BJU Int 2009;103:1406-9.

11. WhiteWM, Haber GP, Goel RK, et al. Single-port urological surgery: single-center experience with the first 100 cases. Urology 2009;74:801-4.

12. Desai MM, Berger AK, Brandina R, et al. Laparoendoscopic singlesite surgery: initial hundred patients. Urology 2009;74:805-13.

13. Desai MM, Aron M, Berger A, et al. Transvesical robotic radical prostatectomy. BJU Int 2008;102:1666-9.

14. Tsimoyiannis EC, Tsimogiannis KE, Pappas-Gogos G, et al. Different pain scores in single transumbilical incision laparoscopic cholecystectomy versus classic laparoscopic cholecystectomy: a randomized controlled trial. Surg Endosc. In press. DOI:10.1007/s00464-010-0887-3.

15. Canes D, Berger A, Aron M, et al. Laparo-endoscopic single site (LESS) versus standard laparoscopic left donor nephrectomy:matched-pair comparison. Eur Urol 2010;57:95-101.

16. Raman JD, Bagrodia A, Caddedu JA. Single-incision, umbilical laparoscopic versus conventional laparoscopic nephrectomy: a comparison of perioperative outcomes and short-term measures of convalescence. Eur Urol 2009;55:1198-206.

17. Park YH, Park JH, Jeong CW, Kim HH. Comparison of laparoendoscopic single-site radical nephrectomy with conventional laparoscopic radical nephrectomy for localized renal-cell carcinoma. J Endourol 2010;24:997-1003.

18. Ganzer R, Blana A, Gaumann A, et al. Topographical anatomy of periprostatic and capsular nerves:

quantification and computerized planimetry. Eur. Urol. 2008;54:353-61.

19. Lunacek A, Schwentner C, Fritsch H, Bartsch G, Strasser H. Anatomical radical retropubic prostatectomy: "curtain dissection" of the neurovascular bundle. BJU Int 2005;95:1226-31.

20. Kaiho Y, Nakagawa H, Saito H, Ito A, Ishidoya S, Saito S, et al. Nerves at the Ventral Prostatic Capsule Contribute to Erectile Function: Initial Electrophysiological Assessment in Humans. Eur. Urol. 2009;55:148-55.

21. Alsaid B, Bessede T, Diallo D, Moszkowicz D, Karam I, Benoit G, et al. Division of Autonomic Nerves Within the Neurovascular Bundles Distally into Corpora Cavernosa and Corpus Spongiosum Components: Immunohistochemical Confirmation with Three-Dimensional Reconstruction. Eur. Urol. 2011;59:902-9.

22. Schreiter F, Noll F. Mesh graft urethroplasty using split thickness skin graft or foreskin. J Urol. 1989;142:1223-6.

23. Barbagli G, Palminteri E, Rizzo M. Dorsal onlay graft urethroplasty using penile skin or buccal mucosa in adult bulbourethral strictures. J Urol. 1998;160:1307-9.

24. Andrich DE, Mundy AR. What is the best technique for urethroplasty? Eur. Urol. 2008;54:1031-41.

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CHOICE OF ORGAN PRESERVING TREATMENT OF SUBMUCOUS UTERINE MYOMA BASED ON RATIONAL DIAGNOSTIC CRITERIA

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ОРГАНОСОХРАНЯЮЩЕЕ ОПЕРАТИВНОЕ ЛЕЧЕНИЕ СУБМУКОЗНОЙ МИОМЫ МАТКИ, ОСНОВАННОЕ НА РАЦИОНАЛЬНОМ ВЫБОРЕ ДИАГНОСТИЧЕСКИХ КРИТЕРИЕВ

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Субмукозная миома матки — вариант лейкомиомы матки, который отличается высокой частотой осложнений, среди них ведущую роль играют менометроррагии, бесплодие и невынашивание беременности.

Стремительное развитие малоинвазивной хирургии требует усовершенствования подходов диагностики доброкачественных процессов полости матки. Это касается и диагностического алгоритма у больных с субмукозной миомой матки.

Мы предлагаем расширить перечень обязательных критериев оценки субмукозных узлов. Это даст возможность хирургу иметь более четкое представление об особенностях оперативного лечения, а значит, повысить эффективность пред- и интраоперационных мероприятий, а также реабилитации в раннем и позднем послеоперационном периоде.

В основу созданных критериев закладывались такие анатомические особенности миоматозных узлов: степень пенетрации в миометрий, размеры узлов и их количество, высота расположения узла в полости матки, величина площади узла, которая непосредственно контактирует с миометрием, расположение относительно стенок матки, васкуляризация. Основываясь на субъективной оценке сложности гистероскопической миомэктомии для хирурга, в каждом из критериев мы выделили параметры в балах от 0 до 3.

Для анализа эффективности предложенной системы оценки субмукозной миомы матки (СОС) мы провели ретроспективное исследование 64 случаев гистероскопических миомэктомий.

Проанализировав полученные данные, мы пришли к выводу, что предложенная СОС представляет собой рациональную, эффективную и понятную оценку анатомических особенностей субмукозных миоматозных узлов, а также является простым и быстрым способом оценки сложности запланированного оперативного лечения.

Ключевые слова: субмукозная миома матки, гистероскопия, диагностические критерии.

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CHOICE OF ORGAN PRESERVING TREATMENT OF SUBMUCOUS UTERINE MYOMA BASED ON RATIONAL DIAGNOSTIC CRITERIA

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Submucous uterine myoma differs from the other types of myoma with a high rate of complications. Among them menorrhagia, infertility and loss of pregnancy.

Impetuous progress of minimal invasive surgery demands the improvement of the diagnostic algorithms for patient with uterine benign tumors especially submucous myoma.

Widen criteria for submucous nodules assessment using ultrasound were offered in this study. It may give surgeons the opportunity to have clearer view about features of the operative treatment and

as result to enhance the efficiency of pre- and intraoperative measures and of cause rehabilitation in early and late postoperative period.

We took several basic anatomical features of the submucous nodules: the penetration of the nodule into the myometrium, the size and the amount of nodules, the size of the surface that contacts with the myometrium, topography, vascularization. In each particular criteria we picked out the parameters of the complexity of hysteroscopic myomectomy for surgeon using balls from 0 to 3.

Analysis of the proposed system of submucous myoma assessment (SMAS) efficiency was made using retrospective study of randomly picked 64 hysteroscopic myomectomies.

The following conclusions were made. Proposed SMAS is rational, effective and understandable assessment of the anatomical features of the submucous nodules. SMAS is simple and quick way to evaluate the complexity of hysteroscopy and to choose the effective preoperative treatment when needed.

Key words: submucous uterine myoma, hysteroscopy, diagnostic criteria.

Introduction

Uterine myoma is the most common benign tumor in women's reproductive system. As many as 1 in 4 women may have fibroids during their childbearing years. Half of all women have fibroids by age 50.

Continuous growth of uterine myoma cases in women population widens the criteria for surgical treatment. By-turn we need to increase the amount of organ preserving gynaecological operations.

Submucous fibroids differ from the other myoma types with high level of complications among them pain, menorrhagia, infertility and miscarriage.

First of all it depends on anatomical defect, changes in blood circulation and biochemical property in uterine wall and adjacent endometrium affected by nodule.

For the time being hysterectomy still is the most effective and radical operative treatment but at the same time the most traumatic and noncompatible with future reproductive function.

Hysteroscopic myomectomy as contrasted to hysterectomy is organ preserving methodic for patients that want to retain reproductive potential and/or refuse to experience hysterectomy.

Rapid development of minimal invasive surgery requires an improvement of diagnostic approaches. It concerns the diagnostic algorithm in patient with submucous fibroids.

In our opinion today's surgeon using the existing classification of submucous myoma proposed by European Society for Gynaecological Endoscopy (ESGE) doesn't have the clear view about the case before the hysteroscopy. That happens because of lack of information and appears to be a dangerous practice. ESGE scale (using Type 0, I, II) describes only one characteristic of fibroid its penetration into the uterine wall.

Sometimes hysteroscopic myomectomy is very complicated procedure and fails to be completed several times. That's why surgeon should use all the possible criteria to evaluate the complexity of the future operation and chose the rational complex of treatment activities.

We believe that the optimal characteristics of submucous myoma that has to be studied before the hysteroscopy are the quantity of fibroids, the size of fibroids, the level of penetration into the uterine cavity, the volume of fibroid that is in contact with myometrium, the level of the nodule localization, the topography (in which part of the uterine cavity fibroid placed), the intensity of fibroid vascularization. All this characteristics can be easily estimated by careful ultrasound investigation.

Using all this parameters we can estimate the complexity of the case and build the optimal individual program for surgical and nonsurgical treatment. This can increase the effectiveness of hysteroscopic myomectomy and postoperative rehabilitation of patients.

Materials and Methods

The aim of the study is to build simple and efficient clinical classification of submucous myoma and program of treatment based on it.

On first stage we used the proposed ultrasound criteria to build the clinical classification of submucous fibroids using the 0 to 3 point scale for each parameter.

The quantity of fibroids:
— 0 p. — 1 nodule;
— 1 p. — 2 nodules;
— 2 p. — 3–4 nodules;
— 3 p. — > 5 nodules.

The size of fibroids:
— 0 p. — ≤ 20 mm;
— 1 p. — 21–30 mm;
— 2 p. — 31–40 mm;
— 3 p. — ≥ 40 mm.

The level of penetration into the uterine cavity (Fig. 1):
— 0 p. — 100% of the fibroid in the uterine cavity;
— 1 p. — > 50% of the fibroid in the uterine cavity;
— 3 p. — < 50% of the fibroid in the uterine cavity.

The volume of fibroid that is in contact with myometrium (Fig. 2):
— 0 p. — ≤ 1/3 of the fibroid volume;
— 2 p. — 1/3–2/3 of the fibroid volume;
— 3 p. — ≥ 2/3 of the fibroid volume.

The level of nodule localization (Fig. 3):
— 1 p. — lower flour;
— 0 p. — middle flour;
— 2 p. — upper flour.

The topography:
— 0 p. — posterior wall;
— 1 p. — side walls;
— 2 p. — anterior wall and fundus;
— 3 p. — uterine corners.

Vascularization:
— 0 p. — none visible vessels on dopplerography;
— 1 p. — small single vessels on dopplerography;
— 2 p. — wide system of blood vessels on dopplerography.

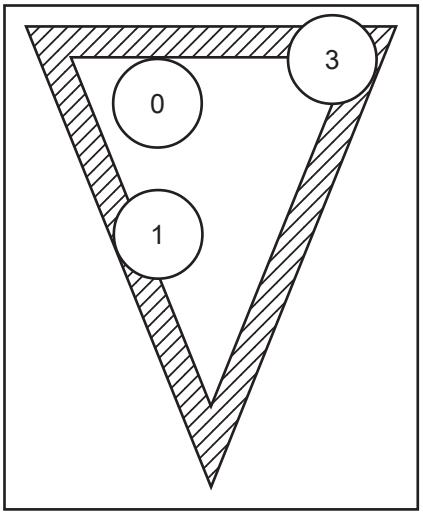

Fig. 1

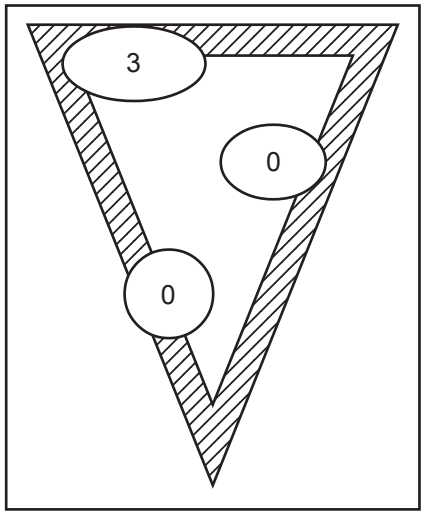

Fig. 2

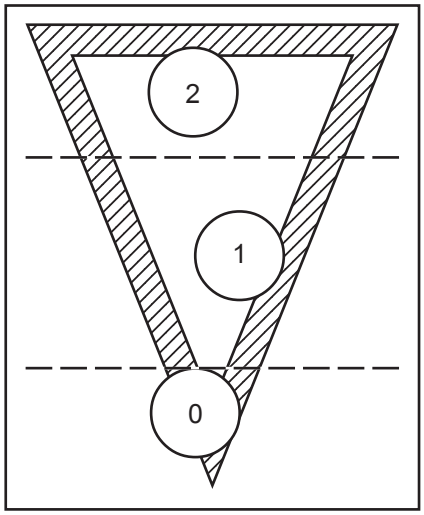

Fig. 3

Final calculation was made using the table 1.

The level of complexity of hysteroscopic myomectomy was calculated by total amount of points in each patient. Three classes of clinical cases were formed:

— Class I (0–6 points);
— Class II (7–10 points);
— Class III (≥11 points).

According to class of clinical case we propose next three types of action for surgeon:

In patients with **Class I** of submucous myoma — hysteroscopy can be performed without any preoperative treatment.

In patients with **Class II** of submucous myoma — preoperative treatment with GnRH-A should be made for a period of 2–3 months under control of ultrasound. Hysteroscopy should be recommended after the end of treatment.

In patients with **Class III** of submucous myoma — preoperative treatment with GnRH-A should be made for a period of 3–5 months under control of ultrasound. Hysteroscopy should be performed in case of conversion from Class III to Class II or I. Otherwise hysterectomy should be recommended because of high level of complexity of hysteroscopy.

To analyze the efficiency of proposed submucous myoma assessment system (SMAS) we

Table 1

Final Calculation of Fibroids' Parameters and Points

Parameter	Points			
	0	1	2	3
1. The quantity of fibroids	1 nodule	2 nodules	3–4 nodules	≥ 5 nodules
2. The size	≤ 20 mm	21–30 mm	31–40 mm	≥ 41 mm
3. The level of penetration into the uterine cavity	100%	> 50%	—	< 50%
4. The volume of fibroid that is in contact with myometrium	≤ 1/3 of the fibroid volume	—	1/3–2/3 of the fibroid volume	≥ 2/3 of the fibroid volume
5. The level of nodule localization	middle flour	lower flour	upper flour	
6. The topography	posterior wall	side walls	anterior wall and fundus	uterine corners
7. Vascularization	none visible vessels on dopplerography	small single vessels on dopplerography	wide system of blood vessels on dopplerography	—

studied 64 cases of hysteroscopic myomectomy performed in the Women's Health Center, Dnipropetrovsk Railway Hospital, Ukraine. All cases were randomly picked.

64 patients were divided in two groups based on year of operation and results of ultrasound investigation. Group I presents 34 hysteroscopies that were made in 2010–2011 using SMAS. Group II presents 30 hysteroscopies that were made in 2004–2006 based on submucous myoma classification by ESGE.

The average age in Group I was (38.0±5.17) years.

The average age in Group II was (38.5±5.74) years.

Before hysteroscopy transvaginal ultrasound investigation with empty bladder was performed in Group I and II in secretory phase of menstrual cycle.

When it was impossible to identify all needed parameters sonohysterography was made.

Standard physical examination was made along with laboratory analysis.

The results of ultrasound showed the next picture (Table 2, 3).

Table 2

Group I — 34 Women (According to SMAS Scale)

Class	Women
I	15
II	14
III	5

Table 3

Group II – 30 Women (According to ESGE Scale)

Type	Women
0	15
I	10
II	5

Results and Discussion

One-phase hysteroscopy was recommended for all patients with Class I myoma. Patients with Class II and III myoma underwent treatment with GnRH-A under ultrasound control. The final ultrasound investigation showed the next picture:

— **Class I** — 21 women;
— **Class II** — 12 women;
— **Class III** — 1 woman.

The table shows significant decrease of high complexity cases.

After conservative treatment all patient with Class I and II myoma underwent hysteroscopy. Successful one-stage operation was performed in 29 (85.3 %) cases. Complete two-stage hysteroscopy was performed in 4 (11.8%) cases. We recommended and successfully made Laparoscopic hysterectomy with tubes for 1 (2.9%) patient with Class III myoma.

Patients from Group II with myoma Type 0 and I underwent hysteroscopy without any preoperative medical treatment. Successful one-stage operation was performed in 17 (56.7%) cases. Complete two-stage hysteroscopy was performed in 6 (23.3%) cases. 2 (6.7%) hysteroscopies failed to be completed on stage two. Laparoscopic hysterectomy was recommended and performed in all 5 (16.7%) cases with Type II myoma and in 2 (6.7%) cases with incomplete hysteroscopy. 7 (23.3%) hysterectomies was made in total.

Presented data show significant difference in successful one-stage hysteroscopies and overall successful hysteroscopies in Group I comparing with Group II. In addition total amount of hysterectomies was significantly lower in Group I.

Average duration of hysteroscopy in Group I was 32.4 min. Average duration of hysteroscopy in Group II was 37.5 min.

Average blood loss in Group I was 81 cc. Average blood loss in Group II was 117 cc. This shows the significant difference between two Groups.

Fluid deficit in Group I was counted as 245 cc. Fluid deficit in Group II was counted as 314 cc.

3 (8,8%) patients from Group I experienced excessive bleeding in early postoperative period. That was stopped by additional administration of uterotonics and by placing the Folly catheter into uterine cavity for 1–4 hrs.

Episode of excessive bleeding was detected in 5 (16,7%) cases in Group II. The described earlier technique was performed to stop bleeding successfully.

No other complication was detected in two Groups.

Conclusions

Through the analysis of collected data we made a conclusion that proposed submucous myoma assessment system (SMAS) is rational, effective and understandable assessment of the anatomical features of the submucous nodules. SMAS is simple and quick way to evaluate the complexity of operative treatment assessment. We believe that SMAS gives the clear view on clinical situation to surgeon which helps to prepare for operation much better. Classifying submucous fibroids using the SMAS permits greater correlation with complete or incomplete removal of the myoma by hysteroscopic myomectomy.

Proposed SMAS helps to reduce complications and increases the effectiveness of hysteroscopy. And can be recommended for practical use by gynaecological surgeons.

REFERENCES

1. Alborzi S, Parsanezhad ME, Mahmoodian N, Alborzi S, Alborzi M. Sonohysterography versus transvaginal sonography for screening of patients with abnormal uterine bleeding. Int J Gynaecol Obstet. 2007;96(1): 20-3.

2. Campo S, Campo V, Gambadauro P. Short-term and long-term results of resectoscopic myomectomy with and without pretreatment with GnRH analogs in premenopausal women. Acta Obstet Gynecol Scand. 2005;84:756-760.

3. Cravello L., Agostini A., Beerli M. et al. Results of hysteroscopic myomectomy Gynecol Obstet. 2004; 32: 825-828.

4. Farquhar C, Ekeroma A, Furness S, Arroll B. A systematic review of transvaginal ultrasonography, sonohysterography and hysteroscopy for the investigation of abnormal uterine bleeding in premenopausal women. Acta Obstet Gynecol Scand. 2003;82(6): 493-504.

5. Fiona R., Anthony R.S. Reducing the complications of minimal access pelvic surgery. Recent advances in obstetrics and gynecology. 2003;22: 145-158.

6. Lasmar RB, Xinmei Z, Indman PD, Celeste RK, Di Spiezio Sardo A. Feasibility of a new system of classification of submucous myomas:a multicenter study. Fertil Steril. 2011 May; 95(6):2073-7. Epub 2011 Feb 21.

7. Lefebrve G, Vilos G, Allaire C, Jeffrey J. The management of uterine leiomyomas. J Obstet Gynaecol Can. 2003;128:396-418.

8. Mavrelos D, Ben-Nagi J, Davies A, Lee C, Salim R, Jurkovic D. The value of pre-operative treatment with GnRH analogues in women with submucous fibroids:a double-blind, placebo-controlled randomized trial. Hum Reprod. 2010 Sep;25(9):2264-9. Epub 2010 Jul 27.

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MAPPING THE DISEASE GENE IN TWO CONGENITAL MOTOR NYSTAGMUS FAMILIES

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Backgrounds. Congenital motor nystagmus CMN is a subtype of Congenital nystagm and usually diagnosed after sensory defect nystagmus is excluded. Although four sites have been located on X chromosome but we think there is still another disease gene on X chromosome. So in our study, we will narrow down the candidate region and identify the candidate gene for X-linked CMN of two Congenital motor nystagmus families.

Methods. Two families with CMN were investigated. Genotyping and linkage analysis were conducted in these two Chinese families.

Results. These two families were affected by X-linked CMN with incomplete penetrance. Two-point linkage analysis revealed significant maximum logarithm of odds (LOD) scores of 8.55 (DXS1047, sita = 0) and 3.91 (DXS1211 and DXS1205, sita = 0) at the family nys-01 and the family nys-02 respectively. Haplotype construction and multipoint linkage analysis also confirmed the locus and refined the locus to a 7.1 cM interval between the markers DXS8044 and DXS8041 in chromosome Xq25-q26.3.

Conclusion. We have mapped the nystagemus gene to an interval of 7.1 cM, at the location of Xq15-q26.3, such interval shares no overlap with previous Xq26-q27 locus.

Key words: congenital motor nystagmus, X-linked, linkage analysis, X-chromosome randomly-inactivation, gene map.

Congenital nystagmus (CN) is a hereditary disease characterized by bilateral ocular oscillations that begin in the first 6 month of life [1]. Congential nystagmus always accompanied with other diseases such as leukotrichia, the monochromasia, cataracts and optic atrophy et al. Congenital motor nystagmus CMN is a subtype of CN and usually diagnosed after sensory defect nystagmus is excluded [2]. CMN is a genetic heterogeneity eye disease to date, various inheritance patterns for CMN have been reported including autosomal dominant, autosomal recessive and X-linked [3]. Among these types, X-linked dominant inheritance with incomplete penetrance is the most probable mode of inheritance. So far, four sites have been located, Xp11.4-p11.3 [4], Xq26-q27 (NYS1, OMIM 310700, X-linked dominant and recessive inheritance) [3; 4], 6p12 (NYS2, OMIM 164100) [5; 6] and 7p11.2 (NYS3, OMIM 608345) [7].The virulence gene of Xq26-q27 is *FRMD7* [8], but there maybe another virulence genes in this site [9].

Methods

Subjects

Two families with CMN from Shangdong and Henan province were investigated they were respectively named nys-01 and nys-02. There are four generation of family nys-01 including 15 patients 22 normal individuals and 15 spouse (Fig. 1). There are four generation of family nys-02 9 patients 9 normal individuals and 8 spouse included (Fig. 2). 69 individuals of the two families gave consent informed to the study protocol which was approved by the Ethics committee of Tianjin Eye Hospital (Tianjin, China). 53 members of them were invited for a detailed clinical examination including direct-flashlight test, visual loss test, examination with slit-lamp microscope and examination of the fundus. Criteria for the diagnosis of CMN included onset of nystagmus before the age of 6 month and ocular examination findings that were normal except for visual acuity and nystagmus: normal color vision, pupillary light reflexes, intraocular pressure, anterior segment, optic nerves, and retina [4]. Electroretinography, which is useful in the evaluation of the patient with nystagmus, was performed in two random selected individuals.

Linkage analysis

As we investigated there is no male-to-male transmission but frequent male-to-female transmission; about half unaffected female were born to affected men, and some unaffected women passed the disease to the next generation. These indicated the disease gene of CMN is in X chromosome and its inheritance mode is X-linked dominant inheritance with incomplete penetrance. So we scanned the X chromosome only.

Blood samples were collected with informed consent from 69 pedigree members of the two families. Genomic DNA of all 23 affecteds family members were

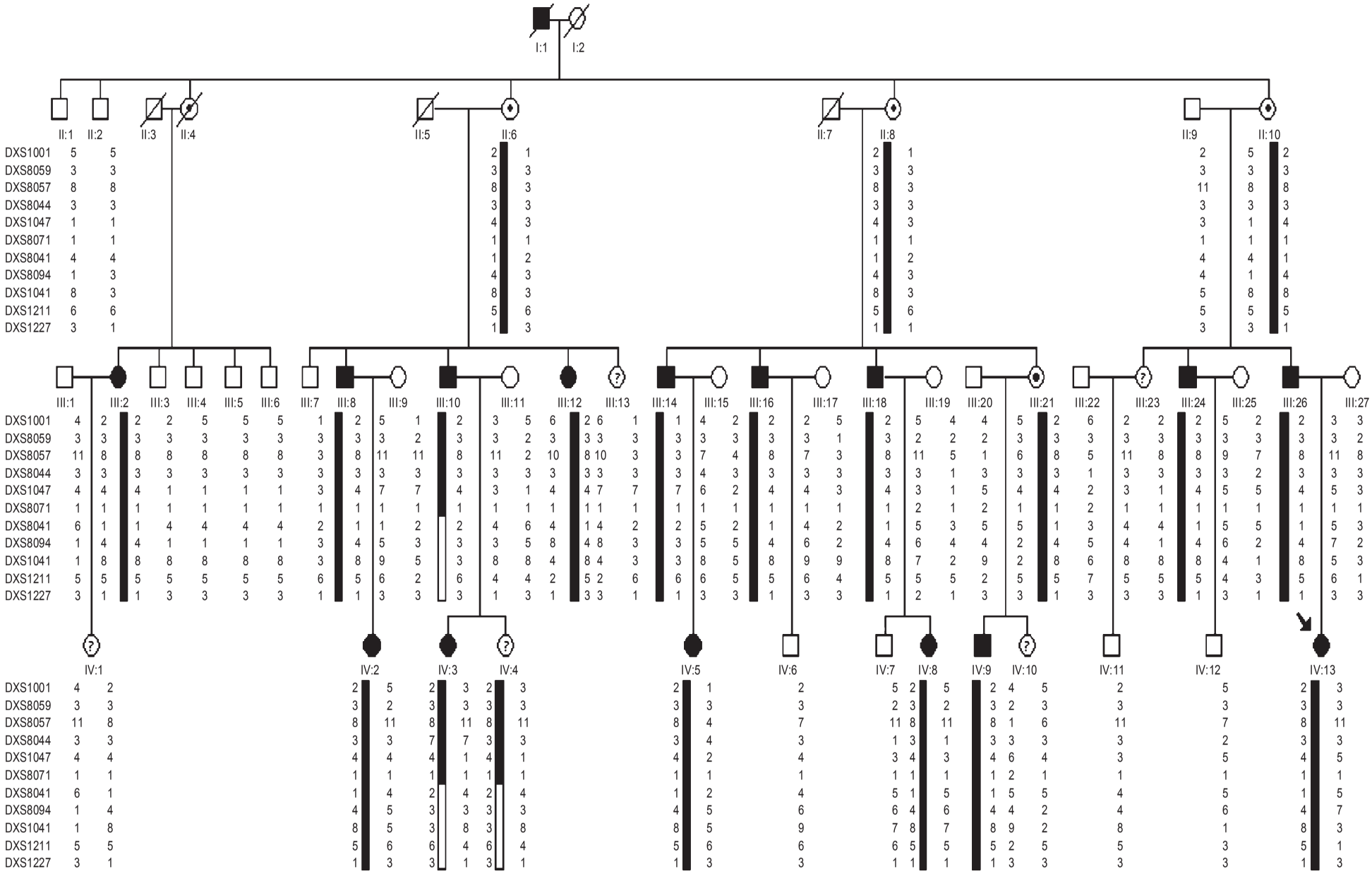

Fig. 1. Haplotype analysis of Family nys-01. Markers are listed from top to bottom:
centromere-DXS1001-DXS8059-DXS8057-DXS8044-DXS1047-DXS8071-DXS8041-DXS8094-DXS1041-DXS1211-DXS1227-telomere

isolated from peripheral blood samples by standard procedures. All specimens were quantified by spectrophotometry and diluted to 50 ng/мL for polymerase chain reaction (PCR) amplificaton. At the same time we take family CEPH-02 from CEPH for control group. Genome-wide screening was performed with 382 markers spaced about 10 cM interval (ABI PRISM Linkage Mapping Set, Version 2.5, Applied Biosystems, USA). Fine mapping was accomplished using fluorescein-labeled primers from the Decode linkage map (Kong et al., 2002). Multiplex PCR was performed in standard techniques with primers and Ampli Taq Gold DNA polymerase from Perkin Elmer. The reaction products 1 мL, Liz Size Standard-500 0.2 мL and Hi-Di formanamide 9 мL,were electrophoresed and visualized on 3130 Genetic Analyzer. Alleles were analyzed by GENESCAN Analysis version 3.7 and GENOTYPER version 3.7 software. Two-point LOD scores were calculated by the MLINK program of the LINKAGE package (version 5.1). We assumed the disease is an autosomal dominant trait with 99% penetrance. Marker allele frequencies were set at 1/*n*, where *n* is the number of alleles observed. We assumed gene frequencies of 0.0001 and no sex difference in recombination rates. Multi-point linkage analysis was used to estimate the optimal position. For multi-point linkage calculation, the genetic distance between loci was calculated by the Gene Browser (http://www.genome.ucsc.edu). The haplotype was constructed using the Cyrillic program to define the borders of the cosegregating region.

Results

Clinical findings

After clinical diagnose 23 members of the two families were affirmed have been affected

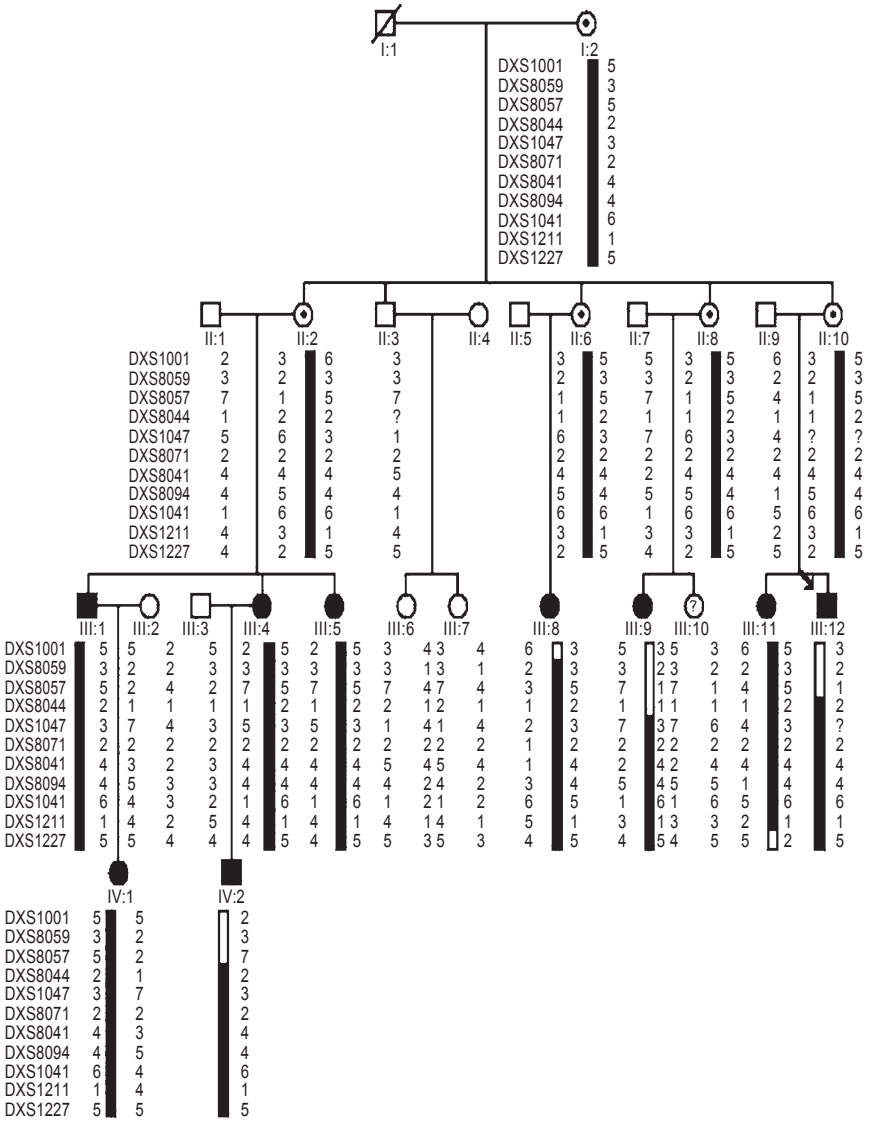

Fig. 2. Haplotype analysis of Family nys-02. Markers are listed from top to bottom:centromere-DXS1001-DXS8059-DXS8057-DXS8044-DXS1047-DXS8071-DXS8041-DXS8094-DXS1041-DXS1211-DXS1227-telomere

CMN. All of these patients have different visual loss 0.2–1.2 no other oculopathy accompanied except CMN and there was no history of other ocular or systemic abnormalities of their spouse.

Genetyping and Linkage Analysis

69 members of the two families 23 clinically affected 46 unaffected were genetyped. Linkage study was performed using 16 microsatellite markers at about 10 cM intervals on the X chromosome. Microsatellite marker DX1047 in both families, generated significant positive LOD scores with LOD2 and = 0. Later, linkage study was performed using 20 microsatillite markers around DXS1047,in nys-01 family, some microsatillites such as DX8059, DX8071 and so on,also revealed positive high LOD scores (Table 1). While, we also got high LOD scores between DXS1047 and DXS1205 in family nys-02 (Table 2). Haplotypes analysis of family nys-01 shows that there are special haplotypes between DXS8055 and DXS1211 in all affecteds and carries, recombination occurred in individual 10, 20 and 22 (see fig. 1). Therefore we assigned a locus for CMN to a 13 cM interval between DXS1001 and DXS8041 in family nys-01. Haplotypes were also constructed for the

Table 1

Two-point LOD Score with Polymorphic DNA Markers on the X Chromosome (Family nys-01)

Order	Position, Mb	LOD score at 0 =					Z_{max}	θ_{max}
		0.0	0.1	0.2	0.3	0.4		
DXS8055	114.5	-0.44	2.72	2.38	1.69	0.84	2.72	0.1
DXS8053	115.4	2.85	3.90	3.14	2.14	1.00	3.90	0.1
DXS8059	122.0	2.59	1.76	1.68	1.29	0.72	2.59	0.0
DXS8078	126.3	3.77	3.15	2.45	1.67	0.84	3.77	0.0
DXS1047	128.8	8.55	7.17	5.63	3.87	1.86	8.55	0.0
DXS8071	131.2	3.65	3.04	2.37	1.61	0.81	3.65	0.0
DXS8041	133.4	1.11	6.42	5.17	3.59	1.73	6.42	0.1
DXS8074	133.8	3.72	3.01	2.25	1.46	0.67	3.72	0.0
DXS8033	133.9	-3.66	4.00	3.16	2.09	0.93	4.00	0.1
DXS8094	136.0	-3.85	6.47	5.23	3.64	1.76	6.47	0.1
DXS1041	136.3	-6.44	4.21	3.36	2.25	1.02	4.21	0.1
DXS1211	138.0	-6.73	3.97	3.17	2.11	0.95	3.97	0.1

Table 2

Two-point LOD Score with Polymorphic DNA Markers on the X Chromosome (Family nys-02)

Order	Position, Mb	LOD score at 0 =					Z_{max}	θ_{max}
		0.0	0.1	0.2	0.3	0.4		
DXS8059	121.9	-4.11	-0.12	0.22	0.29	0.20	0.29	0.3
DXS8098	122.6	-3.69	0.81	0.85	0.58	0.22	0.85	0.2
DXS8057	123.3	-9.79	0.41	0.75	0.65	0.33	0.75	0.2
DXS8009	125.8	-3.07	2.03	1.67	1.10	0.44	2.03	0.1
DXS8044	126.3	-4.89	0.32	0.42	0.36	0.22	0.42	0.2
DXS1047	128.8	3.61	3.02	2.35	1.60	0.78	3.61	0.0
DXS1041	136.2	1.81	1.49	1.13	0.73	0.31	1.81	0.0
DXS1211	138.0	3.91	3.27	2.56	1.75	0.86	3.91	0.0
DXS1205	139.9	3.91	3.27	2.56	1.75	0.86	3.91	0.0
DXS1227	140.5	-3.99	1.34	1.23	0.95	0.54	1.34	0.0

analyzed markers on family nys-02 (see Fig. 2). On individual 18 and 22, recombination events were found. Then according our multipoint linkage analysis on the two families Fig. 3 for nys-01, Fig. 4 for nys-02, the disease gene were located between DXS8044 and DXS1227. Finally, according with the genetypes of nys-01 and nys-02, we located the disease gene of CMN to a 7.1 cM interval between DXS8041 and DXS8044 on Xq25-26.3 (Fig. 5).

So we located the CMN virulence genes to a 7.1 cM interval between Xq25 and Xq26.3 and supposed there were two independent CMN virulence gene.

Discussion

This study suggested that the most common mode of inheritance for CMN is X-linked dominant with incomplete penetrance and the morbidity of the female family members is 60%.This study also validated a classical hypothesis — Lyon hypothesis. As we all known, female with two X chromosomes just have equal X chromosome common gene products with male this means that both males and females rely on the information from only a single X chromosome. Therefore, it is only one X chromosome that provides genetic information in both males and females. This phenomenon was interpreted as a means of dosage compensation for X-linked genes. On 1960 Ohno and his colleagues showed that female mice consisted of a single condensed X-chromosome. On 1961 geneticists Mary Lyon proposed the condensed X chromosome is inactivated that's famous Lyon Hypothesis. (1) In the day 15–16 of embryonic development one of the two copies of the X chromosome present in female mammals is inactivated while the whole cell number is about 5000. (2) The choice of which X chromosome will be inactivated is random it may be from father or mother. (3) Once an X chromosome is inactivated it will remain inactive throughout the lifetime of the cell and its descendants in the organism. But in the next meiotic mitosos term the inactivated X chromosome will be resurrection and on the next new random inacvation trip again. This hypothesis can explain why some female carriers such as 14, 28, 42 didn't affected CMN it may because the disease gene just right on the inactivated X chromosome.

On 1999 Three families with CMN inherited in an X-linked, irregularly dominant pattern were investigated with linkage analysis by Kerrison. He located NYS1 gene between GATA172DO5 and DXS1192 on Xq26-q27 [4] later this gene were located to 15.8 cM interval between ATA59C05 and DXS1192 [10]. On 2011 he narrowed the CMN locus down to a region between ATA9909 and DXS1211 [11]. However, these results is still overlaps 8.7 cM than our defined region in this study. It's interesting there is a report find another inheritance pattern — X linked dominant pattern with 100% penetrance, in a Chinese family, and they refines a locus for X-linked dominant CMN to a 4.4 cM re-

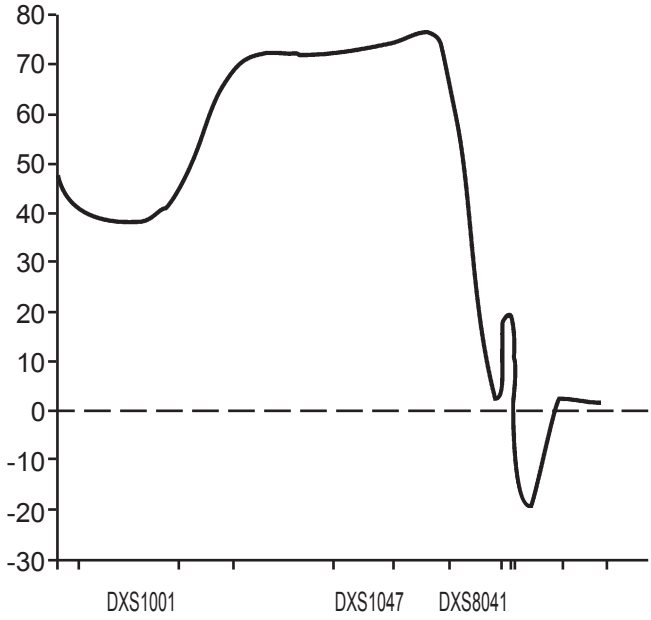

Fig. 3. Multipoint LOD score with support interval localizes the gene in a region between DXS1001 and DXS8041 in family nys-01. The markers and intervals: DXS8055-0.9cM-DXS8053-4.2cM -DXS1001-2.3cM -DXS8059-4.2cM –DXS 8078- 2.53cM -DXS1047-2.3cM -DX8071-2.26cM -DXS8041-0.38cM -DXS8074-0.1cM -DXS8033-2.1cM -DXS8094-0.03cM -DXS1041-1.77cM -DXS1211

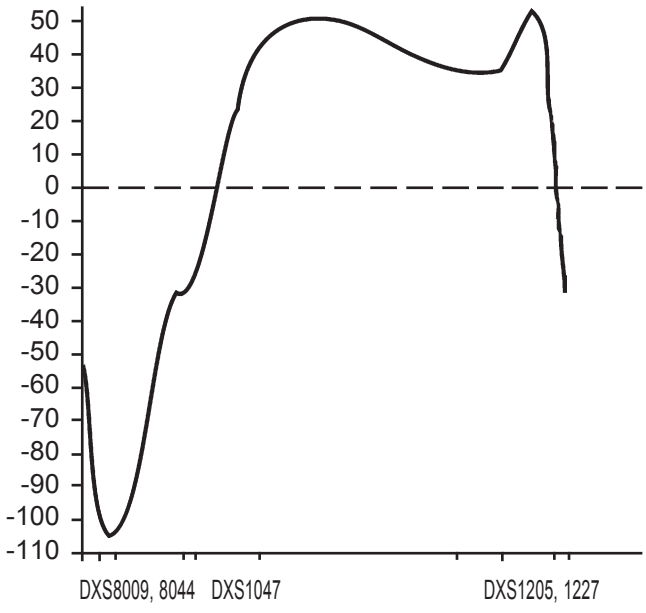

Fig. 4. Multipoint LOD score with support interval localizes the gene in a region between DXS8044 and DXS1227 in family nys-02. The markers and intervals: DXS8059-0.65cM-DXS8098-0.66cM-DXS8057-2.6cM-DXS8009-0.43cM-DXS8044-2.47cM-DXS1047-7.46cM-DXS1041-1.76cM-DXS1211-1.95cM-DXS1205-0.54cM-DXS1227

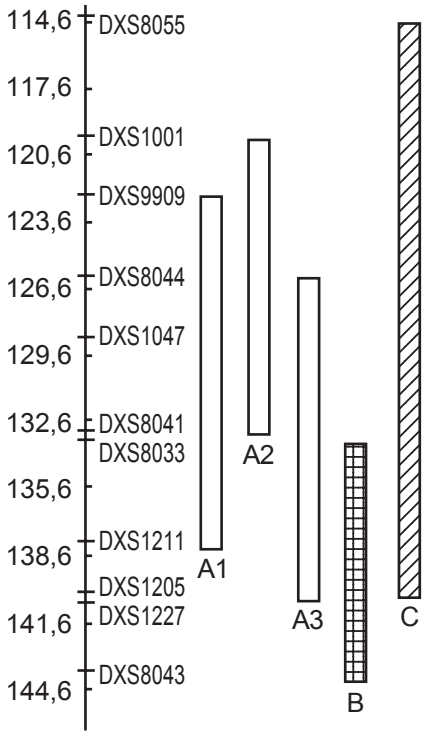

Fig. 5. Xq-linked nystagmus with different inheritance pattern Series A shows the X-linked dominant pattern with incomplete penetrance (A1, assigned by Kerrison et al., 2001; A2 and A3 refined in family nys-01 and nys-02, respectively). B shows the X-linked dominant pattern with 100% penetrance. C shows the X-linked recessive pattern

gion at Xq26.3-q27 [9], and in another study performed in two X-linked recessive pattern families by, the CMN disease gene were located to Xq23-27 [2].

REFERENCES

1. Tkalcevic LA, Abel LA. The effects of increased visual task demand on foveation in congenital nystagmus. Vision Res.2005, 45(9):1139-46.

2. Guo XM, Li SQ, Jiang XY, Xiao XS, Wang PF, Zhang QJ. Linkage analysis of two families with X-linked recessive congenital motor nystagmus. J Hum Genet. 2006, 51(1):76-80.

3. Cabot A, Rozet JM, Gerber S, Perrault I, Ducrog D, Smahi A et al. A Gene for X-linked Idiopathic Congenital Nystagmus (NYS1) Maps to Chromosome Xp11.4-p11.3. Am. J. Hum. Genet. 1999, 64:1141-1146.

4. John B. Kerrison, M. Reza Vagefi, M. Michael Barmada, and Irene H. Maumenee. Congenital Motor Nystagmus linked to Xq 26-27. Am.J.Hum. Gnent. 1999, 64:600-607.

5. John B. Kerrison, Veronique J Arnould, M. Michael Barmada, Robert K Koenekoop, Barbara J Schmeckpeper, Irene H Maumenee. A Gene for Autosomal Dominant Congenital Nystagmus Localizes to 6p12. Genomics, 1996, 33, 623-526.

6. Kerrison JB, Koenekoop RK, Arnould VJ, Zee D, Maumenee IH. Clinical Features of Autosommal Dominant Congenital Nystagmus linked to Chromosome 6p12. American Journal of Ophthalmology, 1998, 125:64-70.

7. Patton MA, Jeffrey S, Lee N, Hogg C. Congenital nystagmus cosegregating with a balance 7;15 translocation. J Med Genet, 1993, 30:526-528.

8. Tarpey P, Thomas S, Sarvananthan N, Mallya U, Lisgo S, Talbot CJ, et al. Mutations in FRMD7, a newly identified member of the FERM family, cause X-linked idiopathic congenital nystagmus. Nat Genet. 2006 Nov;38(11): 1242-4.

9. Zhang BR, Xia K, Ding MP, Liang DS, Liu ZR, Qian P, et al. Confirmation and refinement of a genetic locus of congenital motor nystagmus in Xq26.3-q27.1 in a Chinese family. Hum Genet, 2005, 116:128-131.

10. Mellott ML, Brown J Jr, Fingert JH, Taylor CM, Keech RV, Sheffield VC, et al. Clinical Characterization and linkage analysis of a family with congenital X-linked nystagmus and deuteranomaly. Arch Ophthalmol, 1999, 117: 1630-1633.

11. Kerrison JB, Giorda R, Lenart TD, Drack AV, Maumenee IH. Clinical and genetic analysis of a family with X-linked congenital nystagmus (NYS1). Ophthalmitc Genetics, 2001, 22(4): 241-248.

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ENDOSCOPIC TREATMENT OF AMPULLARY TUMORS

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УДК 616-006-089-072.1
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ЭНДОСКОПИЧЕСКОЕ ЛЕЧЕНИЕ АМПУЛЯРНЫХ ОПУХОЛЕЙ
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Ампулярные аденомы являются предраковыми новообразованиями и встречаются примерно от 0,04 до 0,12 % случаев. В последнее время эндоскопическая папиллэктомия все чаще используется с лечебной целью для этих новообразований. Эндоскопическое лечение было таким: эндоскопическая папиллэктомия — 21 (13 %), супрапапиллярная холедохотомия — 91 (55 %), стентирование нитиноловым стентом — 31 (19 %), стентирование пластиковым стентом — 22 (13 %) случая. Осложнения эндоскопической папиллэктомии имели место в 7 случаях и были такими: кровотечение — 4, острый панкреатит — 2, перфорация — 1. Коагуляция была использована для достижения гемостаза у 2 пациентов, наложение hemoclip — в 1 случае и ангиографическое пособие понадобилось у 1 пациента. Все случаи панкреатита лечили консервативно. В 1 случае перфорации была проведена операция. За время наблюдения (в среднем 30 мес.) 12 из 21 пациента (49 %) не имели рецидива, 5 имели рецидивные аденомы (средний период до прогрессирования — 27 мес.), двое умерли от болезней, не связанных с заболеванием. Все резидуальные опухоли были удалены при повторной эндоскопической процедуре.
Ключевые слова: эндоскопия, ампулярные опухоли, стентирование.

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ENDOSCOPIC TREATMENT OF AMPULLARY TUMORS
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Background. Ampullary adenomas are premalignant neoplasms and occur in about 0.04 to 0.12% of the general population based on autopsy series. Recently, endoscopic snare papillectomy has increasingly been used with curative intent for ampullary neoplasms.

Methods. Between January 2005 and October 2011, 230 patients with ampullary tumors underwent various surgical operations at our institute: pancreatoduodenectomy (Whipple procedure) — 45, transduodenal papillectomy — 29, palliative surgical operations — 78, endoscopic treatment — 165 cases. Endoscopic treatment of ampullary neoplasms was as following: endoscopic papillectomy — 21 (13%), suprapapillary choledochostomy — 91 (55%), nitinol biliary stenting — 31 (19%), plastic biliary stenting — 22 (13%) cases. En bloc resection of adenoma (< 3 cm) was performed in 10 patients, piecemeal removal (> 3 cm) — in 11 cases. Covered and uncoverd metal stents (1 cm × 6 cm) were used in 31 (19%) cases.

Results. Complications of endoscopic papillectomy occurred in 7 cases and were as follows: bleeding — 4, acute mild pancreatitis — 2, perforation — 1. Epinephrine spray and argon-plasma coagulation was used to attain hemostasis in 2 patients, hemoclip placement — in 1 case and angiographic management was necessary in 1 patient. All cases of pancreatitis were treated conservatively. In 1 case of perforation surgery was performed. During follow-up (mean 30 months) 12 of 21 patients (49%) had no recurrence, 5 — had recurrent adenoma (mean time interval to recurrence 27 months), two died of unrelated illnesses and 2 are awaiting follow-up. All residual tumors were eradicated by repeated endoscopic procedures.
Key words: endoscopy, ampullary tumours, stenting.

Introduction

Ampullary adenomas are premalignant neoplasms and occur in about 0.04 to 0.12% of the general population based on autopsy series [1; 2]. Surgical treatment of ampullary tumors includes palliative operations, transduodenal local resection and pancreaticoduodenectomy (Whipple procedure) [4]. In the early years endoscopic management consisted mainly of palliative treatment such as stent placement for obstructive jaundice. Recently, endoscopic snare papillectomy has increasingly been used with curative intent for ampullary neoplasms [3; 5].

Patients and Methods

Between January 2005 and October 2011 230 patients with ampullary tumors underwent various surgical operations at our institute: pancreatoduodenectomy (Whipple procedure) — 45, transduodenal papillectomy — 29, palliative surgical operations — 78, endoscopic treatment — 165 cases. Mean age was 62 years (range 27 to 86 years). There were 132 women and 98 men. Clinical presentation was as following: obstructive jaundice — in 82% patients, pancreatitis — 6%, cholangitis — 19%, gastrointestinal bleed-

ing — 8%, abdominal pain — 7%, asymptomatic — 9% cases. Diagnosis was confirmed preoperatively in all patients using ultrasonography, CT, MRI, EUS, endoscopy and biopsy. Endoscopic treatment of ampullary neoplasms was as following: endoscopic papillectomy — 21 (13%), suprapapillary choledochostomy — 91 (55%), nitinol biliary stenting — 31 (19%), plastic biliary stenting — 22 (13%) cases.

As endoscopic papillectomy became effective procedure in the treatment of ampullary tumors we want to represent our experience in the management of 21 patients.

The Technique of Endoscopic Papillectomy

Endoscopic papillectomy was performed in 21 cases. Papillary adenoma was in 13 patients, tubular adenoma — in 8 cases. Sedation consisted of carefully titrated doses of meperidine and/or midazolam with buscopan as necessary to inhibit duodenal motility. Continuous hemodynamic monitoring was employed, and all procedures were performed using the Olympus TJF-150 or TJF-130 videoduodenscopes with needle-type papillotomes, endoscopic snares and 40 W-s of blended diathermy current. Indications for endoscopic papillectomy were: tumor size less than 3 cm, no endoscopic evidence of malignancy, soft consistency to palpation with any device, benign histopathologic features in prior forceps biopsy specimens.

Features of unresectability were ulceration, friability, more than 50% lateral extension, obvious duodenal infiltration, and intraductal extension of more than 1 cm at ERCP. After performing duodenoscopy a cholangiogram and pancreatogram were obtained. A standard polypectomy snare using blended electrosurgical current was used to tighten around the lesion and transect it (Fig. 1, 2).

En bloc resection of adenoma (< 3 cm) was performed in 10 patients, piecemeal removal (> 3 cm) — in 11 cases. A dilute solution of epinephrine (1 : 10,000) was injected submucosally to elevate the tumor — in 5 patients. In 3 cases incision was made with needle knife circumferentially around the lesion to facilitate snare capture. A biliary sphincterotomy was performed with blended current, whereas the pancreatic sphincterotomy was done with pure cut current by using a monofilament papillotome. Endoscopic stenting of pancreatic duct was performed in 7 cases.

All tissue was retrieved and sent for histopathologic evaluation. If needed, thermal energy (argon plasma coagulation was used to treat any residual tissue. Endoscopic success was defined as complete excision of the tumor. All patients returned 4 to 8 weeks after the initial papillectomy for stent removal, routine biopsies, and further treatment, if needed. Follow-up was then performed at 3, 6, 12 and 24-month intervals.

Endoscopic choledochostomy was performed in 91 cases as follows: the intraduodenal segment of the distal common bile duct was identified by endoscopic examination as a bulge in the suprapapillary portion of the papilla. The distal common bile duct proximal to the cancerous tissue was then punctured with a neddle-knife by using pure coagulation electrosurgical current. When flow of bile through the choledochoduodenal fistula was noted then transfistula cannulation of the bile duct was attempted with the aid of guidewire. Then artificial fistula was extended by means of standard shincterotome or balloon dilation.

Plastic biliary stenting was performed in 22 (13%) cases. We used a stiff polyethylene inner catheter with radiopaque markers over a guidewire. Then the plastic biliary stent (10 F) was advanced over the complex guidewire-inner catheter using an outer pusher device as a three-layer system.

Covered and uncoverd metal stents (1 cm x 6 cm) were used in 31 (19%) cases (Fig. 3).

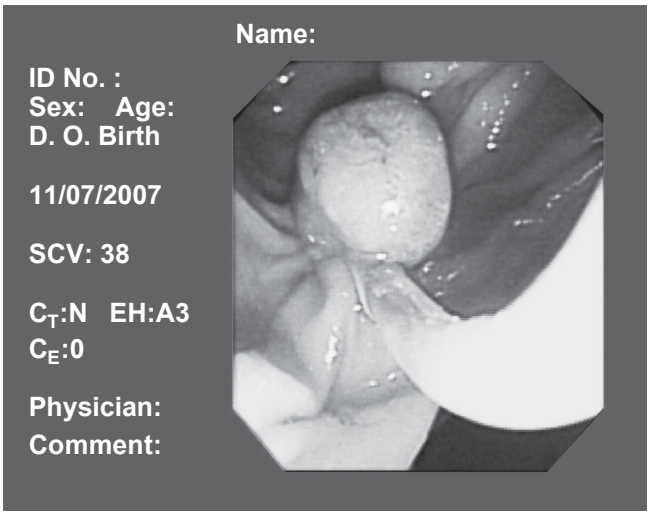

Fig. 1. Tumor capture with endoscopic snare

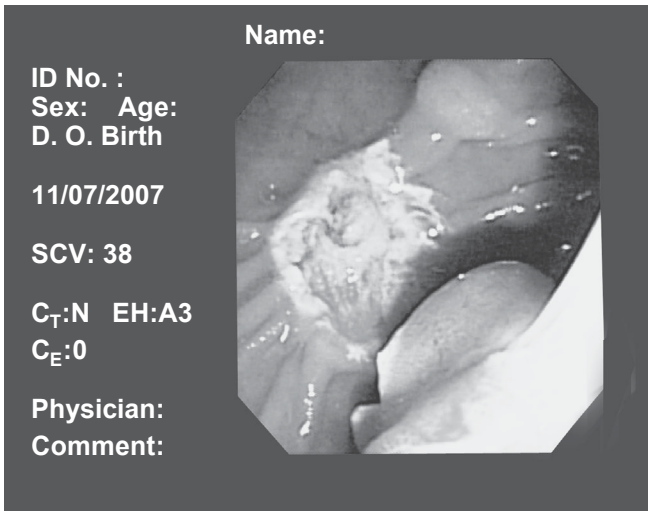

Fig. 2. Transsecting the tumor

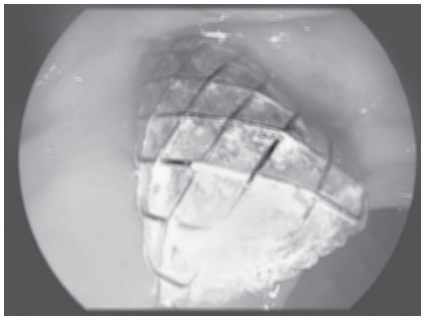

Fig. 3. Metal stenting of ampullary cancer

After biliary sphincterotomy, the length of each stricture was determined and the origin of the cystic duct insertion was noted in patients who had a gallbladder. The stent delivery system was advanced proximal to the stricture over a guide wire, where the stent was partially deployed and positioned within the stricture. When anatomically feasible stents were deployed so as to avoid occlusion of the cystic duct insertion, particularly in patients with a gallbladder.

Results and Discussion

Complications of endoscopic papillectomy occurred in 7 cases and were as follows: bleeding — 4, acute mild pancreatitis — 2, perforation — 1. Epinephrine spray and argon-plasma coagulation was used to attain hemostasis in 2 patients, hemoclip placement — in 1 case and angiographic management was necessary in 1 patient. All cases of pancreatitis were treated conservatively. In 1 case of perforation surgery was performed. During follow-up (mean 30 months) 12 of 21 patients (49%) had no recurrence, 5 had recurrent adenoma (mean time interval to recurrence 27 months), two — died of unrelated illnesses and 2 are awaiting follow-up. All residual tumors were eradicated by repeated endoscopic procedures.

Conclusions

(1) Endoscopic therapy appears to be a reasonable alternative to surgery for management of benign papillary tumors. (2) Papillary adenoma after endoscopic resection recurs in about a third of cases. (3) Recurrences are usually small and benign, and can be successfully treated endoscopically. (4) Further studies with long-term follow up are needed to determine the ultimate outcome of endoscopic treatment in patients with papillary neoplasms. (5) Metal biliary stenting is effective procedure in the treatment of unresectable cases.

REFERENCES

1. *Endoscopic* resection of benign tumors of the papilla of Vater / S. Bohnacker, N. Soehendra, H. Maguchi [et al.] // Endoscopy. – 2006. – Vol. 38. – P. 521–525.

2. *Predictors* of failure after pancreaticoduodenectomy for ampullary carcinoma / R. D. Kim, P. S. Kundhal, I. D. McGilvray [et al.] // J Am Coll Surg. – 2006. – Vol. 202. – P. 112–119.

3. *Ogorodnik P. V.* Endoscopic surgery of the duodenal large papilla tumors / P. V. Ogorodnik, A. G. Deinichenko // Klin Chir. – 2011. – Vol. 4. – P. 9–12.

4. *Focal* early stage cancer in ampullary adenoma: surgery or endoscopic papillectomy? / S. M. Yoon, M. H. Kim, M. J. Kim [et al.] // Gastrointest Endosc. – 2007. – Vol. 66. – P. 701–707.

REFERENCES

1. Bohnacker S., Soehendra N., Maguchi H., et al. Endoscopic resection of benign tumors of the papilla of Vater. Endoscopy 2006; 38: 521-525.

2. Kim R.D., Kundhal P.S., McGilvray I.D., et al. Predictors of failure after pancreaticoduodenectomy for ampullary carcinoma. J Am Coll Surg 2006; 202: 112-119.

3. Ogorodnik P.V. Deinichenko A.G. Endoscopic surgery of the duodenal large papilla tumors. Klin Chir 2011; 4: 9-12.

4. Yoon S.M., Kim M.H., Kim M.J., et al. Focal early stage cancer in ampullary adenoma: surgery or endoscopic papillectomy? Gastrointest Endosc 2007; 66: 701-707.

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ANTIBIOTIC PROPHYLAXIS ON THE TIME OF CATHETER REMOVAL FOLLOWING LAPAROSCOPIC RADICAL PROSTATECTOMY

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Objective. To assess the interaction between antibiotic prophylaxis and bacteriuria, leukocyturia after catheter removal following laparoscopic radical prostatectomy (LRP).

Patients and methods. A prospective randmized study enrolled 180 patients undergoing LRP, who were randomized either for receiving 7 days of prophylactic antibiotics starting at urinary catheter removal, or not. A urine specimen was collected for urinalysis on removal of the catheter, 1, 4 and

8 weeks after operation. Another urine specimen was collected for urine culture on removal of the catheter and 4 weeks later. The groups were compared for the bacteriuria, leukocyturia occuring within 8 weeks after catheter removal.

Results. Antibiotic prophylaxis was given to 80 of 145 LRP patients (55.17%), while the remainnig 65 patients did not receive antibiotic prophylaxis. The total incidence of bacteriuria after catheter removal following LRP was 20% (29/145), which was showed no significantly differences between the two groups (with or without prophylaxis, 16/80, 13/65, P>0.05). However, antibiotic resistance occurred most frequently in the antibiotic prophylaxis group and was significant difference between 2 groups (P=0.025). Moreover, postoperative change in urine leukocyte counts were not significantly different between the 2 groups (P>0.05).

Conclusion. Bacteriuria and luekocyturia should be safely managed with culture-specific antibiotic prophylaxis and careful monitoring after catheter removal following LRP. There is no detectable significant benefit in using antibiotic prophylaxis to reduce the urine leukocyte counts after LRP.

Key words: prostate cancer, radical prostatectomy, bacteriuria, luekocyturia.

Introduction

After laparoscopic radical prostatectomy (LRP), short-term catheterization is usually used to ensure that the bladder remains empty during a period of vesicourethral anastomotic healing. Bacteriuria is one of the most common complication after LRP, and the reported rate of bacteriuria increases about 5–10% for each day [1]. Antibiotic prophylaxis is widely accepted during the perioperative period. However, the benefit of antibiotic prophylaxis during removal of the catheter is controversial [2; 3]. In addition, urine culture results are not usually available before 24 hours after collection, most of physicians are often prescribe the empiric antibiotics as a result of urinalysis (urinary leukocyte counts) for the patient [4]. Herein, the present study was undertaken to assess the interaction between antibiotic prophylaxis and bacteriuria (symptomatic or asymptomatic), and leukocyturia occuring within 8 weeks immediately after catheter removal in patients undergoing LRP.

Patients and Methods

Consecutive men who underwent LRP at our institution from January 2010 to December 2011 by a single surgeon (Xin Gao) were enrolled in this study. The study was approved by the Institutional Ethical Committee and all patients provided written informed consent before entry to the study. The perioperative management of both groups was similar. Intravenous ciprofloxacin (0.5 g) was administered half an hour before surgery plus 3-day doses postoperatively as surgical prophylaxis. The vesicourethral anastomosis was performed using a 3-0 Vicryl suture in a continuous or intermitted manner at the discretion of the surgeon [5]. The drains and indwelling urinary catheters were removed before discharge. Patients who presented with clinical urinary tract infection (UTI) before catheter removal, required additional transurethral manipulations (urethrotomy, dilatation of the urethra), or received prolonged antibiotics (>7 days) for other complications were excluded. Based on whether to receive antibiotics at the time of urinary catheter removal, the patients divided into 2 groups. Antibiotic prophylaxis group routinely prescribed a 7-day oral course of antibiotics (ciprofloxacin, 500 mg, once daily) starting the day at catheter removal. Patients allergic to ciprofloxacin were given (Cefaclor, 375 mg, twice daily). Patients in the other group did not receive any antibiotics at this time.

Demographic and clinical data, including age, history disease, prostate-specific antigen (PSA), Prostate volume, Neoadjuvant androgen ablation therapy, operative time, estimated blood loss, transfusion, duration of catheter, final Gleason score and complications were recorded prospectively. Two urine specimens of each patient, one for urinalysis (urinary leukocyte counts) was collected immediately after catheter removal, 1, 4 and 8 weeks after catheter removal, and one for urine culture immediately after catheter removal and 4 weeks after catheter removal. In our institution, all urine samples were collected in a sterile device that reduces the manipulation of the sample to a minimum. Patients with at least 10^5 cfu/ml in any of these 2 postoperative urine cultures were considered to have present bacteriuria. Leukocyturia was defined as 18.0 leukocytes/ul according to the result of urinalysis (Sysmex UF-1000i). At follow-up period, all patients were seen by a study-blind specialist in urology to assess subjective symptoms after catheter removal.

Data were presented as median (interquartile) for continuous variables and as frequencies (percentage) for categorical variables. Statistical analysis was performed using the t-test, χ^2 test or Fisher's exact test. Postoperative changes in the urine leukocyte counts between the 2 groups were compared by two-factor repeated measure ANOVA. All analysis was done using SPSS 15.0 software (SPSS, Chicago, Illinois, USA) and P values of less than 0.05 was considered statistical significance.

Result

Between January 2010 and December 2011, a total of 177 patients were randomized (T1c-T3b). 32 patients were excluded receiving prolonged antibiotic therapy for clinical UTI before catheter removal (11), chest infection (5), remote infection (4), surgical site infection (3), intraoperative rectal injury (2), and for not completing the follow-up required for this study (7). Statisti-

cal analysis was therefore based on 145 patients. Demographic and clinical characteristics showed no significant difference between the patients remaining in both groups except the operative time (P=0.047, Table 1). The urinary catheters were left in the place for 11±A3.5 days in the prophylaxis group and for (10.0±2.7) days in the group without prophylaxis (P=0.069). Perioperative prophylaxis was given in all patients for a median duration of 3 days.

Among 145 patients analyzed, antibiotic prophylaxis was given to 80 patients (55.17%), 76 patients received ciprofloxacin, and 4 patients received Cefaclor for known or suspected allerge to the former.

Among 145 patients, 29 (20%) developed a postoperative bacteriuria in the both groups (Table 2). In the prophylaxis group, these cases of postoperative bacteriuria were discovered on removal of the catheter (7), 4 weeks after catheter withdral (9). The pathogens in 11 patients were resistant to ciprofloxacin. In the non-therapy group, 9 patients had bacteriuria on removal of the catheter, 4 patients 4 weeks after catheter removal. 10 patients in non-antibiotic group were sensitive to ciprofloxacin. There was no significant difference in the bacteriuria rate (symptomatic or asymptomatic) on the time of catheter removal and 4 weeks later between the antibiotic prophylaxis and non-antibiotic group (P=0.330, 0.385 respectively). However, antibiotic resistance occurred most frequently in the antibiotic prophylaxis group and was significant difference between 2 groups (P=0.025). Lower urinary tract symptoms (LUTS) such as frequency, urgency and burning sensation were not significant difference between the 2 groups (P=0.134). In antibiotic group, 3 patients with fever starting at the 2, 3, 5 days after urinary catheter removal respectively, and fever was observed in 2 patients in no-antibiotic group only (fever < 38°C). These fever suspicious for UTI continued antibiotic therapy in antibiotic group and all decreased gradually thereafter. No serious infectious sequelae occured up to 4 weeks after LRP. No adverse or allergies events from receiving the antibiotic prophylaxis were noted.

In total, 145 urine samples were collected immedialtely prior to catheter removal. Of 1160 urine specimens, the mean con-

Table 1

Clinical Characteristics, Perioperative Data and Complications within 1 Year of Surgery

Indices	Antibiotic prophylaxis at catheter removal		P
	No (n=65)	Yes (n=80)	
Clinical characteristics			
Age, years	70 (57, 77)	67 (55, 74)	0.932
Hypertension	20 (30.7%)	29 (36.3%)	0.488
Diabetes	15 (23.1%)	23 (28.8%)	0.440
Previous TURP	6 (9.2%)	5 (6.3%)	0.542
Serum PSA, ng/ml	17.6 (6.7, 34.6)	23.4 (2.3, 40.8)	0.092
Prostate volume, ml	39.7 (22.7, 89.6)	35.3 (21.9, 108.6)	0.239
Neoadjuvant androgen-ablation therapy	7 (10.8%)	9 (11.3%)	0.927
Perioperative data			
Operative time, min	172 (121, 308)	165 (115, 350)	0.047
Estimated blood loss	132 (65, 450)	116 (50, 389)	0.052
Transfusion	3 (4.6%)	2 (2.5)	0.657
Catheter duration, days	9 (7, 21)	8 (7, 14)	0.058
Final Gleason score > 7	44 (67.7%)	51 (63.7%)	0.619
Postoperative complications			
Urinary retention	1 (1.5%)	0	—
Incontinence	2 (3.1%)	3 (3.8%)	1.000
Anastomotic stricture	2 (3.1%)	1 (1.3%)	0.578

Note. Data are given as median (interquartile range) or frequency (percentage).

Table 2

Summary of Bacterial Isolates and Species Resistant to Ciprofloxacin from Two Groups Patients within 4 Weeks after Catheter Removal Following LRP

Species	No. of cultures (Species resistant to ciprofloxacin)	
	No-antibiotic group (n=65)	Antibiotic group (n=80)
Escherichia coli	6 (1)	5 (4[a])
Pseudomonas aeruginosa	4	3 (3[b])
Klebsiella pneumoniae	1 (1)	4 (2[c])
Staphylococcus epidermidis	1 (1)	2 (1)
Coagulase Negative Staphylococcus	1	0
Enterobacter cloacae	0	1 (1)
Enterococcus faecalis	0	1
Total	13 (3)	16 (11)

Note. a — two cases with fever when urine culture was obtained; b/c — one case with dysurea when urine culture was obtained.

centration of leukocyte counts were highest on the time of catheter removal and decreased gradually thereafter (with vs without antibiotics: (436.82±106.5) vs (444.81±97.06) leukocytes/ul). In addition, postoperative change in urine leukocyte counts were not significantly different between the 2 groups within 8 weeks after catheter removal (P>0.05, Table 3). ANOVA for repeated measures be used to perform the data analysis. The results showed that the interaction between antibiotic therapy and time effects was not significant (P=0.106), the main effect of the treatment was not significant (P=0.097), while the time effect was significant (P=0.042, Table 3).

Table 3

Postoperative Change in Urine Leukocyte Counts and Urine Culture Results between the 2 Groups within 8 Weeks after Catheter Removal

Time point after catheter removal	Antibiotic prophylaxis at catheter removal		P
	No (n=65)	Yes (n=80)	
Urine leukocyte counts	—	—	Group=0.097; time=0.042; Group*time= 0.106@
At catheter removal	444.81±97.06	436.82±106.53	0.932*
1st week	243.32±89.46	215.68±57.42	0.488*
4th week	170.67±63.89	142.70±52.78	0.440*
8th week	25.17±16.87	27.16±35.65	0.542*
Urine culture results			
At catheter removal	9 (13.8%)	7 (8.8%)	0.330#
8th week	4 (6.2%)	9 (11.3%)	0.385#
Resistant to quinolones	3 (23.1%)	11 (68.8%)	0.025#

Note. @ — Two-factor repeated measure ANOVA. Factor 'group' consists of antibiotic and non- antibiotic groups, while factor 'time' consists of at catheter removal, 1 week, 4 week, and 8 week for urinalysis (urine leukocyte counts) and at catheter removal, 1 week for Urine culture results. 'Group × time' indicates interaction; * — t-test; # — χ^2 test or Fisher's exact test.

Discussion

We know from the publications that the incidence of bacteriuria is 5–10% for each day the catheter is in the place [1]. Among the patients with LRP in our institute, the median time to catheter removal was 8 days, which equates to a rate of bacteriuria of at least 40% on the time of catheter removal. There are two critical times for the development of infectious complications following prostatic surgery: the perioperative period and the time of catheter removal [3; 6]. The AUA guidelines recommend that 24 h of oral antibiotics (fluoroquinolones or TMP-SMX) on the time of urinary catheter removal if the patient has infection-related risk factors, and urinary tract surgery should be considered a risk factor for bacteremia [7]. However, there are few specific recommendations and studies concerning antibiotic prophylaxis at the time of catheter removal following LRP.

Several studies try to deciding if administration of antibiotic prophylaxis at catheter removal following radical prostatectomy is appropriate. In prospectively collected data, retrospective analysis study of prophylactic ciprofloxacin in LRP patients after catheter removal, urinary tract infection (UTI) was observed less frequently among patients receiving antibiotic therapy (ABT): 3.1 vs. 7.3% in those not receiving ABT (p=0.019). A number needed to treat to prevent 1 UTI is 24. Hospital readmission for febrile UTI was observed only in patients who did not receive ABT (n=5, 1.1 vs. 0%, p=0.16). One would need to prescribe ABT for 91 LRP patients to prevent 1 case of febrile UTI. They suggested that it is reasonable to treat LRP patients with antibiotics after catheter removal [8]. Jessica A and colleagues [9] prospectively examined urine culture results collected from 334 RP patients who received prophylactic antibiotics 1 day before, the day of, and for 5 days after catheter removal. They found out that 25% (83/334) had positive culture results, of which 7% were resistant to ciprofloxacin. They also suggested a high frequency of bacteriuria but low risk of clinical infectious complications using extended fluoroquinolone prophylaxis at catheter removal after RP.

However, in the present randomized prospective study, there was no significant difference in the bacteriuria rate at the time and 8 weeks later after catheter removal between the antibiotic prophylaxis and non-antibiotic groups (P=0.330, 0.385 respectivley). By contrast, antibiotic resistance occurred most frequently in the antibiotic prophylaxis group and was significant difference between the two groups (P=0.025). Fever is infrequently encountered after catheter removal following LRP, its treatment is usually up to the physician's discretion. Based on our experience, we suggest that fever greater then 38.5°C might be a reasonable ceriteria for administration of antibiotics. In case of the necessity of antibiotic therapy, repeat urine cultures for bacterial species and antimicrobial susceptibilities might seem rational. As we suppose, another concerning, that identified bacteriuria resulting in a peri-anastomotic inflammatory

response leads to anastomosis fibrosis, ischaemia and scarring, which may contribute to anastomotic stricture and would seem to favor antibiotic administration. Due to the growing number of resistant strains of bacteria, we feel that it is more reasonable to treat the patient with culture-specific antibiotic prophylaxis and careful monitoring [10; 11].

The presence of bacteriuria is relatively common of patients after LRP [8; 9]. As yet, however, few investigations have been done the change of urine leukocyte counts after LRP. In several studies of leukocyturia after transurethral resection of the prostate (TURP), a high concentration of leukocytes in urine samples were present on removal of the catheter and 1 week after operation, but at 4 weeks postoperatively, the mean leukocyte counts in urine had become less than before. They presumed that the leukocyturia was probably associated with exudation of infammatory cells of the surgical wounds, but leukocyturia cannot refect the possibility of postoperative bacteriuria [12; 13]. As urinalysis is one of the most common diagnostic screening tests in clinical practice, and urine culture results are available not before 24 h after collection, an antibacterial drug is usually empirically prescribed after urinalysis but before the urine culture results are known [4]. In present study, urine leukocyte counts were highest on the time of catheter removal and decreased gradually thereafter. Postoperative changes in the urine leukocyte counts between the two groups by two-factor repeated measure ANOVA show that the time effect was significant, but not the effect of antibacterial drugs.

Several limitations of our study warrant mention. First of all, our study population was relatively small. Additionally, in our institution, a seven day treatment with orally taken quinolones is the first-line treatment, and the length of antibacterial administration is arbitrary. Another possible confounding factor is the time to catheter removal, our populations tended to have longer time to catheter removal than patients in western country studies [14]. It is possible that early removal of the catheter is reduce the risk of bacterial ascension. Finally, we did not treat our control group patient with placebo, as the results of urinalysis and urinary culture are unlikely to be affected by blinding the patients.

Conclusion

Notwithstanding the limitations, our results suggest that the risk of bacteriuria and luekocyturia after catheter removal following LRP is real, which should be safely managed with culture-specific antibiotic prophylaxis and careful monitoring. There is no detectable significant benefit in using antibiotic prophylaxis to reduce the urine leukocyte counts after LRP.

REFERENCES

1. Sedor J, Mulholland SG. Hospital-acquired urinary tract infections associated with the indwelling catheter. Urol Clin North Am 1999;26:821-8.

2. Wazait HD, Patel HR, van der Meulen JH, Ghei M, Al-Buheissi S, Kelsey M, Miller RA, Emberton M: A pilot randomized double blind placebo-controlled trial on the use of antibiotics on urinary catheter removal to reduce the rate of urinary tract infection: the pitfalls of ciprof loxacin. BJU Int 2004; 94:1048-1050.

3. Wazait HD, van der Meullen J, Patel HR, Brown CT, Gadgil S, Miller RA, Kelsey MC, Emberton M: Antibiotics on urethral catheter withdrawal: a hit-and-miss affair. J Hosp Infect 2004;58:297-302.

4. Grude N, Tveten Y, Jenkins A, Kristiansen BE. Uncomplicated urinary tract infections: Bacterial findings and efficacy of empirical antibacterial treatment. Scand J Prim Health Care. 2005 Jun;23(2):115-9.

5. Gao X, Pu XY, Si-Tu J, Huang WT. Single-centre study comparing standard apical dissection with a modified technique to facilitate vesicourethral anastomosis during laparoscopic radical prostatectomy. Asian J Androl. 2011 May;13(3):494-8. Epub 2011 Feb 7.

6. Tenke P, Kovacs B, Bjerklund Johansen TE, et al. European and Asian guidelines on management and prevention of catheter-associated urinary tract infections.Int J Antimicrob Agents. 2008 Feb 31;Suppl 1:S68-78.

7. Wolf JS Jr, Bennett CJ, Dmochowski RR, Hollenbeck BK, Pearle MS, Schaeffer AJ. Urologic Surgery Antimicrobial Prophylaxis Best Practice Policy Panel: Best practice policy statement on urologic surgery antimicrobial prophylaxis. J Urol 2008;179: 1379-1390.

8. Rodrigo Pinochet, Lucas Nogueira, Angel M. Cronin. Role of Short-Term Antibiotic Therapy at the Moment of Catheter Removal after Laparoscopic Radical Prostatectomy. Urol Int 2010;85:415-420.

9. Banks JA., McGuire BB., Loeb S. et al. Bacteriuria and antibiotic resistance in catheter urine specimens following radical prostatectomy. Jan 25. Urol Oncol. 2012 Jan 25. [Epub ahead of print]

10. Bakken JS: The f luoroquinolones: How long will their utility last? Scand J Infect Dis 2004;36:85-92.

11. Ljuca S, Zvizdic S, Hamzic S, Kalajdzija M, Ljuca A. Antimicrobial susceptibility of bacteria isolated from inpatients and outpatients urine samples. Med Arh. 2010;64(3):161-4.

12. Huang X, Shi HB, Wang XH, Zhang XJ, Chen B, Men XW, Yu ZY. Bacteriuria after bipolar transurethral resection of the prostate: risk factors and correlation with leukocyturia. Urology 2011 May;77(5):1183-7.

13. Mustafaev EM, Martov AG, Naumov AG, et al. The role of ozone therapy in prevention of pyoinflammatory complications after transurethralresection of prostatic adenoma. Urologiia 2007;Jan-Feb;(1):18-23, 27.

14. Koch Mo, Nayee AH, Sloan J, et al. Earyl catheter removal after radical retropubic prostatectomy: long-term follow up. J Urol 2003;Jun;169(6): 2170-2172.

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OUR EXPERIENCE OF COLORECTAL CANCER LAPAROSCOPIC TREATMENT

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НАШ ОПЫТ ЛАПАРОСКОПИЧЕСКОГО ЛЕЧЕНИЯ КОЛОРЕКТАЛЬНОГО РАКА
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В статье приведен опыт использования лапароскопических методов хирургического лечения колоректального рака у 30 пациентов. Проанализировано состояние онкологических больных по стадиям заболевания, локализации опухолей и методикам оперативных вмешательств. Доказано, что при колоректальном раке лапароскопические операции являются альтернативой традиционным хирургическим вмешательствам и могут быть выполнены в адекватном объеме.
Ключевые слова: онкология, колоректальный рак, лапароскопические технологии.

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OUR EXPERIENCE OF COLORECTAL CANCER LAPAROSCOPIC TREATMENT
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Introduction. Laparoscopic technology for colorectal cancer allows the surgeon to use new, more sophisticated methods of operation. At the same time one often have to prove the need for laparoscopic technologies or their combination with conventional surgical techniques in a single transaction.

Objective. To share our experience with laparoscopic techniques for surgical treatment of CRC.

Materials and methods. Since 2011 30 patients with tumors of colon and rectum have been operated by laparoscopic technology. Among them women — 11, men — 19. Age of cancer patients ranged from 32 to 68 and averaged (59.0±8.7) years ($p<0.05$), dominated in elderly people: 14 patients were over 60 years.

Results. We have used these techniques of laparoscopic surgery: radical: right side hemocolectomy — 7 patients (23.3%) by high performance right-perianal incision, followed by withdrawal of the drug mobilized and further resection of the right half of colon tumor formation and ileotransversoanastomosis bifariamous hand stitch indulgent vicryl threads.

Discussion. For adequate laparoscopic operation on the large colon and rectum cancer (provided technical operability) one must consider compliance with these basic principles. Regardless of stage of disease and the nature of tumor growth it was carried out: a full selection of great vessels with displacement of tissue from lymph nodes in the direction of the drug, tissue above the lymph collectors isolated individual sections for separation of lymphatic vessels and interrupt tract metastasis; necessarily performed lymphadenectomy (aorto-femoral).

Conclusions. Favorable results of laparoscopic operations for colorectal cancer are associated with low traumatic interventions. Laparoscopic colorectal cancer surgery is an alternative to traditional operations and can be made in adequate volume. Laparoscopic intervention in colorectal cancer patients reduce length of stay in hospital and in the manual mode of formation of anastomosis — are more economically feasible.
Key words: oncology, colorectal cancer, laparoscopic technologies.

Introduction

Colon cancer and rectal tumor are real scourges of modern industrialized countries. Among older people in some cases it falls to the second place of cancer patients.

The concept of colorectal cancer (CRC) in modern medicine brings together different in form and structure, and localization of malignant epithelial tumors of the intestine and, in fact, the anal canal. It is equally related tumors of the colon ("colon") and tumors of the rectum ("rectum"), and the most malignant in their course are adenocarcinoma of the colon and sigmoid colon adenocarcinoma.

Ukraine has registered an average prevalence of CRC, which is 36.5 new cases per 100 thousand population annually. CRC is the second by prevailence malignant tumor in men (after bronchopulmonary cancer) and the third in women (after bronchopulmonary cancer and tumors of the breast). Every year in Ukraine 15–17 thousand new cases of CRC and about 8 thousand people die. CRC is revealed frequently in the later stages — frequency of detection of 3–4th stage is 70% of all cases [1].

Surgical treatment of diseases of the colon is one of the most difficult problems of Coloproctology. Improvement of methods of surgical treatment of colon cancer associated with a wide laparotomy does not reduce the frequency of postoperative complications, which sometimes reaches 20% [2–4]. The risk of wound and intra-postoperative complications with equal probability limits of radical surgery

in frail and elderly patients, which significantly affects the immediate results of treatment, often leading to disability. Therefore, the use of laparoscopic surgery for CRC can significantly reduce the incidence of postoperative complications, and injury and improve operating results of treatment. Rapid introduction of revolutionary technologies in laparoscopic surgery over the past decade has greatly enhance the classical surgery in the treatment of colorectal cancer. Now it is not questioned advisability of different kinds of sphincter-preserving surgery. Laparoscopic technology for colorectal cancer allows the surgeon to use new, more sophisticated methods of operation. At the same time we often have to prove the need for laparoscopic technologies or their combination with conventional surgical techniques in a single transaction [5–8].

Objective. To share our experience with laparoscopic techniques for surgical treatment of CRC.

Materials and Methods

Since 2011, 30 patients with colon and rectum tumors were operated with laparoscopic technology: women — 11, men — 19. Cancer patients age ranged from 32 to 68 and averaged (59.0±8.7) years ($p<0.05$), dominated in aged and elderly patients: 14 patients over 60 years. Among operated patients are men — 63.3%.

Tumor localized in the blind and ascending colon — in 7 (23.3%) cases, in the sigmoid — 11 (36.6%) and in the rectum — 12 (40%) cases.

Distribution of patients according to stage of disease was responsible pathohistological classification of TNM, developed by the International Committee Anticancer Association in 1997 (Table 1).

The predominance of patients with II stage of CRC is associated with targeted screening the patients to prevent complications in stages of initial set of operational experience.

Patients with IV stage of disease were performed to palliative operation in order to eliminate effects of intestinal obstruction.

Preoperative evaluation of patients was carried out by standard methods using endoscopic study of gastric and colon irrigoscopy, ultrasound or CT studies of the abdomen, X-ray examination of the chest, and generally accepted clinical and laboratory blood and urine.

Results

We have used the following techniques of laparoscopic surgery. Radical: right side hemocolectomy — 7 (23.3%) patients by high performance right-perianal incision, followed by withdrawal of the drug mobilized and further resection of the right half of colon tumor formation and ileotransversoanastomosis bifariamous hand stitch indulgent vicryl threads.

There have been performed 7 (23.3%) sigmoid colon resections by execution of left-oblique incision in the left iliac region and 7 (23.3%) laparoscopic anterior resection of the rectum. It was used a circular suturing device Ethicon Endosurgery CDH-29.

The transition from laparoscopic to open surgery option (conversion) was performed in 2 (6.6%) cases, the reasons were large tumor size, tumor went out the limits of the colon wall. The operation was completed by traditional laparotomic access.

7 patients with IV stage of CRC with metastatic lesions of the liver or peritoneal carcinomatosis with symptoms of chronic intestinal obstruction were operated. All patients were with tumors localized in the left half, or rectum. This contingent was performed colostomy formation of additional metastases biopsy liver (3–10%) and peritoneum (2–6.6%).

Due to a relatively short period of observation, we did not have laparoscopic surgery for cancer of the transverse colon and descending colon.

Discussion

For adequate laparoscopic operation on the large colon and rectum cancer (provided technical operability) must consider compliance with these basic principles. Regardless of stage of disease and the nature of tumor growth it was carried out: a full selection of great vessels with displacement of tissue from lymph nodes in the direction of the specimen, tissue above the lymph collectors isolated individual sections for separation of lymphatic vessels and interrupt metastasis way; necessarily performed lymphadenectomy (aorto-femoral).

Duration of surgery was (187.0±5.2) min, intraoperative blood loss — (150±10) ml.

Restoration of peristalsis after laparoscopic surgery occurred in 2.1 days, independent stool appeared to 3–4-day of the postoperative period. At the same time need in analgesics significantly decreased, some patients began to walk in a day after surgery.

Observations have shown that laparoscopic surgery half reduces the stay of patients in hospital, the average duration of treatment was (6.1±1.3) days.

Complications and deaths after laparoscopic surgery are not observed.

Conclusions

1. Favorable results of laparoscopic operations for colorectal cancer are associated with low traumatic interventions.

Table 1

Distribution of Patients According to Disease Stage, abs.

Stage	Men	Women
1. $T_{1-2,}$ N_0M_0	8	5
2. $T_{3-4,}$ N_0M_0	4	3
3. $T_{1-4,}$ N_1M_0	2	1
4. $T_{1-4,}$ N_xM_1	5	2
Total	19	11

2. Laparoscopy in colorectal cancer surgery is an alternative to traditional operations and can be made in adequate volume.

3. Laparoscopic intervention in colorectal cancer patients reduce length of stay in hospital and in the manual mode of anastomosis formation are more expedient economically.

REFERENCES

1. *Просоленко К. А.* Адекватная курация пациентов с толстокишечными полипами — эффективная профилактика колоректального рака / К. А. Просоленко, В. Б. Жукова // Здоров'я України. – 2006. – № 21/1. – С. 23–24.

2. *Аксель Е. М.* Злокачественные новообразования желудочно-кишечного тракта: основные статистические показатели и тенденции / Е. М. Аксель, М. И. Давыдов, Т. И. Ушакова // Современная онкология. – 2001. – Т. 3, № 4. – С. 141–145.

3. *Барсуков Ю. А.* Современные возможности лечения колоректального рака / Ю. А. Барсуков, В. И. Кныш // Современная онкология. – 2006. – Т. 8, № 2. – С. 7–16.

4. *Колоректальный* рак и предопухолевая патология: новые методики эндоскопической диагностики и требования к подготовке толстой кишки [Электронный ресурс] / Б. К. Поддубный, С. В. Кашин, Я. В. Политов, Р. О. Куваев. – Режим доступа : http://www.eurolab.ua/encyclopedia/565/46054/.

5. *Uraoka T.* What are the latest developments in colorectal endoscopic submucosal dissection? / T. Uraoka, Y. Saito, N. Yahagi // World J Gastrointest Endosc. – 2012. – Vol. 4 (7). – P. 296–300.

6. *Secondary* prevention of colorectal cancer — The roles of endoscopy for early detection and treatment / T. Matsuda, M. Sekiguchi, T. Sakamoto [et al.] // Nihon Shokakibyo Gakkai Zasshi. – 2012. – Vol. 109, N 7. – P. 1156–1165.

7. *Hitchins C. R.* Clinical outcome of laparoscopic and open colectomy for right colonic carcinoma / C. R. Hitchins, J. P. Trickett, H. J. Scott // Ann. R. Coll. Surg. Engl. – 2012. – Vol. 94 (4). – P. 288.

8. *Colorectal-cancer* incidence and mortality with screening flexible sigmoidoscopy / R. E. Schoen, P. F. Pinsky, J. L. Weissfeld [et al.] // N. Engl. J. Med. – 2012. – Vol. 366 (25). – P. 2345–2357.

REFERENCES

1. Prosolenko KA, Zhukova VB. Adequate Supervision of patients with colonic polyps — effective prevention of colorectal cancer Zdorov'ja Ukraïni 2006;21/1;23-24.

2. Aksel' EM, Davydov MI, Ushakova TI. Malignant tumors of the gastrointestinal tract;basic statistics and trends Sovremennaja onkologija 2001;3 (4);141-145.

3. Barsukov JuA, Knysh VI. Modern treatment options for colorectal cancer Sovremennaja onkologija 2006;8 (2); 7-16.

4. Poddubnyj BK, Kashin SV, Politov JaV, Kuvaev RO Colorectal cancer and precancerous pathology;new methods of endoscopic diagnosis and training requirements of the colon [Jelektronnyj resurs]. Rezhim dostupa;http://www.eurolab.ua/encyclopedia/565/46054/.

5. Uraoka T, Saito Y, Yahagi N. What are the latest developments in colorectal endoscopic submucosal dissection? World J Gastrointest Endosc 2012;4 (7);296-300.

6. Matsuda T, Sekiguchi M, Sakamoto T, Nakajima T, Saito Y, Sano Y, Fujii T. Nihon Shokakibyo Gakkai Zasshi 2012;109 (7);1156-1165.

7. Hitchins CR, Trickett JP, Scott HJ Clinical outcome of laparoscopic and open colectomy for right colonic carcinoma Ann R Coll Surg Engl 2012;94 (4);288.

8. Schoen RE, Pinsky PF, Weissfeld JL, Yokochi LA, Church T, Laiyemo AO, Bresalier R, Andriole GL, Buys SS, Crawford ED, Fouad MN, Isaacs C, Johnson CC, Reding DJ, O'Brien B, Carrick DM, Wright P, Riley TL, Purdue MP, Izmirlian G, Kramer BS, Miller AB, Gohagan JK, Prorok PC, Berg CD; PLCO Project Team Colorectal-cancer incidence and mortality with screening flexible sigmoidoscopy N Engl J Med 2012;366 (25);2345-2357.

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COMPARATIVE CHARACTERISTICS OF THE EFFECTIVENESS OF VARIOUS METHODS OF SURGICAL AND CONSERVATIVE TREATMENT OF ECTOPIC PREGNANCY

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СРАВНИТЕЛЬНАЯ ХАРАКТЕРИСТИКА ЭФФЕКТИВНОСТИ РАЗЛИЧНЫХ МЕТОДОВ ОПЕРАТИВНОГО И КОНСЕРВАТИВНОГО ЛЕЧЕНИЯ ВНЕМАТОЧНОЙ БЕРЕМЕННОСТИ

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Изучены 166 историй болезней пациентов с внематочной беременностью. Исследована эффективность различных методов оперативного и консервативного лечения внематочной беременности. Полученные результаты убедительно свидетельствуют о преимуществе применения по показаниям лапароскопического доступа при лечении нарушенной трубной беременности, что позволяет рекомендовать его как метод выбора. Метод консервативного лечения прогрессирующей трубной беременности с использованием метотрексата позволяет сохранить анатомическую и функциональную целостность маточной трубы в 72,5 % случаев.

Ключевые слова: внематочная беременность, метотрексат, консервативное и оперативное лечение.

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COMPARATIVE CHARACTERISTICS OF THE EFFECTIVENESS OF VARIOUS METHODS OF SURGICAL AND CONSERVATIVE TREATMENT OF ECTOPIC PREGNANCY

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166 patient records with an ectopic pregnancy were studied. The effectiveness of different operative and conservative methods of ectopic pregnancy treatment was investigated. These results clearly demonstrate the superiority of laparoscopic access by indications in ectopic pregnancy treatment, which can be recommended as a choice method.

Method of conservative treatment of advanced tubal pregnancy with methotrexate preserves the anatomical and functional integrity of the uterine tube in 72.5% of cases.

Key words: ectopic pregnancy, methotrexate, conservative and operative treatment.

Ectopic pregnancy is characterized by abnormal implantation of fertilized egg outside the uterus. The name “ectopic pregnancy” came from the Greek words “inappropriate”, “not in place”.

The studied pathology still remains valid. From 6 to 10% of women patients enter the gynaecological hospital with a diagnosis of “suspected ectopic pregnancy”. This pathology is one of a major cause of intra-abdominal bleeding; every 4th or 5th woman patient has repeated ectopic pregnancy every 5th or 6th woman — adhesive process in the pelvis and abdominal cavity in 75% of women after salpingectomy because of ectopic pregnancy secondary infertility develops.

Despite of significant achievements in modern gynaecology, which help to improve diagnosis and timely treatment, ectopic pregnancy continues to be one of severe pathologies. There is no single conception of examination and treatment of the patients with suspected ectopic pregnancy. The reason for ectopic pregnancy is multi-factorial, because of which the implanted fertile egg develops outside the uterus.

Pathological localization of the fertilized egg and its development cause intensive blood supply at the implantation place. Only the uterus during the growing of the fertilized egg is designated to ensure optimal life activity of the fetus. With the progression of ectopic pregnancy there arises a risk of rupture of the fallopian tube, massive bleeding, which sometimes leads to the woman’s death.

According to various authors, ectopic pregnancy is one of the leading causes of death related to pregnancy during the first trimester and is 0.2–0.11%. According to the ICD-10 classification there are distinguished the following kinds of ectopic pregnancy by the course, i.e. progressive and impaired (by type of tubal abortion, rupture of the uterine tube).

The aim of our study is to evaluate the effectiveness of different methods of operative and conservative therapy by ectopic pregnancy.

Materials and Methods

We conducted a retrospective study of 224 treatment results of the patients with ectopic pregnancy during the period from 2009 to 2011 in the gynaecological department of Ternopil City Hospital N 2. The share of the operative therapy because of ectopic pregnancy for the last 3 years amounts to (16.5+0.5)%.

The most frequent localization of ectopic pregnancy is fallopian tubes (95–98%).

For the analyzed period 166 women had operative therapy. 58 patients were treated conservatively (methotrexate).

All the examined women patients, depending on the method of treatment, were divided into 3 groups.

The group I included 114 (50.4%) of the patients, who underwent operative therapy with laparotomic approach. Laparotomy was performed in all cases, when the volume of blood loss exceeded 400.0–800.0 ml. In these situations, this method was optimal because of the widest possible access into the abdominal cavity to the source of bleeding and reduction of preparation time for the surgery. The average age of women was (26.24±3.12) years. The group II included 52 (23.0%) of the patients, who underwent operative therapy with laparoscopic approach. The average age of the patients in this group was (24.76±1.26) years. Laparoscopic treatment of tubal pregnancy was conducted with absence of contraindications: severe condition of the woman patient because of hemorrhagic shock, adhesive process in the abdominal cavity, size of fertilized eggs up to 3.5 cm and interstitial pregnancy. The group III included 58 (25.6%) of the patients who were undergone conservative therapy with methotrexate under the order of the Ministry of Health of Ukraine N 676 of 31.12.2004. The average age of women in this group was (23.24±3.12) years.

Both methods of operative therapy of compromised tubal pregnancy consisted in unilateral salpingectomy, which made 69.8% of the total number of surgeries, and in 30.2% of cases organ preserving surgeries on the tube, where the fertilized egg was implanted, were performed.

Performing organ preserving surgery in ectopic pregnancy is accompanied by risk of postoperative persistence of tropho-

blast as a result of its incomplete removal from the fallopian tube and abdominal cavity. The most effective method of preventing this complication was careful toilet of the abdomen cavity with 2–3 l of physiological saline and a single dose of methotrexate of 75–100 mg IM during the first or the second day after surgery.

Methotrexate is a folic acid antagonist that inhibits trophoblast cells proliferation.

Pharmaceutical treatment with methotrexate was used by the women patients with stable hemodynamics and clinic of "acute abdomen" absence by the uterine tube diameter less than 3 cm, chronic gonadotropine levels less than 5000 mIU/ml, absence of the signs of compromised ectopic pregnancy, possibility of echographic and laboratory (chorionic gonadotropine level) control, absence of pathological changes of hematological parameters.

Methotrexate was administered 75–100 mg i/m, after methotrexate there was monitored administration level of β-chorionic gonadotropine, which was stopped by concentrations achievement of 15 mIU/ml, what was observed, on the average, in a month. A characteristic feature was concentration increase of β-chorionic gonadotropine level during the first days after injection of methotrexate, due to destruction of trophoblast cells and admission of chorionic gonadotropine into blood in larger quantities. During the 4th–5th day the level of β-chorionic gonadotropine reached its maximum and then began to decline and achieved the initial line at the 7th–8th day. Mandatory determination of β-chorionic gonadotropine was conducted at the 4th and the 7th days after the methotrexate injection. If the concentration of β-chorionic gonadotropine as at the 7th days was less than the initial or decreased by more than 15% of the maximum concentration (as at the 4th day), weekly control of β-chorionic gonadotropine was still held until "negative" results achievement, i.e. < 15 mIU/ml. If the concentration of β-chorionic gonadotropine at the 7th day was higher than the initial or decreased to less than 15% of the maximum concentration, repeated administration of methotrexate was carried out.

Side effects of methotrexate are associated with depression of bone and cerebral blood formation, toxic effects on the mucous membranes, liver and lungs. During ectopic pregnancy therapy with methotrexate, complications are extremely rare and are nearly absent after a single dose. The probability of their occurrence may be increased by presence of serious pathology of the internal organs, which is to be taken into account while determining the therapy method in such patients. Absolute contraindications for methotrexate were anemia, leukopenia, thrombocytopenia (< 100 thousand/mole), renal and liver failure; acute infectious diseases that cause immunoinhibition, AIDS; gastric ulcer and duodenal ulcer, ulcerative colitis. In addition, during treatment with methotrexate one should refuse medications that increase its side effects. These medications include aspirin, nonsteroidal anti-inflammatory drugs, sulfonamides, tetracycline, laevomycetin, aminobenzoic acid.

Treatment Results and Their Discussion

The results showed that during surgery intraperitoneal bleeding 501.0–700.0 ml was mostly often found (43.6±2.2)% of cases. In (42.9±4.2)% of cases the volume of intraperitoneal bleeding was less than 500.0 ml, and massive bleeding was registered only in (13.7±2.2)% of cases. Restoration of blood volume was performed using macromolecular plasma succenturiate solutions and fresh frozen plasma for blood loss of more than 900.0–1000.0 ml (Table 1).

Evaluating the effectiveness of treatment with laparoscopic access (20 patients) was conducted in comparison with the group of women (20 patients) who underwent laparotomy. The main criterion for selection of the patients in the studied groups were volume of blood loss up to 500.0–600.0 ml to unify its impact on the severity of the woman health condition and postoperative period. Compared with the patients who underwent laparotomy, significant reduction of duration of laparoscopic surgeries by 32.9% ($p<0.05$), reduction of analgesics usage term in the postoperative period 2.7 times ($p<0.05$) and reduction of bed rest period by 12–14 hours were determined, subfebrility was rarely recorded ($p<0.05$). The results clearly show the advantage of applying laparoscopic access by indications in treatment of tu-

Table 1

Long-term Results of Ectopic Pregnancy Treatment

Method of surgery	Groups of patients		
	Laparotomic access	Laparoscopic access	Conservative treatment
Total	35 (52.7%)	19 (30.9%)	15 (27.2%) Operative therapy 7 (45%)
Tubectomy	34 (95.1%)	12 (62.4%)	4 (34.7%)
Reconstructive and plastic surgeries	1 (5.7%)	9 (48.5%)	3 (25.7%)

bal pregnancy, and can be recommended as a method of choice.

According to the literature data, the long-term results of ectopic pregnancy treatment cannot be considered as favourable.

Study of cases of organs preserving surgery with ectopic pregnancy showed that following uterine pregnancy occured in 54% and repeated ectopic one — in 13% of women; 25–35% of women were infertile.

According to the literature, the fallopian tubes after use of methotrexate remain passable in 71–81% of women.

This scope of statistics depends on the clinical course of ectopic pregnancy (the nature of the damaged uterus or elsewhere and the stage of blood loss), the volume and technique of surgical treatment, the completeness and duration of rehabilitation in the postoperative period.

Conclusions

The proposed therapy scheme results showed advantages of surgical laparoscopy versus laparotomy with ectopic pregnancy, what was reflected in the maximal visualization of the pelvic organs with minimal access, reduction surgery duration ($p<0.05$), early mobilization of women ($p<0.05$), small septic risk, insignificant use of medications and lower economic cost for treatment by 1.4 times, reduction of scar changes at the anterior abdominal wall, better cosmetic effect.

The method of conservative treatment of progressive tubal pregnancy with methotrexate IM by the scheme provides effective resorption of the fertilized egg with the small side effects; helps preserve anatomical and functional integrity of the fallopian tubes by 72.5% of cases.

REFERENCES

1. *Гуриев Т. Д.* Внематочная беременность / Т. Д. Гуриев, И. С. Сидорова. – М. : Практическая гинекология, 2007. – 96 с.

2. *Клинические* лекции по акушерству и гинекологии / под ред. А. Н. Стрижакова, А. И. Давыдова, Л. Д. Белоцерковской. – М. : Медицина, 2000. – 379 с.

3. *Краснопольский В. И.* Репродуктивные проблемы оперированной матки / В. И. Краснопольский, Л. С. Логутова, С. Н. Буянова. – М. : Миклош, 2006.

4. *Кулаков В. И.* Оперативная гинекология / В. И. Кулаков, Н. Д. Селезнева, В. И. Краснопольский. – Н. Новгород : НГМА, 1999. – 504 с.

5. *Маркін С. Б.* Позаматкова вагітність / С. Б. Маркін, О. О. Матвієнко, С. А. Маркін. – Львів, 1999. – 106 с.

6. *Внематочная* беременность / А. Н. Стрижаков, А. И. Давыдов, М. Н. Шахламова, Л. Д. Белоцерковская. – М. : Медицина, 1998. – 201 с.

REFERENCES

1. Guriyev TD, Sidorova IS Vnyematochnaya Beryemennost. M. Prakticheskaya Ginekologiya 2007:96.

2. Klinicheskiye Lektsiyi po Akusherstvu & Ginekologii // Pod red Strizhakov AN, Davydov AI, Byelotserkovskaya LD:M: Medicina, 2000: 379.

3. Krasnopolskyy VI, Lohutova LS, Buyanova SN Ryeproduktivnyye Problemy Opyerurovanoy Matki:Moscow: “Miklosh”;2006.

4. Kulakov VI, Seleznyova ND, Krasnopolsky VI Operative gynaecology. – N. Novgorod : NGMA, 1999. – 504 p.

5. Markin SB, Matviyenko OO, Markin SA Pozamatkova Vahitnist. Lviv 1999: 06.

6. Stryzhakov AN, Davydov AI, Shakhlamova MN, Byelotserkovskaya LD Vnyematochnaya Beryemennost M.: Medicina 1998:201.

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MANAGEMENT AND ENDOSURGICAL TREATMENT OF BENIGN OVARIAN CYSTIC FORMATIONS IN PREGNANCY

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ТАКТИКА ВЕДЕНИЯ И ЭНДОХИРУРГИЧЕСКОЕ ЛЕЧЕНИЕ ДОБРОКАЧЕСТВЕННЫХ КИСТОЗНЫХ ОБРАЗОВАНИЙ ЯИЧНИКОВ У БЕРЕМЕННЫХ

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В работе рассмотрены вопросы дифференциальной диагностики доброкачественных кистозных овариальных образований во время беременности, оценки показаний для оперативного вмешательства, разработки соответствующей тактики ведения и выбора хирургического доступа при выполнении вмешательств.

Крайне важно, чтобы акушер был специалистом в области диагностики и лечения овариальных образований во время беременности. Использование ультразвука для характеристики злокачественного потенциала овариальных образований дает возможность выбора нескольких вариантов ведения пациентки. Наблюдение осуществляется при бессимптомных, доброкачественных, без признаков злокачественности, образований, отмеченных на ультразвуковом изображении. Для пациенток с комплексными образованиями с риском озлокачествления может быть предложено до- и послеродовое наблюдение как приемлемый вариант.
Ключевые слова: беременность, доброкачественные кистозные образования яичников, тактика ведения, эндохирургическое лечение.

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MANAGEMENT AND ENDOSURGICAL TREATMENT OF BENIGN OVARIAN CYSTIC FORMATIONS IN PREGNANCY
The Scientific-Research Institute of Family Medical Problems of the Donetsk National Medical University named after M. Gorky, Ukraine
This paper gives an experience on the differential diagnosis of benign cystic ovarian structures during pregnancy, assessing the indications for surgery, development of management and choice of surgical approach in carrying out interventions.

Therefore important that obstetrician should be a specialist in the diagnosis and treatment of ovarian lesions during pregnancy. Using ultrasound to characterize the malignant potential of ovarian formations gives the patient the possibility of more options. Observation is a viable option for asymptomatic, benign formations with no signs of malignancy detected by US. For patients with complex formation with the risk of malignancy observation may also be offered to childbirth as a viable option.
Key words: pregnancy, benign ovarian cystic formation, management, endosurgical treatment.

Registered incidence of ovarian formations during pregnancy ranges from 1 in 81 to 1 in 8,000 pregnancies or from 1 in 76 to 1 in 2,328 births, but studies based on ultrasound detection of this pathology, showed a higher prevalence — from 1 case in 19 childbirths to 1 in 88 [1; 2].

Most ovarian formations are diagnosed by chance during the first trimester ultrasound screening (US) [3; 4; 6]. Ovarian formation remained in the second trimester of pregnancy are at risk of torsion, rupture, or obstruction in labor.

The question of differential diagnosis of ovarian formations during pregnancy, evaluation of indications for surgical intervention, the development of appropriate strategy managing ovarian formations during pregnancy is relevant.

Differential Diagnosis. Like in non-pregnant state, functional cysts are the most common ovarian formations of uterine appendages during pregnancy. Differential diagnosis during pregnancy should be made with the benign tumors, such as benign cystic teratoma (7–37% of cases), serous (5–28%) and mucinous (3–24%) cystadenoma, endometrioma (0,8–27%), paraovarian cysts (< 5%) and leiomyoma (1–2.5%) [2; 5]. Ovarian malignancy (including with low malignant potential) is approximately 1,8% of all ovarian formations during pregnancy [6; 7].

Diagnosis. Ovarian formation during pregnancy is asymptomatic in 65–80% of cases [1]. Most of them are diagnosed by chance during ultrasound screening in the first trimester [2], it is believed that between 50% and 80% of ovarian formations are detected in the first two trimesters of pregnancy [1]. If the tumor of the uterus is palpated on examination, ultrasound is the preferred method of radiological confirmation because of its ability to differentiate the morphology. This allows the stratification of risk without harm to the mother and fetus [8]. The ultimate goal of ultrasound evaluation is to assist to the doctor in a prior determination of the histological structure of formation, that determines the choice between conservative treatment and surgery.

Ultrasound is very accurate in determining tumors with the malignant potential. Ultrasound characteristic of the complexity and size of ovarian formations may help in predicting malignancy. Prognostic sign of malignancy is the presence of septa, solid structure, nodes, papillary components or average diameter larger than 5 cm. Thus, the higher complexity of formation — higher risk of malignancy.

Recent studies have assessed the usefulness of adding Doppler flow evaluation by gray scale ultrasonography to improve the sensitivity of prenatal diagnosis of malignant neoplasms. There is evidence that the 3D-Doppler investigation can help in stratification of complex ovarian formations.

Other terms of image processing such as computed tomography (CT) and magnetic resonance imaging (MRI) may be a useful addition when the ultrasound image does not give the required results. CT provides better access to identify nonobstetrical causes of abdominal pain. Although CT relatively safe during pregnancy, the mother and fetus received the absorbed dose of at least 2=4 rads during one investigation [8]. Contrast agents may pass the placental barrier and should be used with caution, because their action is not really known [3]. MRI is considered as generally safe during

pregnancy. There are two specific situations in which MRI is the method of choice. MRI better detect paraovarian cystic lesions, which can then be carried out conservatively during pregnancy [3]. MRI also can provide the best features of tissue allowing more accurate assessment of large formations that are difficult to fully visualize with ultrasound. MRI can also determine the degree of malignancy and possible help in the diagnosis of acute process of the gastrointestinal tract such as appendicitis and intestinal inflammation [3]. However, the purpose for MRI examinations during pregnancy should be reasonable and it should be used exclusively as an explanation for the results inconclusive ultrasound data.

Tumor markers should be used with caution in pregnant women due to big differences in results and interpretation of these tests during pregnancy. Level of CA-125 increases during pregnancy, especially in the first trimester [9], and its detection has a limited role. Levels of CA-125 is also elevated in other benign processes, such as uterine leiomyoma, endometriosis and others [6; 8]. Other tumor markers are useful for stratification of germ cell malignancy such as α-fetoprotein, β-human chorionic gonadotropin, lactatedehydrohenase, are of limited use because they can significantly change during pregnancy [2; 9].

The main value of determination of tumor markers during pregnancy lies in determining their levels as indicators of tumor control, but it should not be considered as a basis for therapeutic activity, especially in case of presence of asymptomatic ovarian formations.

Management. Currently, management of ovarian formations during pregnancy is arguable, some researchers recommend observation, others — surgery [2; 6; 7].

Most ovarian formations identified during pregnancy regress spontaneously, and surgury is not required. Characteristics favorable for observation are the following: simple cysts according to ultrasound, the diameter of structures smaller than 5–6 cm, the diagnosis established before 16 weeks of pregnancy [3]. The large size and complex structure with more complex morphology rarely regress spontaneously, may represent tumor process [10] and lead to complications during pregnancy: torsion (1–22%), rupture (0–9 %), labor obstruction (2–17%) [4; 6].

Surgical treatment is recommended when a persistent or large ovarian formation represents an increased risk of acute abdomen, secondary torsion or rupture [4; 6]. In addition, 10% of persistent complex ovarian formations will eventually be exhibited diagnosis of malignant tumors; the observation may worsen outcome [6; 10]. Finally, researchers that support the surgical treatment suggest a tendency to improve mother and fetus condition through the use of surgery in mid-pregnancy (12–27 weeks) [4; 7]. Finally, the decision about observation or surgical intervention should depend on individual patient's symptoms and the degree of malignancy probability.

Observation. The management mode of cystic ovarian formations during pregnancy is connected to the fact that 71% of them reduce in size or regress. Some of them with more complex structure self-regreses too [8; 9].

Consensus of Society of Radiologists for Ultrasound was published in 2010 and provides instructions for management of accidentally discovered by ultrasound asymptomatic ovarian lesions in nonpregnant women. The purpose of this project was to determine which ovarian formation did not require or needed further ultrasound follow up, or require surgery. This consensus proposed ultrasound criteria for further evaluation. Simple cysts (unechogenic, with smooth, thin wall, without membranes) size to 5–7 cm in premenopausal women or larger than 1 cm in postmenopausal women should be reviewed each year.

Hemorrhagic cysts more than 5 cm in size in premenopause should be reviewed in 6–12 weeks. Hemorrhagic cysts of any size in early menopause (within 1–5 years after the last menstrual period) should be reviewed in 6–12 weeks, however hemorrhagic cysts of any size in the late menopause (> 5 years since last menstrual period) require surgical treatment. Endometrioid cyst (homogeneous hypoechogenic formation) or dermoid cystoma (focal or diffuse hyperechogenic component) should be screened annually if not surgically removed at any age. Hydrosalpinx and peritoneal cysts should be reviewed if they have clinical manifistations. Cysts with thin membranes should be revised once in 6–12 weeks or, if they are stable, can be examined annually up to the menopause. However, surgical approach should be considered in postmenopausal women. Cystic formation containing nodules with blood flow or thick membrane (> 3 mm) obligatory require surgical treatment at any age. These recommendations are intended for non-pregnant women with accidental detection on ultrasound [7].

Thus, the observation is a viable option for ovarian formations with low complexity, detected by ultrasound [6].

Using transvaginal ultrasound for risk stratification and low probability of malignancy in pregnancy, you can use delay surgery even in complex formations in asymptomatic pregnant women.

Surgical approach. Traditionally, surgery on the ovarian formations during pregnancy were performed by laparotomy.

However, recently there are many opposing views about the role of laparoscopy in the surgical treatment of ovarian formations during pregnancy [4]. Supporters of laparotomy exhibit concerns about laparoscopy, including lack of data on the effects of pneumoperytoneum, the possibility of penetration of carbon dioxide into the uterus, damage of pregnant uterus by Veresh needle, trocar or surgical instruments, as well as the risk of fetal acidosis by maternal conversion of carbon dioxide to carbon dioxide [10].

On the other hand, supporters of laparoscopy emphasize on reducing postoperative pain, less use of narcotic analgesics, shorter hospital stay and less need for traction of the uterus, resulting in less irritation of the uterus during surgery. In addition, laparoscopy leads to faster physical recovery and return to normal activities, which is very important during pregnancy because of the phenomenon of hypercoagulation [7].

Currently there are no prospective studies that compare laparotomy and laparoscopic accesses to determine which approach is better. This is unlikely due to the limited number of pregnant patients who require surgery to remove ovarian formations [22]. However, several review studies have shown that laparoscopic removing of ovarian formations during pregnancy is technically feasible and should no longer be regarded as contraindicated in pregnancy [4; 5].

A large number of reports and observations in the world scientific literature have shown the benefits of laparoscopic surgery in relation to reducing pain, reducing hospital stay, earlier mobilisation, reducing blood loss, low levels of infection. All these provide advantages over traditional open laparotomy access.

Although data suggest a similar risk to the fetus during laparoscopic access, there are still disputes the impact of CO_2 by imposing pneumoperitoneum on the fetus. There are reports of more than 500 laparoscopic operations in pregnant patients [26]. From this literature, only one publication includes reports of adverse effects on the fetus compared with the expected at laparotomy [4].

When considering the surgery for ovarian formations during pregnancy surgeon should weigh both: the mother result and fetal condition during surgery. Pregnant women who had undergone surgery have increased general risk of preterm delivery (22%) compared with those without surgery, regardless of surgical access [8]. In addition, those who are needed urgent surgical intervention, such as in cases of rupture or torsion, usually have higher risk to the fetus compared with planned surgery [8]. However, other researchers have concluded that fetal condition probably related to the nature of underlying diseases, which leads to the necessity of surgical intervention rather than surgical intervention alone [4; 9].

Laparoscopic removal of ovarian lesions should be performed only by qualified surgeons in countries with advanced laparoscopy and the presence of gynecological oncology. The Society of American Gastrointestinal and Endoscopic Surgeons published the following recommendations for laparoscopy during pregnancy [8]:

— laparoscopy can be performed at any gestational age, but nonurgent cases should optimally be scheduled at 16–20 weeks. This recommendation is based on providing time for spontaneous regression of ovarian formations, optimizing visualization of ovarian structures with an increase of uterus size, and reducing the frequency of preterm birth associated with a greater term of pregnancy;

— patient should be placed on the left or right tilt to reduce compression on the vena cava and improving cardiac return;

— should be used intraoperative monitoring of CO_2 capnographia;

— there is no necessity for routine blood gas monitoring;

— open Hasson technique is the best way for initial laparoscopic access, because it offers the possibility of visual input, although the use of Veresh needle is not contraindicated. The surgeon may consider using Veresh needle in combination with ultrasound control;

— trocar should be placed at least 6 inches above uterine fundus or in the upper left quadrant;

— intraoperative intra-abdominal pressure must be maintained below 15 mm Hg at Trendelenburg position to ensure adequate venous return and utero-placental blood flow;

— currently no evidence for using tocolytics.

Personal experience. In department of endoscopic surgery of the Donetsk Regional Center of Mother and Child during the period from 2000 to 2011 there were operated 72 pregnant women with benign ovarian cystic formations. In 37 (51.39%) cases it was the first pregnancy, in 17 (23.61%) — the second, in 14 (19.44%) — the third, in 1 (1.39%) — the fourth, in 2 (2.78%) — fifth and in one (1.39%) — the tenth. The average time detection of ovarian cystic formations at pregnancy was (9.29±0.57) weeks of gestation. The size of formationsrange from 4 to 30 cm and at the time of operation was in average (10.94±0,70) cm. 68 (94.44%) women had a unilateral formation and 4 (5.56%) — bilateral. In 3 (4.17%) patients were observed rupture of cysts, in 14 (19.44%) — torsion.

In 58 (80.56%) surgery were performed through laparoscopic

access, in 14 (19.44%) — laparotomic. Laparotomy was rational with a high risk of injury of pregnant uterus, technical difficulties if laparoscopic surgery performed at gestational term more than 16 weeks of pregnancy, suspected malignancy. In 1 (1.39%) case was performed conversion from laparoscopy to laparotomy due to gestation 17–18 weeks and adhesive process in the pelvis around endometriosis cyst with size 8 × 8 cm.

When conducting laparoscopy surgery it was used the technique of applying four troacar ports and the use of bipolar current in cutting and coagulation mode. The average time of surgery was (35.4±8.5) min. All surgical interventions were without complications. Sutures were removed on the fifth-seventh day. All wounds were healed by primary intention.

Among operated were 9 (11.11%) women with mature cystic teratoma, 15 (20.83) — with mucinous cystadenoma, 30 (41.67%) — with serous cystadenoma, 3 (4.17%) — with persistent functional cysts, 7 (9,72%) — with endometrioid cysts, 3 (4.17%) — with paraovarian cysts, 2 (2.78%) — with cystadenocarcinoma.

Conclusions

Because of widespread use of prenatal ultrasound and aneuploidy screening detection of ovarian formations during pregnancy is becoming more common. It is therefore important that obstetrician should be a specialist in the diagnosis and treatment of ovarian lesions during pregnancy. Using ultrasound to characterize the malignant potential of ovarian formations gives the patient the possibility of more options. Observation is a viable option for asymptomatic, benign formations with no signs of malignancy detected by US. For patients with complex formation with the risk of malignancy observation may also be offered until childbirth as a viable option.

The decision on whether to postpone the surgical treatment of complex formation to delivery or after delivery should be based on the balance of risks and benefits: malignancy risk against unnecessary surgical risk for mother and fetus. Patients selected for observation should be informed about a possibility of torsion, rupture, need for surgery in late pregnancy and the potential delay in diagnosis of malignancy. They should also know that anteor prenatal surgery may be necessary if symptoms or formations change with time.

Those patients who need surgical treatment have no benefits for choosing a particular surgical approach. Laparoscopy and laparotomy have a similar risk of complications during pregnancy. Taking into account advantages that laparoscopy versus laparotomy in relation to pain, hospital stay, infection risk and recovery time, laparoscopic approach should be considered affordable in the presence of appropriate skills and training.

REFERENCES

1. Aggarwal P. Ovarian tumours in pregnancy: a literature review. P. Aggarwal, S. Kehoe. Eur. J. Obstet. Gynecol. Reprod. Biol. 2010;155:119-124.

2. Giuntoli R. Evaluation and management of adnexal masses during pregnancy. R. Giuntoli, R. Vang, R. Bristow. Clin. Obstet. Gynecol. 2006; 49:492-505.

3. Glanc P. Adnexal masses in pregnant patient: a diagnostic and management challenge. P. Glanc, S. Salem, D. Farine. Ultrasound Q. 2008;24:225-240.

4. Ko Ma-Lee. Laparoscopic management of complicated adnexal masses in the first trimester of pregnancy. Ma-Lee Ko, T. Lai and S. Chen. Fertil. Steril. 2009;92:283-287.

5. Laparoscopic management of ovarian cysts in pregnancy. [Y.Lenglet, H.Roman, B.Robishong et al.].Gynecol.Obstet.Fertil.- 2006.-Vol.34.-P.101-106.

6. Leiserowitz G. Managing ovarian masses during pregnancy. G. Leiserowitz. Obstet. Gynecol. Surv. 2006;61: 463-470.

7. Management of asymptomatic ovarian and other adnexal cysts imaged at US: Society of Radiologists in Ultrasound consensus conference statement. [D. Levine, D.L. Brown, R.F. Andreotti et al.]. Ultrasound Q. 2010; 26:121-131.

8. Predicting risk of malignancy in adnexal masses. [J.M. McDonald, S. Doran, C.P. DeSimone et al.]. Obstet. Gynecol. 2010;115:687-694.

9. Sarandakou A. Tumor markers in biological fluids associated with pregnancy. A. Sarandakou, E. Protonotariou, D. Rizos. Crit. Rev. Clin. Lab. Sci. 2007;44:151-178.

10. Whiteside J. Laparoscopic management of the ovarian mass: practical approach. J. Whiteside, H. Keup. Clin. Obstet. Gynecol. 2009;53:327-334.

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CURRENT APPROACHES TO DIAGNOSTICS AND TREATMENT OF OVARIAN APOPLEXY

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СОВРЕМЕННЫЕ ПОДХОДЫ В ДИАГНОСТИКЕ И ЛЕЧЕНИИ АПОПЛЕКСИИ ЯИЧНИКА
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Цель. Анализ оказания медицинской помощи женщинам с апоплексией яичника, определение основных клинических, лабораторных и ультразвуковых критериев, влияющих на выбор лечебной тактики, оценка ближайших и отдалённых результатов лечения яичниковых кровоизлияний.

Материалы и методы. Изучено оказание медицинской помощи 888 женщинам с апоплексией яичника. В зависимости от объема гемоперитонеума пациентки были разделены на три группы: I группа — 480 (54,0 %) пациенток, у которых объем гемоперитонеума не превышал 200 мл; II группа — 283 (31,8 %) женщин с внутрибрюшным кровотечением объемом от 200 до 500 мл; III группа — 125 (14,1 %) пациенток с объемом гемоперитонеума более 500 мл. В I группе 108 (40,0 %) пациенток после прекращения яичникового кровотечения и получения курса медикаментозной терапии были с диагностической и лечебной целью лапароскопически прооперированы в «холодном» периоде (I«К»Л^{x} подгруппа).

Результаты исследования. Средний возраст больных — (28,3±5,2) года. Ведущим клиническим симптомом у всех пациенток была тазовая боль. Интенсивная острая боль чаще встречалась у пациенток II и III групп (62,2 и 92,3 % соответственно). По данным трансвагинального УЗИ, выполненного в сагиттальной плоскости, наблюдалась линейная зависимость между уровнем свободной жидкости относительно матки и объемом гемоперитонеума ($r=0,63$, $P<0,05$). У пациенток при отсутствии спаечного процесса при яичниковых кровотечениях чаще наблюдался больший объём внутрибрюшного кровотечения, чем у пациенток с сопутствующим спаечным процессом. Так, средний объём гемоперитонеума, обнаруженного у пациенток с апоплексией яичника, при отсутствии спаечного процесса составил (273,5±21,3) мл, тогда как у пациенток с выраженным спаечным процессом органов малого таза он был (141,4±35,5) мл. Во время операции более чем у половины пациенток I«К»Л^{x} подгруппы наиболее частой интраоперационной находкой был спаечный процесс малого таза. Формирование персистирующего КГОЯ на фоне внешнего эндометриоза обнаружено у трети женщин этой подгруппы. Наибольшая частота рецидива АЯ, формирование КГОЯ и самый продолжительный срок субфертилитета наблюдались у женщин IК группы.

Выводы. Выраженность клинических симптомов при апоплексии яичника зависит от объема внутрибрюшного кровотечения. Анализ данных трансвагинальной эхографии позволяет с высокой степенью точности количественно определить объем интраабдоминального кровотечения и морфологическое состояние пораженного яичника. Лапароскопия является не только «золотым стандартом» в диагностике и лечении АЯ, но и способствует предупреждению яичниковых кровоизлияний в будущем.

Ключевые слова: гемоперитонеум, апоплексия яичника, лапароскопия.

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CURRENT APPROACHES TO DIAGNOSTICS AND TREATMENT OF OVARIAN APOPLEXY
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Objective. Analysis of rendering the medical aid to women with apoplexy of the ovary, determination of the basic clinical, laboratory and ultrasonic criteria which influence the choice of management, the evaluation of the immediate and long-term results of treatment of ovarian hemorrhages.

Materials and methods. There was studied medical aid to 888 women with ovarian apoplexy (OA) who referred to the gynecologic clinic of the Military Medical Clinical Center of the Southern region, in Odessa (Ukraine) from 2001 to 2009. Depending on the volume of hemoperitoneum the patients were divided into three groups: I group — 480 (54.0%) patients with hemoperitoneum under 200 ml; II group — 283 (31.8%) women with intraperitoneal hemorrhage with volume from 200 to 500 ml; III group — 125 (14.1%) patients with volume of hemoperitoneum over 500 ml. The group I consisted of IC group — 270 (30.4%) women who were given conservative treatment of OA, and IL group — 210 (23.6%) patients whose main diagnostic and treatment measure was laparoscopic intervention. In IC group 108 (40.0%) patients after controlling ovarian hemorrhage and obtaining the course of drug therapy were laparoscopically operated on with the diagnostic and therapeutic purpose in the “cold” period (I“C”L^{C} subgroup).

Results and discussion. The average age of the patients was 28.3±5.2. The pelvic pain was the leading clinical symptom in all patients. Intense acute pain was more frequently encountered in patients of II and III groups (62.2 and 92.3% respectively). According to the data of the transvaginal US made in the saggital plane, a linear dependence was observed between the level of free liquid and the volume of hemoperitoneum ($r=0.63$, $p<0.05$). In 792 (89.2%) patients the diagnosis of apoplexy of the ovary and intraperitoneal hemorrhage was made, and surgical intervention was indicated on the basis of clinical picture and US data. In the remaining cases — 92 (10.4%) diagnostic laparoscopy was required for confirming the diagnosis. The most frequently performed hemostatic operation was resection of the ovary — 477 (77.2%) interventions. The great volume of intraperitoneal hemorrhage was observed more frequently in the patients with ovarian hemorrhages in absence of the adhesive process, than in patients with the associated adhesive process. Thus, the average volume of hemoperitoneum discovered in patients with AO, in absence of the adhesive process was (273.5± ±21.3) ml, whereas in patients with the pronounced adhesive process of the small pelvis organs it was (141.4±35.5) ml. The cause of AO was the corpus luteum or cyst of the corpus luteum in more than the half of the cases — 348 (56.3%). The most frequent intraoperative finding in more than a half of patients of I"C"L^X subgroup during the operation was an adhesive process in the small pelvis. The formation of persisting CHFO against a background of external endometriosis is found in one third women of this subgroup. The greatest frequency of AO relapse, formation of CHFO and the most prolonged period of subfertility were observed in the women of I"C"L^C subgroup.

Conclusions. The manifestation of the clinical symptoms in apoplexy of the ovaries depends on the volume of intraperitoneal hemorrhage. The data analysis of transvaginal echography allows to determine quantitatively, with a high degree of accuracy the volume of intraabdominal hemorrhage and the morphological state of the affected ovary. Laparoscopy is not only a "gold standard" in diagnosis and treatment of AO, but also contributes to the prevention of ovarian hemorrhages in future. The application of laparoscopy as a main therapeutic and prophylactic method in AO allows to preserve, and sometimes to restore the reproductive function of a woman and to reduce the rate of the disease relapse development.

Key words: hemoperitoneum, ovarian apoplexy, laparoscopy.

Introduction

The pathologic states which require rendering emergency aid, take a special place in the structure of gynecological diseases. More than half of urgent gynecological operations are performed for acute gynecological pathology, complicated by intraperitoneal hemorrhage [1; 2]. Apoplexy of the ovary (AO) occupies the second place among the causes of intraperitoneal hemorrhages in the work of the gynecological hospital, giving place only to the disturbed ectopic pregnancy [3]. Videoendoscopic technologies have been "the gold standard" of diagnosis and treatment of the practically entire urgent gynecological pathology, including apoplexy of the ovary already for a period of several decades [2; 5; 6]. In the individual clinical cases the sudden pathologic rupture of the ovarian tissue is not accompanied by extensional hemoperitoneum, and hemorrhage neither exceeds the limits of the ovarian capsule nor is accompanied by minimum intraabdominal hemorrhage. Patients with the localized intraovarian hemorrhage or insignificant intraperitoneal hemorrhage, which is controlled, in presence of the moderate pain syndrome, require conservative treatment [7; 8].

Objective. Analysis of rendering aid to women with apoplexy of the ovary, determination of the basic clinical, laboratory and ultrasonic criteria, which influenced the choice of therapeutic tactics, evaluation of the immediate and long-term results of treatment of ovarian hemorrhages.

Materials and Methods

To achieve this aim we have analyzed aid to 888 women with AO, who had referred to the clinic of gynecology of the Military Medical Clinical Center of the Southern region of Odessa within last 8 years. All patients were divided into three basic groups depending on the volume of hemoperitoneum, revealed intraoperatively or established by noninvasive methods of examination. I group was composed of 480 (54.0%) patients whose volume of hemoperitoneum did not exceed 200 ml and it was considered as minimum; II group consisted of 283 (31.8%) women with moderate intraperitoneal hemorrhage ranged from 200 to 500 ml; III group was formed by 125 (14.1%) patients whose amount of blood in the abdomen exceeded 500 ml, we considered this hemorrhage as significant. The main group I consisted of IC group (treated conservatively) — 270 (30.4%) women whose attack of ovarian apoplexy was treated by drugs; and IL group (treated laparoscopically) — 210 (23.6%) patients whose main diagnostic and treating measure was laparoscopic intervention. Of the women who were subject to conservative therapy, 105 (38.8%) patients were given out-patient treatment; 108 (40.0%) patients of IC group after cessation of ovarian hemorrhage and obtaining the course of drug therapy during the period from 1 to 7 weeks were operated on laparoscopically for the diagnostic and therapeutic purpose in the so-called "cold" period. These patients were united in I"C"L^C subgroup. The patients of IC group who could be followed up to fix long-term results of treatment, were united in IC^{LT} subgroup.

In referring to the center patients there were made general

clinical, biochemical studies of the blood, urine, urotest for pregnancy, a bacterioscopic and bacteriological study of discharge from the vagina and cervical canal. Ultrasonic examination of the abdominal and small pelvis organs was made by the apparatus ALOKA-650 and SA-8000 SE, vaginal sensor with a frequency of 6.0–7.5 MHz.

Surgical intervention was performed either immediately after the establishment of the diagnosis of apoplexy of the ovary and hospitalization of the patient or after an attempt of the conservative treatment, and also in absence of the possibility to exclude another threatening acute surgical and gynecological pathology. Laparoscopy was performed employing the conventional procedure under the endotracheal anesthesia with the use of mono- and bipolar electro-surgical technology [2]. The women of III group were performed the retransfusion of the autologous blood intraoperatively employing our own developed procedure [4] in absence of contraindications. Statistical processing of the results obtained was made by the software Statistica 5.5 (Stat soft inc., the USA).

Ultrasonic diagnosis. All ultrasonic images of the ovaries were divided into 3 types depending on the presence of dense and liquid components on the scan in the tumor-like formation. Type I — tumor-like formation with dense, solid, amorphous hyperechogenic contents. Type II — reticulated or sponge-like pattern is noticeable with the filamentary strips, which pass in different directions against the dense, amorphous hypoechogenic background. Type III — the echogenic formation of the irregular shape was observed in the ovary from 20 to 35 mm in diameter with a slit-shaped cavity.

The volume of free liquid was determined with the aid of transvaginal echograms of the small pelvis made in the saggital plane, which were also divided into three types. Type I — the level of liquid does not rise above the internal opening of the uterus. Type II — the echogenic strip of liquid reaches the middle body of the uterus. Type III — the level of free liquid is at the level of the uterus body and higher.

Results and Discussion

The age of the observed patients varied from 17 to 55 years (on an average — 28.3±5.2). Pelvic pain was a leading clinical symptom in all patients. Intense acute pain was more frequently encountered in patients with moderate and great blood loss (62.2 and 92.3% respectively). In 285 (70.0%) patients of II and III groups the pain attack appeared in the second phase of the menstrual cycle (MC), while in 324 (67.6%) patients of I group the disease developed in the middle of MC. The hospitalized patients of I group with the expressed pain syndrome — 287 (76.5%) women — were characterized by early reference for medical aid (during the first 2 hrs from the beginning of the attack).

When insignificant nagging pelvic pain and stable geodynamics with the medical aid was observed in reference to the centre, the conservative treatment of the formed cystic hemorrhagic formation of the ovary (CHFO) was carried out under the out-patient conditions. The general state of all women of I group was estimated as satisfactory. The average indices of hemodynamics and red blood in the patients of this group were similar: pulse — (72±8) per 1 min, SAP — (124±±6) mm Hg, DAP — (70±8) mm Hg, hemoglobin — (121±16) g/l.

In the women of II group the pain syndrome had a persisting character and was intensified in time. More than half of these patients noted persistent irradiation of pain in the rectum and perineum. The state of the patients as those of I group, was estimated as satisfactory because of absence of the visible hemodynamic disturbances and changes in the red blood: pulse — (86±8) per 1 min, SAP — (122±±6) mm Hg, DAP — (68±8) mm Hg, hemoglobin — (118±16) g/l.

The state of the patients of III group was estimated as satisfactory only in 5 (4.0%) patients, of moderate severity in 57 (45.5%) patients and severe — in 63 (50.4%). The average indices of hemodynamics and red blood in patients of III group were similar: pulse — (104±8) per 1 min, SAP — (87±6) mm Hg, DAP — (68±8) mm Hg, hemoglobin — (74±12) g/l.

According to the US data a linear dependence between the level of free liquid regarding the uterus and volume of hemoperitoneum was revealed intraoperatively ($r=0.63$, $p<0.05$). Thus, in 90 (43.3%) women, whose intraabdominal hemorrhage did not exceed 200 ml, were observed by echograms of the type I, and in 63 (30.0%) cases of the IL group free liquid on the echograms was not revealed at all. In all cases of intraperitoneal hemorrhage with the volume more than 200 ml on the transvaginal echograms made in the saggital plane, a column of free liquid was fixed. In the women of II group the echograms of the type II — 198 (70.3%) cases were most frequently observed. When intraperitoneal hemorrhage reached more than 500 ml, all ultrasonic images were of the type III. In 18 (14.4%) patients of III group US study revealed hyperechogenic free liquid with the echoheterogenic sections in the vesicouterine space and around the ovaries.

In 70.0% of women of I group with the significant pain attack ultrasonic image of CHFO corresponded to the type I. The echogram of the type II was encountered in the majority of cases — 80.0% — in the patients with insignificant pain syndrome who mostly had out-patient treatment. In 281 (68.9%) woman with moderate and significant

hemoperitoneum there was observed the ultrasonic image of the type III.

On the whole in 792 (89.2%) patients the diagnosis of apoplexy of the ovary and intraperitoneal hemorrhage was made before surgical intervention on the basis of the clinical picture and US data. In the remaining cases — 92 (10.4%) it was necessary to perform diagnostic laparoscopy for confirming the diagnosis.

When according to the US data and laboratory indices the volume of the blood in the abdomen did not exceed 200 ml, the hemodynamically stable patients were started conservative treatment, accomplishing dynamic observation with the ultrasonic monitoring. The hemostatic therapy was the first to administer: etamzilat (dicinon), adroxon, menadione, the solution of calcium chloride, tranexam and aminocaproic acids. To reduce the intensity of pelvic pains nonsteroid antipyretic drugs were administered — both in injections and rectal suppositories. When the pain attack peak has already passed and in refusal to be observed at the in-patient department, out-patient treatment with the obligatory medical examination and ultrasonic monitoring was administered on the following day.

After disappearance of danger of the prolonged intraperitoneal hemorrhage further out-patient therapeutic measures were taken, directed at the resolution of the formed CHFO. Taking into account the important role of the infectious inflammatory processes of the small pelvis organs in the development of the tumor-like processes of the ovaries as one of the probable sources of AO, we give antibacterial therapy from the moment of CHFO formation considering the revealed pathogenic agents. To block the pathologic secretion of the gonadotropic hormones the hormonal drugs were administered (combined oral contraceptives or synthetic progestins). According to our observations, up to 90% of CHFO regressed after the first period, which was controlled by the transvaginal US. In case of absence of CHFO regress more than 50% patients were performed laparoscopic intervention.

All patients of II and III groups as well as 210 women of IL group were subject to urgent laparoscopic intervention. The most frequently performed hemostatic operation was resection of the ovary — 477 (77.2%) interventions. In 65 (10.5%) cases the uterine appendages were removed on the side of affection because of the significant destruction of the ovarian tissue by the pathologic process or development of the suppurative inflammatory process in ovarian hematoma, which involved practically the entire ovarian tissue. Diagnostic laparoscopy was performed when the cause of insignificant hemorrhage in the small pelvis and expressed pain syndrome was pathologic ovulation.

There was no revealed adhesive process during the operation in the small pelvis and abdominal cavity in 398 (64.5%) patients; I–II degree of the manifested adhesive process was found in 146 (23.6%) patients. The manifested adhesive process of the small pelvis organs of III–IV degree was present in 74 (11.9%) patients. The larger volume of intraperitoneal hemorrhage was observed more frequently in the patients in absence of adhesive process in ovarian hemorrhages than in the patients with the accompanying adhesive process. Thus, the average volume of hemoperitoneum found in the patients with AO, in absence of the adhesive process was (273.5±21.3) ml, while in the patients with the expressed adhesive process of the small pelvis organs it was (141.4±35.5) ml. The cause of AO in more than the half of the cases — 348 (56.3%) was the corpus luteum or cyst of the corpus luteum. A considerably less frequent cause of ovarian intraperitoneal hemorrhage was other benign tumors and tumor-like formations of the ovaries (serous, follicular, endometrioid cyst).

Besides hemostatic intervention on the ovarian tissue the majority of patients — 348 (56.3%) were performed additional surgical intervention to eliminate the accompanying pathology of the small pelvis organs. The average duration of the surgical intervention was (41.3±1.8) min — from 15 to 110 min. In the postoperative period the basic method of anesthetization was the application of nonsteroid analgesics during the first two days. After surgery the patients were in the hospital from 1 to 3 days, on an average (1.9±0.1) day.

During the operation the most frequent intraoperative finding in the patients of I“C”L^{C} subgroup was the adhesive process of the small pelvis, caused by previous acute inflammatory diseases and open surgical intervention. The adhesive process of I–II degree was revealed in 18 (16.9%) patients of this group, and of III–IV degree — in 39 (36.4%) cases. The formation of persisting CHFO against the background of external endometriosis was detected in 35 (32.1%) women of this group, endometriosis of the peritoneum of I–II degree — in 19 (17.5%) patients, and of III–IV degree in 17 (15.7%) women of I“C”L^{C} subgroup.

After obtaining the results of the histological study further antirelapse therapy was carried out taking into account the morphological structure of the source of ovarian hemorrhage. The monophase low-dose combined oral contraceptives (COC) in the cyclic regimen from 3 to 12 mo, depending on the reproductive intentions of the patient were used for the prevention of relapses of apoplexy from the follicular cysts of the ovary. If the patient was revealed endometrioid

cyst or endometriosis of other localization, the depot — drugs of the gonadotropin-releasing-hormone (aGnRH) agonists were obligatory used in the treatment for the period from 2 to 4 mo. After successful therapy by the preparations of aGnRH, depending on the reproductive intentions of the patient, the long-term therapy with COC or synthetic progestins was used. The latter (noretisteron acetate, didrogesteron) were administered to the patients with cysts of the corpus luteum. When the woman had reproductive intentions in the near future there was used antirelapse therapy with didrogesteron (dufaston) given on the 16th day of MC with the daily dose of 20–40 mg for the period from 10 days to 6 mo. Every 6–9 mo of therapy with COC or synthetic progestins interruption in the hormonal therapy was made during the period from 3 to 5 mo. During the interruption there were used plant and vitamin preparations (remens, tocopherol acetate, ginecohel), utilized for the regulation of the hormonal homeostasis of a woman.

We succeeded in following up the long-term results of treatment in 487 patients (I group — 231 women, II group — 144 patients and III group — 53 patients). The long-term results of treatment of IC^{LT}, IL and I"C"L^{C} subgroups were observed in 58, 100 and 73 patients respectively. The average duration of the patients' follow up was 31.7 mo (from 12 to 47 mo). The long-term results of treatment of AO were evaluated according to the state of the woman's reproductive function and development of the disease relapse (Table 1).

According to the data obtained, the greatest incidence of relapse of apoplexy of the ovary, formation of CHFO and most prolonged period of subfertility were observed in the women of IC^{LT} subgroup. The desired uterine pregnancy began more frequently in the patients of IL, II and III groups — 74 (74.0%), 105 (72.7%) and 39 (73.8%) cases respectively. Within the period of the observation 34 (58.6%) women conceived of those treated conservatively. In the subgroup I"C"L^{C} two thirds of the observed patients conceived — 45 (61.6%). Reduction in the reproductive function in the women of this subgroup is explained by high rate of the extensive adhesive process, observed before the operation. The average period between the treatment of AO and the desired pregnancy was approximately identical in laparoscopically operated women and made 7.5; 7.4; 7.5; 7.8 mo. For IL, I"C"L^{C}, II and III groups respectively, and in women IC^{LT} subgroup this index increased to 9.5 mo.

Relapse of ovarian hemorrhage in the form of CHFO formation was observed in 14 (24.1%) patients of IC^{LT} subgroup, in 21 (14.5%) women of II group and in 8 (15.0%) patients of III group. Within the period of the observation of AO and CHFO relapses were not observed in patients of IL and I"C"^{LT} group. 3 (5.1%) patients of IC^{LT} subgroups had to be performed laparoscopic intervention. AO was controlled conservatively in the remaining patients; 8 (13.7%) patients of IC^{LT} subgroup agreed to diagnostic laparoscopy in a year after AO attack due to recurrence of the cystic formations, during which 5 women were revealed the adhesive process of the II–III degree of extension, 4 had external endometriosis of II degree.

Conclusions

Thus, the manifestation of the clinical symptoms in apoplexy of the ovaries depends on the volume of intraperitoneal hemorrhage. The data analysis of transvaginal echography allows to determine quantitatively, with a high degree of accuracy the volume of intraabdominal hemorrhage and the morphological state of the affected ovary. Noninvasive diagnosis of the volume of hemoperitoneum in AO is used for differentiated selection of patients for the conservative or surgical treatment. Taking into account the fact that the adhesive process and endometriosis of the small pelvis peritoneum frequently accompanies ovarian hemorrhages, especially those clinical forms which are subject to the conservative treatment (hemoperitoneum up to 200 ml), they can be one of the most probable causes of AO. Taking it into account, laparoscopy is a "gold standard" not only in diagnosis and treatment of AO, but also in prevention of possible ovarian hemorrhages. The application of laparoscopy as a

Table 1

Long-term Results of Treatment of Apoplexy of the Ovary

The indices investigated	I group, n=231			II group, n=144	III group, n=5
	IK group, n=58	IL group, n=100	I"C"L^{C} group, n=73		
Reproductive function:					
they became pregnant	34 (58.6%)	74 (74.0%)	45 (61.6%)	105 (72.7%)	39 (73.8%)
the period of subfertility, mo	9.5	7.5	7.4	7.5	7.8
Relapse of apoplexy of the ovary and formation of CHFO	14 (24.1%)	—	—	21 (14.5%)	8 (15.0%)

main therapeutic and prophylactic method in AO allows to preserve and sometimes to restore reproductive function in almost 4 of 5 women with AO and reduce the rate of AO and CHFO relapse development.

REFERENCES

1. *Айламазян Э. К.* Неотложная помощь при экстремальных состояниях в гинекологии / Э. К. Айламазян, И. Т. Рябцева. – М. : Медицинская книга ; Н. Новгород : НГМА, 2003. – 183 с.

2. *Видеоэндоскопические* операции в хирургии и гинекологии / В. Н. Запорожан, В. В. Грубник, В. Ф. Саенко, М. Е. Ничитайло. – К. : Здоров'я, 2000.

3. *Гладчук І. З.* Апоплексія яєчника в сучасній гінекології / І. З. Гладчук, В. Л. Кожаков, О. В. Якименко // Репродуктивное здоровье женщины. – 2005. – № 4 (24). – С. 56–58.

4. *Деклараційний* патент України на винахід 22716, UA, МПК6 : A61B17/00 Спосіб реінфузії автокрові з черевної порожнини при лапароскопічній гінекологічній операції / І. З. Гладчук, М. А. Каштальян, О. Я. Назаренко, О. В. Якименко ; заявник та патентовласник Одеський державний медичний університет. – № u 2006 13335. – Заявл. 18.12.2006 ; опубл. 25.04.2007, Бюл. № 5.

5. *Management* of patients with ectopic pregnancy with massive hemoperitoneum by laparoscopic surgery with intraoperative autologous blood transfusion / A. Takeda, S. Manabe, T. Mitsui, H. Nakamura // J. Minim. Invasive Gynaecol. – 2006, Jan-Feb. – Vol. 13 (1). – P. 43–48.

6. *Comparison* of laparoscopy and laparotomy in managing hemodynamically stable patients with ruptured corpus luteum with hemoperitoneum / S. W. Teng, J. Y. Tseng, C. K. Chang [et al.] // J. Am. Assoc. Gynaecol. Laparosc. – 2003, Nov. – Vol. 10 (4). – P. 474–477.

7. *Ultrasonographic* and Clinical Appearance of Hemorrhagic Ovarian Cyst Diagnosed by Transvaginal Scan / Y. Nemoto, K. Ishihara, T. Sekiya [et al.] // J. Nippon Med. Sch. – 2003. – Vol. 70 (3). – P. 243–249.

8. *Bottomley C.* Diagnosis and management of ovarian cyst accidents / C. Bottomley, T. Bourne // Best Pract Res Clin Obstet Gynaecol. – 2009, Mar 17. – P. 21–23.

REFERENCES

1. Ajlamazjan Je.K., Rjabceva I.T. Neotlozhnaja pomoshh' pri jekstremal'nyh sostojanijah v ginekologii [Emergency care in extreme conditions in gynecology]. Moscow, Medical book: N. Novgorod, NSMA, 2003:183.

2. Zaporozhan V.N., Grubnik V.V., Saenko V.F., Nichitajlo M.E. Videojendoskopicheskie operacii v hirurgii i ginekologii [Video-endoscopic operations in surgery and gynecology]. K., Zdorov'ja, 1999:300.

3. Gladchuk I.Z., Kozhakov V.L., Jakimenko O.V. Ovarian apoplexy in modern gynecology. Reproduktivnoe zdorov'e zhenshhiny. 2005;4(24):56-58.

4. Gladchuk I.Z., Kashtal'jan M.A., Nazarenko O.Ja., Jakimenko O.V. Sposib reinfuzii avtokrovi z cherevnoї porozhnini pri laparoskopichnij ginekologichnij operacii [Method of auto-blood reinfusion from the abdominal cavity during laparoscopic gynecological surgery] Deklaracijnij patent Ukraini na vinahid, № 22716, UA, МПК6 : A61B17/00. Promislova vlasnist', 25.04.2007:5.

5. Takeda A., Manabe S., Mitsui T., Nakamura H. Management of patients with ectopic pregnancy with massive hemoperitoneum by laparoscopic surgery with intraoperative autologous blood transfusion. J. Minim. Invasive Gynaecol 2006;13(1):43-48.

6. Teng S.W., Tseng J.Y., Chang C.K., Li C.T., Chen Y.J., Wang P.H. Comparison of laparoscopy and laparotomy in managing hemodynamically stable patients with ruptured corpus luteum with hemoperitoneum. J. Am. Assoc. Gynaecol. Laparosc. 2003;10(4): 474-477.

7. Nemoto Y., Ishihara K., Sekiya T., Konishi H., Araki T. Ultrasonographic and Clinical Appearance of Hemorrhagic Ovarian Cyst Diagnosed by Transvaginal Scan. J. Nippon Med. Sch. 2003;70(3):243-249.

8. Bottomley C., Bourne T. Diagnosis and management of ovarian cyst accidents. Best Pract Res Clin Obstet Gynaecol. 2009;23(5):711-724.

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OESOPHAGEAL ACHALASIA TREATMENT EFFICACY BY THE METHOD OF ENDOSCOPIC INTRODUCTION OF THE BOTULINIC TOXIN

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ЭФФЕКТИВНОСТЬ ЛЕЧЕНИЯ АХАЛАЗИИ КАРДИИ МЕТОДОМ ЭНДОСКОПИЧЕСКОГО ВВЕДЕНИЯ БОТУЛИНИЧЕСКОГО ТОКСИНА

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Баллонная дилатация нижнего пищеводного сфинктера баллонами диаметром 30–40 мм или введение ботулинического токсина в этой области являются эффективными методами, которые позволяют устранить проявления дисфагии в течение 3–12 мес. Цель — изучить воздействие ботулинического токсина на давление нижнего пищеводного сфинктера и разработать прогностические критерии эффективности терапии ботулиническим токсином. В исследование были включены 32 пациента (22 мужчин, 10 женщин) с 1-й и 2-й стадиями ахалазии, которым проводили эндоскопи-

ческие инъекции ботулинического токсина типа А в области нижнего пищеводного сфинктера (препарат Диспорт). Было установлено, что давление нижнего пищеводного сфинктера и эвакуация бария из пищевода в первый день после этой инъекции являются важным прогностическим индикатором эффективности. Пациентам с хорошим ответом на введение ботулинического токсина лечение должно быть продолжено, а у пациентов с плохим ответом после возобновления симптомов необходимо выполнение кардиомиотомии. Актуальны широкое внедрение оптимизированной терапии ботулиническим токсином в клиническую практику и разработка схем проведения малоинвазивных эндоскопических процедур и показаний к их применению в лечении ахалазии пищевода.
Ключевые слова: ахалазия пищевода, инъекция ботулинического токсина.

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OESOPHAGEAL ACHALASIA TREATMENT EFFICACY BY THE METHOD OF ENDOSCOPIC INTRODUCTION OF THE BOTULINIC TOXIN
The Kharkiv Medical Academy of Postgraduate Education, Kharkiv, Ukraine
Background. Lower esophagial sphincter (LES) balloons dilation with a diameter of 30–40 mm or the introduction of botulinum toxin in this area are more efficient methods that allow to remove manifestations of dysphagia during the period from 3 to 12 months. However, after the expiration period the therapy sessions should be repeated or surgical treatment with the performance of cardiomyotomy should be performed.

The aim was studying effectiveness of botulinum toxin on the performance of pressure in the NPC to develop prognostic criteria for botulinum toxin therapy effectiveness.

Methods. The study included 32 patients (22 men, 10 women) with the 1st and early 2nd stage of AK, which were treated by endoscopic injections of botulinum toxin type A in the area of NPC (the drug Dysport, MO 500/3 mb.)

Results. Analysis of symptoms and level of pressure in the cardia showed no correlation between them and the stage of achalasia. A higher rate of transient relaxations of esophageal-gastric junction in comparison occurred at the 1st and early 2nd stage of achalasia cardia (AC) with later stages. Response to therapy is to reduce the pressure in the cardia, the restoration of peristaltic function of the esophagus, reducing the time delay of barium in the esophagus, which correlated with a decrease in severity of symptoms.

Conclusions. The pressure in the cardia and the evacuation of barium from the esophagus on the first day after injection of botulinum toxin is an important prognostic indicator of the effectiveness of its patients with AC. Patients with good response to the introduction of botulinum toxin treatment should be continued, and in patients with poor response after the resumption of symptoms cardiomyotomy will be performed. Widespread introduction of suitable botulinum toxin therapy in clinical practice, development schemes of performing minimally invasive endoscopic procedures and indications for their use in the treatment of achalasia of the esophagus.
Key words: oesophageal achalasia, botulin toxin injection.

Background

Achalasia cardiae (AC) is idiopathic disease characterized by lack of response of relaxation of the lower esophageal sphincter (LES) in response to swallowing, caused by an imbalance between excitatory (acetylcholin containing or containing substance P) and inhibitory (containing vasoactive intestinal peptide or nitric oxide) neurons as a result of selective loss of inhibitory nerves [1]. Patients with AC revealed degenerative changes in the intramuscular plexus LES [2] and a pronounced decrease in activity of nitric oxide synthesis [3]. Patients with AC noted dysphagia, chest pain, weight loss. The disease has two peaks of age of manifestation — 20–30 and 50–60. The aim of treatment is to reduce the AC pressure pump station and restore its ability to relax. At early stages of the disease can be a temporary effect of intake of nitrates and calcium channel blockers. At present, medical treatment of AC is considered ineffective.

NPC balloons dilation with a diameter of 30–40 mm or the introduction of botulinum toxin in this area are more efficient methods that allow to remove manifestations of dysphagia during the period from 3 to 12 months. However, after the expiration period the therapy sessions should be repeated or surgical treatment with the performance of cardiomiotomy [4]. One of the measurements of the effectiveness of the treatment is to reduce the pressure in the pump station and restore its ability to relax.

The Aim of the Study

To study the effectiveness of botulinum toxin on the performance of pressure in the LES to develop prognostic criteria for the effectiveness of botulinum toxin therapy.

Material and Methods

The study included 32 patients (22 men, 10 women) with the 1st and early 2nd stage of AC, which were treated by endoscopic injections of botulinum toxin type A in the area of LES (the drug Dysport, MO 500/3 mb.). Men's age was 24–69, women's — 20–68 years old.

Medical procedure was performed as follows. Esophagoscopy was performed under local anesthesia. Observing the rules of antisepsis four injections of the drug Dysport were performed. Piercing the mucosa, the drug was injected into the pump station at points corresponding to 3, 6, 9, and 12 hours. At each point it was injected 60 units of the drug. The total dose should not exceed 250 units. Complica-

tions associated with intervention and/or the introduction of the toxin were observed. All patients underwent a comprehensive survey: endoscopy, barium suspension roentgen tests with the definition of the delay time of barium in the esophagus, esophageal manometry with the definition of pressure in the NPS.

After the introduction of botulinum toxin on the 1st and 7th day, the pressure was measured in the NPC, as well as determination of the time delay of barium suspension in the esophagus. Patients were examined 1 month after the procedure, then at intervals of 3 months from the time of drug administration for 1.5 years (the study of pressure in the pump station, the definition of consistency of esophageal peristalsis, X-ray examination with the definition of esophageal emptying time, the analysis of clinical presentations with visual analogue scale of severity of dysphagia with a maximum estimate of 10 points). Statistical analysis of the results was performed using standard statistical tests; data processing was carried out in the program Microsoft Excel XP.

Results and Discussion

Analysis of symptoms and level of pressure in the cardia showed no correlation between them and the stage of achalasia. But at the 1st and early 2nd stage of AC occurred a higher rate of transient relaxations of esophageal-gastric junction in comparison with later stages (Table 1). Response to therapy is to reduce the pressure in the cardia, the restoration of peristaltic function of the esophagus, reducing the time delay of barium in the esophagus, which correlated with a decrease in severity of symptoms (Table 2).

The pressure level in NPC correlated with the time of the evacuation of the esophagus (Spearman correlation coefficient — 0.85, p<0.05). Noted the almost linear relationship between the indicators of pressure in the pump station on the 1st and 7th day after surgery, so for further calculations, we used data from manometry and roentgen tests on the 1st day after surgery.

In the analysis of long-term results were divided into three groups. The first — with the pressure in the cardia after injection of botulinum toxin less than 10 mm Hg, the second — 10–20 mm Hg, the third — more than 20 mm Hg. Results of monitoring patients after treatment are shown on Fig. 1. Differences in the results indicate the possibility of using pressure levels after administration of botulinum toxin as a prognostic criterion of its effectiveness.

The relation between the level of pressure in achalasia car-

Table 1

Monometric Value of Intraoperative Patients

Value	Stage		
	1	1–2	2
Pressure in cardia, mm Hg.	38.6±12.5	45.2±14.4	56.4±12.3
The frequency of cardia relaxation, the hour	2.1±1.2	1.60±0.81*	0.80±0.35*

Note. * — differences were statistically significant (d<0,05).

Table 2

Effectiveness of Botulinum Toxin Therapy in Patients with Achalasia

Effectiveness value	Before introduction of toxin, n=32	After introduction of toxin, n=32
The delay of contrast in the esophagus, sec	364±124	32.0±24.1*
Pressure in cardia, mm Hg	58.6±15.4	13.68±8.90*
Esophageal peristalsis, mm Hg	24.0±15.6	34.0±12.4*
Dysphagia, scores	5.6±2.4	1.4±0.7*
Chest pain, scores	5.3±2.4	2.1±1.2*
Regurgitation, scores	4.2±1.4	1.8±0.8*
Weight lost, %	9.2±2.2	0.7±1.2*

Note. * — differences are scientifically significant (d<0,05).

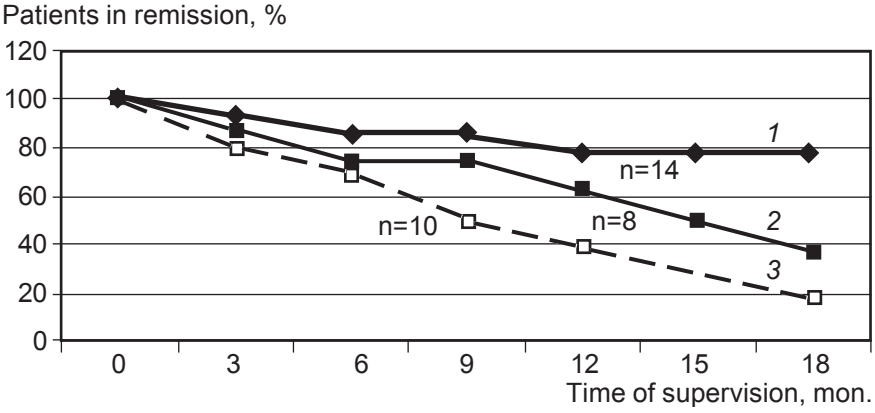

Fig. 1. The probability of recurrence of symptoms, depending on the pressure in the gastric cardia after injection of botulinum toxin. Differences between groups are scientifically significant (d<0,05): *1* — < 10 mm Hg; *2* — 10–20 mm Hg; *3* — > 20 mm Hg

Table 3

The Relationship between the Pressure after the Administration of Botulinum Toxin and the Clinical and Manometric Parameters at 1 and 18 Months

Effectiveness scores, condition	Complex survey	Pressure in the NPS after the introduction of botulinum toxin, mm Hg		
		< 10, n=27	10–20, n=22	> 20, n=16
Pressure in NPS, mm Hg				
beyond remission	1	7.5±3.6	14.0±7.5	24.0±15.6
remission	18	12.4±8.6	24.0±15.6	24.0±15.6
recurrence	18	32.1±15.6	44.0±15.6	56.1±18.6
Integral assessment of symptoms, scores				
beyond remission	1	1.6±1.1	1.8±1.4	2.1±1.2
remission	18	1.23±1.20	1.6±1.1	2.2±1.6
recurrence	18	3.6±2.1	4.8±1.8	5.4±2.4
Weight loss, %				
beyond remission	1	0.71±1.10	0.83±1.20	0.57±1.40
remission	18	0.58±0.21	0.67±0.23	0.71±1.10
recurrence	18	4.2±2.2	9.7±2.2	10.4±2.2

dia after relapse and severity of symptoms (Table 3). Also, the level of pressure of field injection of botulinum toxin has been associated with the intensity of the return of symptoms and the level of pressure in the pump station after the recurrence of achalasia. According to modern concepts, the method of choice for early treatment of AC is the introduction of botulinum toxin in the area of NPC or balloon dilatation. Several studies have shown that the best results compared to these methods which allows early surgical treatment [5]. However, in our opinion, the use of endoscopic techniques is justified with proper patient selection.

Our observations show that patients with good response to therapy with botulinum toxin, which is characterized by a decrease in pressure in the pumping station is less than 10 mm Hg on the first day after injection, decreasing the time delay of barium to normal values and a decrease in the severity of symptoms until the complete regression of dysphagia, it is possible to predict the effectiveness of treatment is not inferior to operative procedures [6], but with the advantage of minimally invasive and convenience for patients. Also, there is no doubt about the advantage of using botulinum toxin in elderly and senile patients, in patients with severe concomitant diseases, and patients who refuse surgery.

Conclusions and Prospects for Further Research

The pressure in the cardia and evacuation of barium from the esophagus on the first day after injection of botulinum toxin is an important prognostic indicator of the effectiveness of its patients with achalasia cardia.

Patients with good response to the introduction of botulinum toxin treatment should be continued, and in patients with poor response after the resumption of symptoms cardiomyotomy will be performed.

Widespread introduction of suitable botulinum toxin therapy in clinical practice, development schemes of performing of minimally invasive endoscopic procedures and indications for their use in the treatment of esophagial achalasia.

REFERENCES

1. Walzer N., Water N., Hirano I. Achalasia. Gastroenterol Clin North Am 2008;37(4):807-825.

2. Gockel L., Bohl J.R., Eckardt V.F. Reduction of interstitial cells of Cajal (ICC) associated with neuronal nitric oxide synthase (n-NOS) in patients with achalasia. Am J Gastroenterol 2008; 103(4):856-864.

3. Bruley des Varannes S., Chevalier J., Pimont S. Serum from achalasia patients alters neurochemical coding in the myenteric plexus and nitric oxide mediated motor response in normal human fundus. Gut 2006;55:319-326.

4. Campos G.M., Vittinghoff E. Rabl C. Endoscopic and surgical treatments for achalasia: a systematic review and meta-analysis. Ann Surg 2009;249:45-57.

5. Wang L., Li Y.M., Li L. Meta-Analysis of Randomized and Controlled Treatment Trials for Achalasia. Dig Dis Sci 2008;24:12-14.

6. Mikaeli J., Yaghoobi J.M., Montazeri G. Efficacy of botulinum toxin injection before pneumatic dilatation in patients with idiopathic achalasia. Dis Esophagus 2004;17:213-217.

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TECHNICAL FEATURES OF THE IMPLEMENTATION OF SLEEVE GASTRECTOMY AND BILIOPANCREATIC DIVERSION IN THE TREATMENT OF OBESE PATIENTS

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ТЕХНИЧЕСКИЕ ОСОБЕННОСТИ ВЫПОЛНЕНИЯ РУКАВНОЙ ГАСТРЭКТОМИИ И БИЛИОПАНКРЕАТИЧЕСКАЯ ДИВЕРСИЯ В ЛЕЧЕНИИ ПАЦИЕНТОВ С ОЖИРЕНИЕМ

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Значительно и неуклонно повышается количество людей, страдающих избыточным весом, особенно во всех экономически развитых странах. По данным Всемирной организации здравоохранения, около 30 % населения имели избыточный вес в конце XX в.

Билиопанкреатическая диверсия (в модификации Hess-Marceau) позволяет добиться устойчивого снижения массы тела и нормализации липидного и карбогидратного метаболизма в течение 2-х лет в среднем % EWL на 72 %.

Рукавная гастрэктомия снижает % EWL до 64 % в течение 2 лет после операции.

Ключевые слова: морбидное ожирение, хирургическое лечение, билиопанкреатическая диверсия, рукавная гастрэктомия.

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TECHNICAL FEATURES OF THE IMPLEMENTATION OF SLEEVE GASTRECTOMY AND BILIOPANCREATIC DIVERSION IN THE TREATMENT OF OBESE PATIENTS

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Background. Steady growth of the number of people with excessive weight is observed almost in all economically developed countries. According to the World Health Organization (WHO), about 30% of people had excessive weight by the end of the twentieth century. Thereby, assimilation and improvement of the methods of bariatric surgeries is an actual task.

Aim of the study. To estimate technical features and the results of sleeve gastrectomy and biliopancreatic diversion (Hess-Marceau modification).

Methods. During the period from 2009 to 2012 year bariatric surgery was performed in 24 patients (16 women and 8 men). Patients' age ranged from 28 to 59, BMI range from 31.6 to 80 kg/m^2. Biliopancreatic diversion (Hess-Marceau modification) was performed on 18 patients (with BMI > 40 kg/m^2). Sleeve gastrectomy was performed in 6 patients (with BMI range from 31.6 to 47.7 kg/m^2).

The main complaints of patients with morbid obesity were a progressive increase in body weight, with no effect from other methods of treatment (diet, drug therapy, intragastric balloon), severe shortness of breath with little exertion, pain in the back and in large joints of lower limbs, different degrees of manifestation of Pickwickian syndrome (night snoring, apnoea, daytime sleepiness). Body mass, carbohydrates and fats metabolism rates were controlled.

Results. All patients reported a significant reduction in appetite after surgery. It was reported a median percentage of excessive weight loss (%EWL) by 49% within the first year after the operation, 64% EWL after two years.

Conclusions. Biliopancreatic diversion (Hess-Marceau modification) leads to a significant reduction in body weight and normalization of lipid and carbohydrate metabolism and in two years a median %EWL is 72%. Sleeve gastrectomy reduces %EWL by 64% within 2 years after surgery.

Key words: morbid obesity, surgical treatment, biliopancreatic diversion, sleeve gastrectomy.

Actuality of the Work

Steady growth of the number of people with excessive weight is observed almost in all economically developed countries. According to the World Health Organization (WHO), about 30% of people had excess we weight by the end of the twentieth century. Today obesity is considered to be a non-infectious epidemic. 60% of the Americans are overweight people and 27% of them are obese; in the countries of Western Europe about 25% of the population have excess we weight. Arterial hypertension, diabetes mellitus and dyslipidaemia are closely associated with obesity; they decrease the quality of patient's life, increase costs of medical treatment and in most cases they are the reason of an untimely death.

Treatment of obesity is a difficult task for a doctor and especially for a patient. Obesity is regarded as a chronic recurrent disease, which needs a lifelong treatment and it is very important to the patient to understand this necessity. Present methods of

conservative treatment contain nutrition and lifestyle changes, longtime therapy, but it is really hard to do for most patients. That is why in 90% of cases conservative treatment is ineffective and after treatment cessation patients have a relapse of the disease.

As for up-to-date methods the most complete and lasting effect can be reached with the help of surgical methods of treatment of morbid obesity [1–5]. All bariatric surgeries are commonly divided into three main groups: restrictive, malabsortive and combined [1; 2; 4; 5].

One of the modern methods of restrictive surgery is sleeve gastrectomy. In recent times this methodology attracts more and more attention of bariatric surgeons and gets wide spread. However, because of the relative novelty of the methodology there is no enough number of observations over the patients in the long term after the operation. This fact causes the high interest to the results of sleeve gastrectomy.

Combined surgery is recommended to the patients with morbid obesity and with accompanying dyslipidaemia, insulin resistance and hypertension. One of the effective combined methodologies is biliopancreatic diversion (Hess-Marceau modification). This methodology allows to achieve a good result with a small number of complications in the early postoperative period and provides a high quality of life in the late period [2–6; 8; 9].

Thereby, assimilation and improvement of the methods of bariatric surgeries is an actual task.

Purpose of the Work

To estimate technical features and the results of sleeve gastrectomy and biliopancreatic diversion (Hess-Marceau modification).

Object and Methods of Research

During the period since 2009 till 2012 year bariatric surgery was performed on 24 patients, there were 16 women and 8 men. Patient age ranged from 28 to 59, BMI range from 31.6 to 80 kg/m^2.

Biliopancreatic diversion (Hess-Marceau modification) was performed on 18 patients (with BMI > 40 kg/m^2). Sleeve gastrectomy was performed on 6 patients (with BMI range from 31.6 to 47.7 kg/m^2).

The main complaints of patients with morbid obesity were a progressive increase in body weight, with no effect from other methods of treatment (diet, drug therapy, intragastric balloon), severe shortness of breath with little exertion, pain in the back and in large joints of lower limbs, different degrees of manifestation of Pickwickian syndrome (night snoring, apnoea, daytime sleepiness).

Body mass, rates of the metabolism of carbohydrates and fats were controlled.

The degree of obesity was defined according to WHO classification (1997 year); BMI was defined as the individual's body mass (kg) divided by the square of his or her height (m^2); ideal body weight was defined according to the international table Metropolitan Height and Weight Tables, Converted to Metric System (1983 year); the percentage of excess weight loss was defined according to the formula

$$\%EWL = \frac{\text{Weight Loss (kg)}}{\text{Excess Weight (kg)}} \cdot 100\%.$$

Results and Discussion

The surgeon together with every patient planned and decided which method of surgical treatment to chose. During the conversation it was determined if expectations of patients were realistic; the advantages and disadvantages of each type of surgery, the expected decrease in body weight were discussed. Will and possibility of the patient to be under medical supervision in long-term periods after surgery were obligatory conditions for the surgery. In our opinion, it is obligatory to obtain consent for surgery not only of the patient but also of the relatives, especially in the cases of younger patients.

All patients underwent a standard preoperative assessment. It was first estimated that 9 patients had hypertension and it caused longer preoperative preparation. All operated patients were in risk of thromboembolic complications, this fact was the reason to carry out specific and non-specific prevention of thromboembolic complications. Compression stockings were used for non-specific prevention, nadroparin (fraxiparine) was used for carrying out specific prevention. In all cases prevention of purulent-septic complications with the use of second-generation cephalosporins was carried out.

Biliopancreatic diversion (Hess-Marceau modification) was performed on 18 patients with class III obesity. Body mass of these patients was from 100 to 248 kg, BMI range from 40 to 80 kg/m^2. In discussing the technical aspects of the operation it should be noted the Harmonic scalpel (Johnson & Johnson) was used to mobilize the greater curvature of the stomach and duodenum, that greatly facilitated the implementation of this phase of the operation, and reduced its time. Resection was performed while gastric tube (12 mm) was inserted, along the lesser curvature of stomach and the line of resection was carried out on the edge of the probe. The line of surgical staples was obligatory peritonized by a continuous encircling stitch. Intraoperative measurement of the stomach showed that the volume of reservoir was from 70 to 150 ml. For the intersection of the stomach and duodenum the suturing devices Ethicon Proximate (with the length of the seam — 75 mm) were used. The length of the total loop was left 80–100 cm. Before intersection of the small intestine the marks were made on

the gut, it allowed to identify clearly the proximal and distal parts of the loop during the surgery.

Discussing the results of the treatment, it should be noted that almost immediately after surgery all patients of this group reported a significant decrease in appetite. Within 2 months after surgery loose stools was noted up to 4 times a day, then this number decreased by 1–2 times a day and depended on the quality of food. All patients regularly take a multivitamin, fat-soluble vitamins, iron and calcium. During the first year after surgery in this patient group, the percentage of excess weight loss ranged from 52 to 87%, a median %EWL for the first year was 58%. Within second year, a median %EWL was 72%. Before surgery, eight patients had disorders of carbohydrate and fat metabolisms; it caused hyperinsulinemia, hypercholesterolemia, hypertriglyceridemia, increased levels of leptin and C-peptide. Also, there were an increase in blood pressure, Pickwickian syndrome and pain in large joints of lower limbs. In the postoperative period carbohydrate and fat metabolism rates, blood pressure numbers were normalized, Pickwickian syndrome was liquidated, and there is no pain in the lower limbs. Indicators of iron, calcium and protein were monitored, they remained within normal limits.

Sleeve gastrectomy was performed on 6 patients (with body mass from 95 to 159 kg and BMI range from 31.6 to 47.7 kg/m^2), and in 4 cases laparoscopic way was used. Talking about the features of surgery it should be noted that the first intersection of the stomach was performed at a distance of 5 cm from the pylorus, and only for the second stitching a gastric tube was inserted (12 mm in diameter). The line of surgical staples was peritonized by a continuous stitch. All patients reported a significant reduction in appetite after surgery. It was reported a median percentage excess weight loss (%EWL) of 49% in the first year after the operation, 64 %EWL after two years.

Conclusions

Biliopancreatic diversion (Hess-Marceau modification) leads to a significant reduction in body weight and normalization of lipid and carbohydrate metabolism and in two years a median %EWL is 72%. Sleeve gastrectomy reduces% EWL 64% within 2 years after surgery.

REFERENCES

1. *Егиев В. Н.* Рестриктивные вмешательства на желудке в лечении больных ожирением / В. Н. Егиев, М. Н. Рудакова, Д. С. Белков. – М. : Медпрактика, 2004. – 99 с.

2. *Лаврик А. С.* Результати хірургічного лікування цукрового діабету II типу у хворих на морбідне ожиріння / А. С. Лаврик, О. С. Тивончук, О. А. Лаврик // Клінічна хірургія. – 2010. – № 8. – С. 21.

3. *Седлецкий Ю. И.* Современные методы лечения ожирения / Ю. И. Седлецкий. – СПб. : ЭЛБИ-СПб, 2007. – 403 с.

4. *Яшков Ю. И.* Гастрошунтирование и билиопанкреатическое шунтирование — первые наблюдения и результаты / Ю. И. Яшков // Хирургическое лечение ожирения и сопутствующих метаболических нарушений : материалы 3-го Рос. симп. Санкт-Петербург, 1–2 июля 2004. – СПб., 2004. – С. 53–54.

5. *Яшков Ю. И.* Этапы развития хирургии ожирения / Ю. И. Яшков // Вестник хирургии. – 2003. – № 3. – С. 53–56.

6. *Biliopancreatic* diversion with duodenal switch / P. Marceau, F. S. Hould, S. Simard [et al.] // World J. Surg. – 1998. – Vol. 22. – P. 947–954.

7. *Twenty* years of biliopancreatic diversion: what is the goal of the surgery? / S. Biron, F. S. Hould, S. Lebel [et al.] // Obes Surg. – 2004. – Vol. 14. – P. 160–164.

8. *Hess D. S.* The biliopancreatic diversion with the duodenal switch: results beyond 10 years / D. S. Hess, D. W. Hess, R. S. Oakley // Obes Surg. – 2005. – Vol. 14. – P. 408–416.

9. *Biliopancreatic* diversion for obesity: state of the art / N. Scopinaro, G. Marinari, G. Camerini [et al.] // Surg Obes. – 2005. – Vol. 1. – P. 317–328.

REFERENCES

1. Egiev V.N., Rudakova M.N., Belkov D.S. Restrictivnye vmeshatelstva na zheludke v lechenii bolnyh oshireniem [Restrictive procedures on stomach for morbid obesity]. Moscow, Medpractica, 2004:99.

2. Lavrik A.S., Tyvonchuk O.S., Lavrik O.A. Results of surgical treatment of type II diabetes associated with morbid obesity. Klinichna hirurgiya 2010;8: 21.

3. Sedletskiy Yu.I. Sovremennye metody lechenia ozhirenia [Modern methods of treatment of obesity] Sanct-Peterburg, Elbi-Spb, 2007:403.

4. Yashkov Yu.I. Gastric and biliopancreatic diversion — first results. Hirurgicheskoe lechenie ozhireniya i soputstvuyuschih metabolicheskih narusheniy: Materialy III Rossiyskogo simpoziuma (Surgical treatment of obesity and related metabolic disorders: Proceedings of III Russian Symposium). Sanct-Peterburg 2004:53-54.

5. Yashkov Yu.I. Etapy razvitiya hirurgii ozhireniya [Steps of evolution of obesity surgery]. Vestnik hirurgii 2003;3: 53-56.

6. Marceau P., Hould F.S., Simard S., et al. Biliopancreatic diversion with duodenal switch. World J Surg 1998; 22:947-954.

7. Biron S., Hould F.S., Lebel S., et al. Twenty years of biliopancreatic diversion:what is the goal of the surgery? Obes Surg. 2004;14:160-164.

8. Hess D.S., Hess D.W., Oakley R.S. The biliopancreatic diversion with the duodenal switch:results beyond 10 years. Obes Surg. 2005;14:408-416.

9. Scopinaro N., Marinari G., Camerini G., et al. Biliopancreatic diversion for obesity: state of the art. Surg Obes. 2005;1:317-328.

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DIFFERENTIATED CHOICE OF THE MINIINVASIVE SURGICAL APPROACH IN SURGICAL TREATMENT OF CHOLELITHIASIS

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ДИФФЕРЕНЦИРОВАННЫЙ ВЫБОР МАЛОИНВАЗИВНОГО ХИРУРГИЧЕСКОГО ДОСТУПА В ХИРУРГИЧЕСКОМ ЛЕЧЕНИИ ЖЕЛЧНОКАМЕННОЙ БОЛЕЗНИ
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С 2009 г. в клинике Одесского национального медицинского университета прооперировано 47 больных с желчнокаменной болезнью. У 26 больных выполнена минилапароскопическая холецистэктомия, у 21 – однопортовая. Все оперативные вмешательства прошли без интраоперационных осложнений. У 5 пациентов из-за анатомических сложностей мы вынуждены были прибегнуть к установке дополнительного троакара в эпигастральной области. Время, использованное для проведения вмешательств, варьировалось от 30 до 130 мин. Больные находились в стационаре от 1 до 4 сут. При наблюдении за пациентами в течение первых месяцев после операции отдаленных осложнений не наблюдалось, отмечен хороший косметический эффект. Спустя 8 месяцев после операции у 1 пациента после однопортовой лапароскопической холецистэктомии диагностирована троакарная грыжа в месте установки порта.
Ключевые слова: минилапароскопическая и однопортовая холецистэктомия.

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DIFFERENTIATED CHOICE OF THE MINIINVASIVE SURGICAL APPROACH IN SURGICAL TREATMENT OF CHOLELITHIASIS
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In 2009 at the University Clinic of the Odessa National Medical University with minilaparoscopic and single-port technology we have operated 47 patients with cholelithiasis. 26 patients were performed minilaparoscopic cholecystectomy, 21 — laparoscopic cholecystectomy using a single laparoscopic access. All surgical interventions had no intraoperative complications. In 5 patients because of anatomic difficulties in removing the gallbladder, we were used to installing an additional trocar in the epigastric region. Time used for interventions ranged from 30 to 130 minutes. Patients were hospitalized after the surgery from 1 to 4 days. Technically, the performance of single-port laparoscopic cholecystectomy was more difficult than the traditional laparoscopic or minilaparoscopic operations due to lack of conditions for the quality triangulation, visualization of anatomical structures in the area of operation and the small angle between the operating instruments. Particular attention was devoted to adequate closure of the abdominal wall defect after installing the port. Pain after use minilaparoscopic surgery was significantly less than with traditional laparoscopic approach. The intensity of pain after single-port operations, was comparable with that of conventional traditional laparoscopy. At follow-up of patients during the first months after surgery separated complications were not observed, marked by a beautiful cosmetic effect. 8 months after surgery 1 patient was diagnosed trocar-site hernia after a single port laparoscopic cholecystectomy.
Key words: minilaparoscopic and single-port cholecystectomy.

Introduction

The use of traditional laparoscopic surgical intervention with the aid of the standard 10 and 5 mm instruments in a definite quantity of patients is accompanied by development of such complications as postoperative ventral ruptures, pyoseptic complications, formation of significant cosmetic defects on the abdominal skin [1; 2]. The use of laparoscopic instruments of small diameter — 2–5 mm allowed to perform operations at the new qualitative level and with smaller traumatic outcome than by the standard laparoscopic operations; however, the need for extraction of the volumetric macro-preparation from the abdominal cavity levels the advantages of minilaparoscopy. In the last few years Notes-technologies began to be applied in the clinical practice, which consisted in the use of natural openings in the human body for the surgical access. Of the widest use became procedures with the use of a single laparoscopic access (SILS-, LESS- operation with setting of the special ports through the navel) [3; 4]. At present there are no developed possibilities of the substantiated application of minilaparoscopic and endoscopic transluminal surgical interventions in the surgery of the gallstone disease, indications and contraindications to their use are not determined; the detailed estimation of the operational technique is absent.

The advantages of the technology of the single surgical access in the treatment of the gallstone disease remain debatable, the long-term results of using this procedure are not studied, and there are no developed measures for prevention of the formation of trocar hernias.

Aim of the work: to improve the results of surgical treatment of patients with the gallstone disease by optimization of the surgical access for performing laparoscopic cholecystectomy.

Results and Discussion

Since 2009 there have been operated 47 patients with the gallstone disease with the use of minilaparoscopic and single port technologies in the University clinic of the Odessa National Medical University. These were predominantly women (34 patients), without decompensated concomitant pathology and obesity. In 12 patients we used the possibility of providing vaginal access for the manipulations on the organs of the abdominal cavity under the videoendoscopic control and for the extraction of the remote organ from the abdominal cavity. 26 patients were performed minilaparoscopic cholecystectomy, 21 — laparoscopic cholecystectomy with the use of single laparoscopic access. 1 patient was performed the simultaneous removal of the nonparasitic cyst of the liver, 1 patient had bilateral adnexectomy, 8 had the plasty of the umbilical hernia, through which the port for performing the single port operation was set.

We used laparoscopes of 2.6, 4.2 and 5 mm in diameter and standard 3 and 5 mm trocars and the systems of single laparoscopic access for introduction as well as long (600 mm in length) 5 mm, endoscopes with the end and 70° optics for using laparoscopy through the posterior formix of the vagina or through the single port system. There were used 3 mm conventional instruments and original, of our own construction, trocar manipulators for traction of the internal organs of 2.6 and 3 mm in diameter. For performing the single port laparoscopic interventions there were used the device of the access of the firms Karl Storz and PPP as well as the port of our own construction, a set of the curved instruments of the firm Karl Storz.

All surgical interventions did not have any intraoperative complications. We were forced to set additional 5 mm trocar in the epigastric region in 5 patients because of the anatomical complexities in removal of the gall bladder. Instead of clipping of the bile duct and artery, the extracorporeal ligation was used in 5 patients, which allowed to perform this manipulation through one trocar. Colpotomic access after the organ removal was not sutured; only tamponade of the vagina was made. The time of the intervention varied from 30 to 130 minutes. The patients' in-hospital stay after the operation was from 1 to 4 days.

Technically the performance of single port laparoscopic cholecystectomies was more complex than traditional laparoscopic or minilaparoscopic ones because of absence of conditions for the qualitative triangulation, visualization of the anatomical formations in the operation zone and small angle between working tools. The presence of even insignificant infiltration or anatomical peculiarities in the zone of Calot triangle made this access dangerous for surgery and we were forced to set additional epigastric trocar. The situations of acute cholecystitis or insufficient effective hemostasis forced to make the drainage of the subhepatic space, which levelled all advantages of the single port access.

Special attention must be paid to the adequate suturing of the abdominal wall defect after setting the port. We used a continuous two-row polypropylene suture with the thread size of 2–0. The use of the provisory threadholders, which we applied before setting the port, facilitates the application of this suture.

Painful syndrome after the use of minilaparoscopic surgical intervention was substantially less than in using traditional laparoscopic access. Pain intensity after single port operations was compared with that of the usual three-trocar laparoscopy. Taking into account the greater duration of performing single port cholecystectomy, its invasiveness (taking into consideration more prolonged anesthesia) is hardly less than during the traditional access.

There were observed no long-term complications during the first months of the follow-up of the patients after the operation, a beautiful cosmetic effect was noted. In 8 months after the operation 1 patient was diagnosed trocar hernia at the site of the port setting after single port laparoscopic cholecystectomy.

Conclusions

The use of minilaparoscopic and combined single port surgical intervention is a perspective trend in development of modern surgical technologies, which needs further improvement and introduction into the practical activity of the specialized surgical centers. Today in chronic calculous cholecystitis preference should be given to minilaparoscopic techniques. Operations with the use of single laparoscopic access are justified when the associated umbilical hernia or the expansion of the umbilical ring is present, which requires its suturing as well as in large size of the concrements and the gall bladder itself, which do not prevent its extraction through the single port system.

REFERENCES

1. *Захараш М. П.* Хирургия единого лапароскопического доступа — новое направление миниинвазивной хирургии / М. П. Захараш, Ю. М. Захараш, Е. В. Усова // Хірургія України. – 2010. – № 3 (35). – С. 100–109.

2. *Однопортові* лапароскопічні втручання. Перший досвід та перспективи використання / О. Ю. Іоффе, О. П. Стеценко, Т. В. Трасюк [та ін.] // Хірургія України. – 2011. – № 3. – С.16–20.

3. *Single*-port laparoscopic appendectomy conducted intracorporeally with the aid of a transabdominal sling suture / O. Ates, G. Hakguder, M. Olguner, F. M. Akgur // Journal of Pediatric Surgery. – 2007. – N 6, Vol. 42. – P. 1071–1074.

4. *Single* Port Access Laparoscopic Cholecystectomy / P. Bucher, P. Pugin [et al.] // World J Surgery. – 2008. – N 5, Vol. 33. – P.1015–1019.

REFERENCES

1. Zakharash M.P., Zakharash Yu.M., Usova E.B. Surgery by single laparoscopic access — a new tendency of noninvasive surgery. Surgery of Ukraine 2010;3(35):100-109.

2. Ioffe O.Yu., Stetsenko O.P., Trasyuk T.V. et al.Single port laparoscopic interventions. First experience and perspectives of application. Surgery of Ukraine 2011;3:6-20.

3. Ates O., Hakguder G., Olguner M., Akgur F.M. Single-port laparoscopic appendectomy conducted intracorporeally with the aid of a transabdominal sling suture. Journal of Pediatric Surgery 2007;6,42:1071-1074.

4. Bucher P., Pugin P. et al. Single Port Access Laparoscopic Cholecystectomy. World J Surgery 2008;5(33): 1015-1019.

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COMPARISON OF THE LONG-TERM RESULTS OF MONOPOLAR AND BIPOLAR TRANSURETHRAL RESECTION OF THE PROSTATE

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СРАВНЕНИЕ ОТДАЛЕННЫХ РЕЗУЛЬТАТОВ МОНОПОЛЯРНОЙ И БИПОЛЯРНОЙ ТРАНСУРЕТРАЛЬНОЙ РЕЗЕКЦИИ ПРЕДСТАТЕЛЬНОЙ ЖЕЛЕЗЫ

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В последние годы внедрено большое количество альтернативных малоинвазивных методов лечения доброкачественной гиперплазии предстательной железы (ДГПЖ). Современные многоцентровые исследования демонстрируют сопоставимость ближайших результатов биполярной ТУР, биполярной и плазмокинетической энуклеации простаты, а также гольмиевого и green-лазера в лечении ДГПЖ по сравнению со стандартной методикой монополярной ТУР. Большинство исследований сравнивают периоперационные и ранние послеоперационные результаты биполярной и монополярной ТУР простаты. Автором статьи поставлена задача оценить качество жизни и характер отдаленных послеоперационных осложнений после биполярной ТУР в сроки от 36 до 60 мес. после операции по сравнению с монополярной ТУР предстательной железы. В результате исследования установлено, что при практически равных интраоперационных и ранних послеоперационных показателях биполярная ТУР предстательной железы имеет преимущества перед монополярной ТУР по отдаленным результатам в связи с меньшим количеством риска рецидива ДГПЖ ($p<0,05$) и отсутствием послеоперационных рубцовых изменений в зоне резекции.

Ключевые слова: биполярная ТУР, монополярная ТУР, ДГПЖ, стриктура уретры, отдаленные результаты.

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COMPARISON OF THE LONG-TERM RESULTS OF MONOPOLAR AND BIPOLAR TRANSURETHRAL RESECTION OF THE PROSTATE

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The monopolar transurethral resection of the prostate (TUR) has long remained a “gold” standard of treatment of benign prostatic hyperplasia (BPH). However, recently there have been introduced a large number of alternative noninvasive methods of BPH treatment. Modern multicenter studies demonstrate the comparability of the intraoperative data and early postoperative characteristics of the monopolar and bipolar TUR.

The author of the paper compare quality of life and nature of the long-term postoperative complications after the bipolar TUR in the period from 36 to 60 months after the operation in comparison with the monopolar TUR of the prostate. There were evaluated the frequency of BPH relapses and infravesical obstruction development, associated with the postoperative scar changes in the urethra and neck of the bladder, which was confirmed by the data of ascending urethrography and urine flowmetry. The patients with the irritative symptoms, associated with the bladder overactivity, were excluded from the study.

The author demonstrates that 6.7% patients after monopolar TUR underwent repeated TUR due to BPH relapse and 13.3% of patients had the infravesical obstruction, associated with the scar changes in the zone of the surgical intervention in the long-term period after the monopolar TUR. The bipolar TUR of the prostate had advantages over the monopolar TUR in the long-term results, regarding smaller quantity of risk of BPH relapse ($p<0.05$) and absence of the postoperative scar changes in the zone of resection. Besides, the amount of patients contented by results of the operation is reliably more after the bipolar TUR ($p<0.05$).

Key words: bipolar TUR, monopolar TUR, BPH, the stricture of the urethra, the long-term results.

Objective

The monopolar transurethral resection (TUR) of the prostate has long remained a "gold" standard of treatment of benign prostatic hyperplasia (BPH) [9; 15; 17; 24]. The standard procedures of the operation have already been developed, special peculiarities of the postoperative period, complications and postoperative results have been studied [15]. However, in the recent years there were introduced a large number of alternative noninvasive methods of BPH treatment [1; 8; 12; 13; 19; 27]. Modern multicenter studies demonstrate the comparability of the immediate results of the bipolar TUR, bipolar and plasmokinetic enucleation of the prostate as well as holmium and green-laser in BPH treatment [20; 21; 25; 26]. The advantages of the new technologies are caused only by the expansion of indications to noninvasive surgical intervention due to absence of limitations in surgery duration, absence of the risk of the TUR-syndrome development and their smaller morbidity, which allows to use data of the procedure in large extension of hyperplasia [2–4; 6; 7; 11; 14; 16].

The authors of studies on this topic, comparing intraoperative data and early postoperative characteristics, have found that the monopolar and bipolar TUR are little distinguished in these indices [5; 10; 13; 15; 16; 18]. However, at present the basic criterion of effectiveness of one or other procedure is customary assumed to consider the patients' quality of life. Based on these positions we did not encounter any studies, which evaluate long-term results of both forms of surgical intervention.

Aim of the work. To compare quality of life and nature of the long-term postoperative complications after the bipolar TUR in the period from 36 to 60 months after the operation in comparison with the monopolar TUR of the prostate.

Materials and Methods

23 patients participated in the study, whom the bipolar TUR of the prostate gland for BHPG was performed from June 2007 to June 2009 with the use of a electro-surgical generator Autocon II 400 (Karl Storz, Germany). The patients' age was (69±12) years. The prostate volume was (85.5± ±32.9) ml. The PSA index was (2.3±1.9) ng/ml. Duration of the operation was (60±25) min. The period of catheterization was (4±2) days. To make the comparison 30 patients were examined who were performed standard, monopolar TUR of the prostate for BPH. The patients' age was (71±6) years. The prostate volume was (58.5±23.6) ml. The PSA index was (2.9±1.4) ng/ml. Duration of the operation was (45±20) min. The period of catheterization was (5±2) days in comparison. That is both groups were compared by the criteria of inclusion in the study. To eliminate the effect of the special peculiarities of the surgical technology and experience of the surgeon all surgical intervention were performed by one specialist. The follow-up period of the patients was from 36 to 60 months. There were evaluated the frequency of BPH relapses, which was revealed with TRUS and frequency of development of the infravesical obstruction, associated with the postoperative scar changes in the urethra and neck of the bladder, which was confirmed by the data of ascending urethrography and uroflowmeter. The patients with the irritative symptoms, associated with the bladder overactivity, were excluded from the study.

Results

Within the follow-up period from 36 to 60 months after the operation as a result of the control examination 20/23 (87%) patients were satisfied by quality of urination by the IPSS scale after bipolar TUR and 24/30 (80%) after monopolar TUR ($p<0.05$). 1/23 (4.3%) patients after bipolar TUR and 2/30 (6.7%) patients after monopolar TUR ($p<0.5$) underwent repeated TUR due to BPH relapse. Strictures of the urethra and scar changes of the neck of the bladder were not noted in the long-term period after bipolar TUR, while after monopolar TUR there were noted 3/30 (10%) scar stenosis of the neck of the bladder and 1/30 (3.3%) had the non-extended stricture of the membranous part of the urethra. Thus, 13.3% of patients had the infravesical obstruction, associated with the scar changes in the zone of the surgical intervention in the long-term period after the monopolar TUR. It is probably possible to explain it by the deeper damaging effect on the mucosa of the urethra and neck of the bladder by the monopolar current. Furthermore, it is not possible to exclude probability by the appearance of anomalous course, which is characteristic for the monopolar electro-surgical effect.

Thus, comparing the results obtained it is possible to note that in practically equal intraoperative and early postoperative indices the bipolar TUR of the prostate has advantages over the monopolar TUR in the long-term results, regarding smaller quantity of risk of BPH relapse ($p<0.05$) and absence of the postoperative scar changes in the zone of resection. Besides, the amount of patients contented by results of the operation is reliably more after the bipolar TUR ($p<0.05$).

Conclusions

1. The bipolar TUR of the prostate does not differ from the monopolar standard TUR of the prostate gland by technique and is compared with the latter by the intraoperative and early postoperative characteristics.

2. The rate of development of the late postoperative complications, such as BPH relapse, scar strictures of the urethra and stenosis of the neck of the bladder

are reliably less in the bipolar TUR of the prostate.

3. The bipolar TUR does not lead to the significant damages of mucosa of the urethra and neck of the bladder due to absence of the risk of the anomalous motion of the electric current.

4. The amount of patients satisfied with the results of the noninvasive operation is reliably more after the bipolar TUR of the prostate gland; therefore the procedure should be widely introduced in the clinical practice.

REFERENCES

1. Alivizatos G, Skolarikos A. Photoselective vaporization of the prostate to manage benign prostatic hyperplasia. J Endourol 2008;22: P. 2117-2119.

2. Finley DS, Beck S., Szabo RJ. Bipolar saline TURP for large prostate glands. Scientific World Journal 2007; 7:1558-1562.

3. Gupta N, Sivaramakrishna, Kumar RR, Dogra PN, Seth A. Comparison of standard transurethral resection, transurethral vapour resection and holmium laser enucleation of the prostate for managing benign prostatic hyperplasia of > 40 g. BJU Int 2006; 97:P.85-89.

4. Hahn RG. Fluid absorption in endoscopic surgery. BJA 2006;96: 8-20.

5. Ho HSS, Yip SKH, Lim KB [et al] A prospective randomized study comparing monopolar and bipolar transurethral resection of prostate using transurethral resection in saline (TURIS) system. Eur Urol 2007;52: 517-524.

6. Horasanli K, Silay MS, Altay B [et al] Photoselective potassium titanyl phosphate (KTP) laser vaporization versus transurethral resection of the prostate for prostates larger than 70 mL: a short-term prospective randomized trial. Urology 2008;71:247-251.

7. Iori F, Franco G, Leonardo C [et al] Bipolar transurethral resection of prostate:clinical and urodynamic evaluation. Urology 2008;71: 252-255.

8. Kuntz RM. Current role of lasers in the treatment of benign prostatic hyperplasia (BPH). Eur Urol 2006;49: P.961-969.

9. Marszalek Martin, Ponholzer Anton, Pusman Marlies [et al] Transurethral Resection of the Prostate. Eur Urol Suppl, Vol.8, issue 6, 2009:504-512.

10. Mamoulakis C, Ubbink DT, de la Rosette JJMCH Bipolar versus monopolar transurethral resection of the prostate:a systematic review and meta-analysis of randomized controlled trials. Eur Urol 2009;56:P.798-809.

11. Michielsen DP, Debacker T, De Boe V [et al] Bipolar transurethral resection in saline-an alternative surgical treatment for bladder outlet obstruction? J Urol 2007;178:P.2035-2039, discussion 2039.

12. Montorsi F, Naspro R, Salonia A [et al] Holmium laser enucleation versus transurethral resection of the prostate:results from a 2-center, prospective, randomized trial in patients with obstructive benign prostatic hyperplasia. J Urol 2004;172:1926-1929.

13. Nuhoglu B, Ayyildiz A, Karaguzel E [et al] Plasmakinetic prostate resection in the treatment of benign prostate hyperplasia:results of 1-year follow up Int J Urol 2006;13: 21-24.

14. Rajbabu K, Chandrasekara SK, Barber GH NJ [et al] Photoselective vaporization of the prostate with the potassiumtitanyl-phosphate laser in men with prostates of > 100 mL BJU Int 2007;100: 593-598, discussion 598.

15. Rassweiler J, Teber D, Kuntz R, Hoffman R. Complications of transurethral resection of the prostate (TURP) — incidence, management, and prevention. Eur Urol 2006;50:969-980.

16. Rassweiler J, Schulze M, Stock C [et al] Bipolar transurethral resection of the prostate-technical modifications and early clinical experience. Minim Invasive Ther Allied Technol 2007;16: 11-21.

17. Reich O, Gratzke C, Stief CG Techniques and long-term results of surgical procedures for BPH Eur Urol 2006;49:970-978.

18. Riccardo A, Rocco D, Di Lorenzo G [et al] Four-Year Outcome of a Prospective Randomised Trial Comparing Bipolar Plasmakinetic and Monopolar Transurethral Resection of the Prostate. Eur Urol 2009;55:922-931.

19. Ruszat R, Seitz M, Wyler SF [et al] GreenLight laser vaporization of the prostate: single-center experience and long-term results after 500 procedures Eur Urol 2008;54:P.893-901.

20. Ruszat R, Wyler SF, Seitz M [et al] Comparison of potassium-titanyl-phosphate laser vaporization of the prostate and transurethral resection of the prostate: update of a prospective non-randomized two-centre study BJU Int 2008;102:1432-1438.

21. Ahyai Sascha A, Gilling Peter, Kaplan Steven A [et al] Meta-analysis of Functional Outcomes and Complications Following Transurethral Procedures for Lower Urinary Tract Symptoms Resulting from Benign Prostatic Enlargement Eur Urol 2010;58:384-397.

22. Seckiner I, Yesilli C, Akduman B [et al] A prospective randomized study for comparing bipolar plasmakinetic resection of the prostate with standard TURP Urol Int 2006;76:139-143.

23. Singh H, Desai MR, Shrivastav P, Vani K. Bipolar versus monopolar transurethral resection of prostate: randomized controlled study J Endourol 2005;19:333-338.

24. Wendt-Nordahl G, Bucher B, Hacker A [et al] Improvement in mortality and morbidity in transurethral resection of the prostate over 17 years in a single center J Endourol 2007;21: 1081-1087.

25. Wilson LC, Gilling PJ, Williams A [et al] A randomised trial comparing holmium laser enucleation versus transurethral resection in the treatment of prostates larger than 40 grams: results at 2 years Eur Urol 2006;50:569-573.

26. Xia S-J, Zhuo J, Sun X-W [et al] Thulium laser versus standard transurethral resection of the prostate: a randomized prospective trial Eur Urol 2008;53:382-390.

27. Yu X, Elliott SP, Wilt TJ, McBean AM Practice patterns in benign prostatic hyperplasia surgical therapy: the dramatic increase in minimally invasive technologies J Urol 2008; 180:241-245.

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COMPARATIVE ASSESSMENT OF THE TRADITIONAL AND ENDOSCOPIC APPENDECTOMY ACCORDING TO THE RESULTS OF PERFORMING FIRST 1,000 LAPAROSCOPIC APPENDECTOMIES

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СРАВНИТЕЛЬНАЯ ОЦЕНКА ТРАДИЦИОННОЙ И ЭНДОСКОПИЧЕСКОЙ АППЕНДЭКТОМИИ ПО РЕЗУЛЬТАТАМ ВЫПОЛНЕНИЯ ПЕРВОЙ 1000 ЛАПАРОСКОПИЧЕСКИХ АППЕНДЭКТОМИЙ

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Цель исследования — улучшение результатов лечения больных острым аппендицитом путем применения лапароскопической техники в диагностике и лечении заболевания.

При применении лапароскопии ошибочно удалено 0,4 % неизмененных червеобразных отростков. При традиционном методе — 6,5 %. Катаральный аппендицит диагностирован у 36,4 % больных в группе открытых аппендэктомий и лишь у 10,5 % — в группе лапароскопических аппендэктомий, что позволяет говорить о неоправданно выполненной в некоторых случаях аппендэктомии.

Выполнение лапароскопической аппендэктомии по поводу острого аппендицита возможно у 95,9 % больных. Продолжительность выполнения эндоскопической аппендэктомии — (53,4±±7,6) мин достоверно не отличается от таковой открытой операции — (49,2±8,7) мин. Продолжительность лечения больных в стационаре после выполнения лапароскопической аппендэктомии составляет (3,4±0,9) дня, что меньше, чем после открытой операции, — (6,2±1,2) дня. Частота послеоперационных осложнений после выполнения лапароскопической аппендэктомии меньше, чем после открытой операции, — соответственно 3,5 и 6,1 %.

Ключевые слова: острый аппендицит, открытая аппендэктомия, лапароскопическая аппендэктомия.

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COMPARATIVE ASSESSMENT OF THE TRADITIONAL AND ENDOSCOPIC APPENDECTOMY ACCORDING TO THE RESULTS OF PERFORMING FIRST 1,000 LAPAROSCOPIC APPENDECTOMIES

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The **aim** of the study is improvement of treatment results of patients with acute appendicitis by application of laparoscopic technique in diagnosis and treatment of the disease.

The laparoscopic diagnosis of acute appendicitis allows to avoid “unnecessary” appendectomy inevitable in traditional clinical and laboratory diagnosis. Performance of laparoscopic appendectomies for acute appendicitis is possible in 95.9% of patients. Intracorporal laparoscopic appendectomy was performed in 704 patients. We withdrew patients from the study if conversion to open appendectomy was necessary (28 patients — 4.0%). The appendix stump closure method was assigned in accordance with appendix base inflammatory changes. The patients were divided into 4 groups according to stump securing method. The appendix stump was controlled by using two or three titanic clips in 356 (52.6%) patients, two separate ligatures — in 252 (37.3%) patients, using a linear stapler in 56 (8.3%), and immersion into the ceacum cupola by a purse-string suture was performed in 12 (1.8%) patients. Operation time and complications were analyzed.

Duration of laparoscopic appendectomy — (53.4±7.6) min does not differ from open surgery — (49.2±8.7) min. Duration of in-hospital treatment after laparoscopic appendectomy — (3.4±0.9) days is shorter than after open surgery — (6.2±1.2) days. The rate of postoperative complications after laparoscopic appendectomy is lower than those after traditional open surgery — 3.5 and 6.1% accordingly.

Key words: acute appendicitis, open appendectomy, laparoscopic appendectomy.

Importance of the study

Acute appendicitis (AA) is the most common acute surgical disease of the abdominal organs. Patients with suspected AA make up to 50% of all patients hospitalized in emergency to general surgical in-patient departments. In Ukraine the AA morbidity rate is on average 4.3–5.4 per 1000 population [1; 4].

The disease hazard is caused by complications, the rate of which is from 33 to 43% in Russia. The complication rate after appendectomy is from 4.2 to 16.2%. These indices reach 32.3% in patients over 50 [1; 2].

Lethal outcome in AA makes from 0.1 до 0.5%. The signifi-

cant task for clinicians is an increase of efficacy of diagnosis as well as clinical approbation of new approaches to treatment of the patients with AA. One of such approaches may be diagnosis and treatment of AA using noninvasive technologies, namely videolaparoscopy [1–4].

The aim of the study is improvement of treatment of patients with AA by using laparoscopic technique.

Materials and Methods

The material of the study is results of treatment of 2,346 patients aged from 16 to 88 hospitalized to the department of urgent surgery of MMCC of SR with the preliminary diagnosis of AA.

311 patients (98 were performed traditional surgery, 213 — were operated with the use of videoendoscopic technique) were diagnosed a firm appendicular infiltrate (30) or a diagnosis of AA was excluded during surgery and other diseases were detected (281). 2.035 patients being performed appendectomy were divided into two groups: the 1st group included 1,092 patients who were performed appendectomy with the use of endovideoappliance; the 2nd group consisted of 943 patients performed appendectomy by the traditional open method. Each group was subdivided into groups of patients depending on morphological signs of the disease — with simple (catarrhal — CA), phlegmonic (PA), gangrenous and perforating appendicitis. Subgroups of patients with gangrenous and perforating appendicitis were combined into a subgroup with gangrenous-perforating appendicitis (GPA).

The selection of patients in the groups studied was homogenous. The groups were comparable by sex, patient's age, severity of the disease course, its duration before hospitalization as well as the criteria used — data of the laboratory and instrumental methods of examination.

Besides generally accepted clinical methods all patients were made purposeful laboratory and instrumental methods of examination, ultrasound investigation of the abdominal cavity, retroperitoneal area and organs of the small pelvis by indication. In diagnostically difficult situations 65 patients were made computer tomography and 10 — magnetic-resonance imaging. On detection of a firm appendicular infiltrate 30 patients were performed irrigoscopy for differentiated diagnosis with other diseases of the large intestine.

All open and endoscopic interventions were performed under general multicomponent anesthesia. To perform endosurgical interventions there were used special sets of equipment and instruments manufactured by "Karl Storz", "Martin", "Aesculap" (Germany), "Circon Acmi", "Ethicon" (the USA), "Endomedium" (Russia), "Contact" (Ukraine).

Laparoscopy was performed by a classical technique under the conditions of carboxiperitoneum. Attention was paid to localization of the appendix, its mobility, elasticity, the state of the appendix mesentery. To evaluate the character of the appendix changes there was determined its rigidity and instrumental palpation was made. Revision of the appendix base and extension of the inflammatory infiltration over the cecum cupula was especially carefully made. According to the laparoscopic revision the corresponding endoscopic diagnosis was made which was compared with clinical data and decision was made to perform surgery. At this stage there was made a final decision as to expediency to perform LAE, determined its kind and stage succession. Extra- and intracorporal technique of LAE was used depending on manifestation of the inflammatory changes in the appendix base area and cecum cupula.

Results and Discussion

The diagnosis was confirmed in 943 (87.3%) of 1,080 patients with preliminary diagnosis of AA operated on by the open method, they were performed VAE (Table 1). The diagnosis of AA was not confirmed in 132 (12.2%) patients, they were diagnosed other diseases (mesadenitis, acute gynecological diseases, acute pancreatitis, etc). Secondary changed appendix was removed in 70 (6.5%) of them. Appendectomy was not performed in 5 (0.5%) patients with diagnosed firm appendicular infiltrate.

1,251 patients were operated on with the use of endovideoappliance, the diagnosis was confirmed in 1,092 (87.0%) patients, and they were performed LAE (Table 1). The diagnosis of AA was excluded in 134 (10.6%) patients according to the results of the diagnostic stage of laparoscopy; the unchanged appendix was removed in 5 cases, which made 0.4%.

Appendectomy was not performed in 25 (2.0%) patients who were diagnosed a firm appendicular infiltrate.

VAE was performed using the McBurney approach. The appendix mesentery was intersected after ligation. The appendix stump was ligated by the catgut

Table 1

Forms of AA and Kinds of Surgical Interventions

Surgery	Amount of observations of AA morphological forms			
	CA	PA	GPA	Total
VAE	345 (36.6%)	453 (48.0%)	145 (15.4%)	943 (100%)
LAE	126 (11.5%)	711 (65.1%)	255 (23.5%)	1,092 (100%)
Including conversion	—	10	25	35
Total	471	1164	400	2035

ligation, and then immersed into the purse-string and Z-like sutures. In presence of gangrenous and perforating appendicitis the wound was closed before the subcutaneous cellular tissue.

Among 1,092 patients operated on for AA with the use of endovideoappliance the intracorporal technique of appendectomy was used in 1,035 (94.8%) patients, extracorporal — in 55 (5.2%). The most important stage of LAE is treatment of the mesentery and appendix base.

There were used different methods (Table 2) to treat the appendix mesentery: clipping of its vessels in 34 (3.1%) patients, ligation — in 81 (7.4%), ultrasound scalpel — in 119 (10.9%), electrocoagulation — in 838 (76.7%), endostapler — in 20 (1.8%).

In application of the intracorporal technique of LAE there were also used different methods to treat the appendix base: clipping — in 522 patients, ligation — in 285, immersion — in 57, dissection of the appendix with the aid of endoscopic stapler — in 138 (Table 3).

Macropreparations were removed from the puncture in the right inguinal area in the container to avoid the contact of the infected macropreparation with tissues of the abdominal wall with preliminary irrigation of the container with antiseptic solution. The application of this method prevents suppuration in the puncture area of the anterior abdominal wall. For this purpose there was devised and patented an original method — a special container for evacuation of the macropreparation (a patent of Ukraine 16016 of 15.02.06). Sanation and drainage of the abdominal cavity during LAE is made more completely than in VAE with the use of McBurney approach.

The method of laparoscopically assisted appendectomy (extracorporal technique of appendectomy) was used in presence of the manifested inflammatory changes in the appendix base and a threat of cutting through the clips or ligatures applied to its base. At the same time there was made a revision of the abdominal cavity and treated the appendix mesentery laparoscopically by one of the mentioned methods (see Table 2). This allows to mobilize the cecum cupola and take out the appendix through the puncture extended up to 2–2.5 cm in the right inguinal area. The appendix base was treated by the immersed method. Laparoscopically assisted appendectomy was performed in 55 (5.2%) patients (a patent of Ukraine 16016 of 15.02.06).

Conversion to the open surgery was made in 35 (3.2%) patients. 16 patients were performed medial laparotomy for GPA complicated by extended purulent peritonitis, 19 were operated by McBurney approach: 10 for GPA complicated by extended purulent peritonitis or formation of the appendicular abscess; 2 — in combination of AA with abscess of Douglas pouch with inflammation of the right uterine appendages involved into the suppurative process; 3 — in considerable infiltrative signs of the cecum; 5 — in impossibility to visualize the appendix due to marked adhesive process in the abdominal cavity after previous open interventions into the abdominal organs.

The postoperative complications in VAE developed in 59 (6.3%) patients (the postoperative adhesive diseases — in 4, intraabdominal bleeding — in 3, intraabdominal abscess — in 5, suppuration of the operative wound — in 47), in LAE there were complications in 35 (3.2%): intraabdominal abscess — in 6, carboximediastinum — in 1, suppuration of the operative wound — in 28. Because of intraabdominal abscesses there were performed relaparoscopies, opening, sanation and drainage of abscesses. Carboximediastinum was manifested by weakness of the cardiac activity, eliminating by itself on the 5th postoperative day. The

Table 2

Methods of Treatment of the Appendix Mesentery During LAE

A method of treatment	Amount of observations of AA morphological forms, pathoanatomical form			
	CA	PA	GPA	Total
Clipping	21	13	0	34
Ligation	39	34	8	81
Electrocoagulation	52	591	160	803
Ultrasound scalpel	14	56	49	119
Endostapler ETS-Flex	—	2	18	20
Total	126	696	235	1057

Table 3

A Method of Treatment of the Appendix Base During LAE (Intracorporal Technique)

A method of treatment	Morphological form of AA			
	CA	PA	GPA	Total
Clipping	76	371	75	522
Ligation	25	183	77	285
Application of the purse-string suture	15	29	13	57
Closure with endostapler ETS–Flex	—	89	49	138
Conversion	—	10	25	35
Total	116	682	239	1,037

patient needed cardiometabolic therapy. Suppuration of the postoperative wounds after laparoscopic appendectomy is treated faster as the size of the wound is considerably smaller. The lethal outcome was 0.1% in both groups. The patients died were 89 and 91 years old with perforating appendicitis. Death occurred on the 3rd and 4th day after surgery due to myocardial infarction and acute kidney failure respectively.

Duration of VAE was (47.4±±8.6) min. LAE duration was (51.2±7.3) min. Thus, the average duration of VAE and LAE did not differ significantly (P>0.05).

The average in-hospital stay after LAE for any form of AA was considerably shorter (on average was 3.1±0.9) than after VAE (6.1±1.3), more significant for CA and PA (2.1 and 2.0 times accordingly, P<0.001). The patients diagnosed with perforating AA were discharged from the hospital 1.5 times faster after LAE than after VAE.

In 133 patients in whom AA was not confirmed during diagnostic laparoscopy only 5 patients had been removed pathomorphologically unchanged appendix which made 0.4%. During open appendectomy the number of removed unchanged appendixes was 6.5% that was reliable evidence of efficacy of the videoendoscopic method. The rate of detection of simple (catarrhal) appendicitis in patients operated on with the use of laparoscopic technique is smaller than in those operated on by the open method — 11.5 and 36.6% accordingly.

Conclusions

1. Videolaparoscopic diagnosis allows to elucidate the diagnosis of acute appendicitis, reveal other diseases of the abdominal organs and avoid unjustifiable appendectomy in 6.5%.

2. Performance of laparoscopic appendectomy for acute appendicitis is possible in 95.9% of patients independent on the anatomical localization of the appendix.

3. Differential approach to selection of the treatment methods of the appendix mesentery and base allows to decrease the complication rate after laparoscopic appendectomy 1.7 times compared with appendectomy by the traditional approach.

4. The same duration of the operation and considerably shorter in-hospital stay after videolaparoscopic appendectomy (3.1±0.9) in comparison with traditional surgery (6.1±1.3) allows to consider laparoscopic appendectomy as a method of choice in treatment of acute appendicitis.

REFERENCES

1. *Лапароскопия* в диагностике и лечении острого аппендицита / А. Ю. Некрасов, С. А. Касумьян, А. А. Прибыткин [и др.] // Эндоскопическая хирургия. – 2009. – № 3. – С. 31–34.

2. *Пронин В. А.* Патология червеобразного отростка и аппендиктомия / В. А. Пронин, В. В. Бойко. – Харьков : ИЗНХ, 2007. – 272 с.

3. *Golash V.* Laparoscopic management of acute appendicitis in situs inversus / V. Golash // J Min Access Surg. – 2006. – Vol. 2. – P. 220–221.

4. *Subramanian A.* A 60-year literature review of stump appendicitis: the need for a critical view / A. Subramanian, M. Liang // The American Journal of Surgery. – 2012, April. – Vol. 203 (4). – P. 503–507.

REFERENCES

1. Nekrasov A.Yu., Kasumyan S.A., Pributkin A.A., Sergeev A.V., Bezaltunnukh A.A. Laparoscopy in diagnosis and treatment of acute appendicitis. Endoscopicheskaya hiryrgia 2009;3: 31-34.

2. Pronin V.A., Boyko V.V. Patologia cherveobraznogo otrostka i appendektomia [Pathology of the appendix and appendectomy]. Harkov, IZNH 2007:272.

3. Golash V. Laparoscopic management of acute appendicitis in situs inversus. J Min Access Surg. 2006;2: 220-1.

4. Subramanian A., Liang M. A 60-year literature review of stump appendicitis: the need for a critical view. The American Journal of Surgery;203(4), April 2012:503-507.

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«ОДЕСЬКИЙ МЕДИЧНИЙ ЖУРНАЛ»

Відомості про видання

«Одеський медичний журнал» засновано у 1926 році. За кілька років він набув неабиякого авторитету серед науковців. У ньому друкували свої праці вчені, чиї імена були всесвітньо відомі вже того часу або здобули визнання в майбутньому. Та згодом, на початку 30-х років, видання журналу було припинено. Поновлений у 1997 році, він за короткий час відновив свій авторитет і посів чільне місце серед наукових видань країни.

Засновниками «Одеського медичного журналу» є Міністерство охорони здоров'я України й Одеський національний медичний університет, видавцем — Одеський національний медичний університет.

Головним редактором з часів відновлення випуску журналу є академік НАМН України лауреат Державної премії України В. М. Запорожан. До складу редакційної колегії та редакційної ради входять відомі вітчизняні та зарубіжні вчені.

Постановами Президії ВАК України № 1–05/2 від 27 травня 2009 року та № 1-05/5 від 31 травня 2011 року «Одеський медичний журнал» включено до переліку видань, у яких можуть публікуватися основні результати дисертаційних робіт з медицини, біології та фармації. Саме це й визначає тематику його публікацій. Щороку у журналі друкується близько двохсот статей і повідомлень.

Журнал виходить шість разів на рік. Він надходить до найвідоміших бібліотек країни, великих наукових центрів, десятків навчальних закладів. Його появу гідно оцінено за межами нашої країни.

Розповсюджується за передплатою. Передплатити журнал можна у будь-якому передплатному пункті. Передплатний індекс — 48717.

ЗМІНЕНО ПРАВИЛА ПІДГОТОВКИ СТАТЕЙ ДО «ОДЕСЬКОГО МЕДИЧНОГО ЖУРНАЛУ»

Статті, прийняті до друку за попередніми правилами, будуть опубліковані. Нові статті приймаються за новими правилами, які надруковано наприкінці цього номера, друкуватимуться у наступних номерах і на сайтах Одеського національного медичного університету **odmu.edu.ua** та Одеського медичного журналу **journal.odmu.edu.ua.**

Зміна попередніх правил викликана необхідністю щонайтіснішої інтеграції нашого видання у всесвітній науковий простір з його розвинутим наукометричним інструментарієм, який дозволяє досить чітко визначити роль будь-якого вченого, будь-якого видання у науковому процесі. Адже не за горами ті часи, коли здобуття наукового ступеня стане неможливим без урахування всесвітнього рейтингу здобувача.

Найбільшою в світі є реферативна наукометрична база даних Scopus. Саме вона за своєю методикою визначає так званий індекс Хірша (h-індекс), який, попри усіляку критику, вважається достатньо об'єктивним і надійним показником внеску вченого в науку та його визнання у науковому світі.

Тож наші вимоги до статей, залишаючись незмінними у своїй основі, зазнали змін саме у тому, що стосується їх використання у наукометричних базах даних. Звертаємо на це особливу увагу авторів, адже вирахуваний системою індекс Хірша багато у чому залежатиме саме від ретельності дотримання автором нижченаведених вимог.

ПРАВИЛА ПІДГОТОВКИ СТАТЕЙ ДО «ОДЕСЬКОГО МЕДИЧНОГО ЖУРНАЛУ»

1. В «Одеському медичному журналі» публікуються теоретичні й оглядові статті, які відображають важливі досягнення науки, підсумки завершених оригінальних клінічних і експериментальних досліджень, основні результати дисертаційних робіт з медицини, біології та фармації, а також матеріали меморіального характеру.

2. До розгляду приймаються проблемні статті загальним обсягом до 8 сторінок, огляди — до 10 сторінок, оригінальні й інші види статей — до 6 сторінок, короткі повідомлення — до 2 сторінок.

3. Не приймаються статті, які вже були надруковані в інших виданнях або запропоновані до публікації кільком виданням водночас, а також роботи, які за своєю сутністю є переробкою опублікованих раніше статей і не містять нового наукового матеріалу або нового наукового осмислення вже відомого матеріалу.

4. У журналі друкуються:

а) результати оригінальних досліджень у пріоритетних напрямах розвитку медичних, біологічних і фармацевтичних наук;

б) роботи з фундаментальних проблем біології, медицини, фармакології та фармації:

— генетики та прикладних аспектів медичної генетики;

— біофізичні та морфофункціональні характеристики клітин організму при різних видах патології;

— роботи з новітніх клітинних технологій;

— новітні розробки в галузі загальної і клінічної фармакології та фармації;

— досягнення в галузі вивчення етіології, патогенезу та діагностики сучасних захворювань;

— профілактика захворювань, щеплення, запобігання особливо небезпечним захворюванням;

в) огляди з сучасних актуальних проблем біології, медицини та фармації;

г) інформація, хроніка, ювілеї.

5. Стаття надсилається до редакції в двох примірниках, підписаних усіма авторами. Своїми підписами автори гарантують, що статтю написано з дотриманням правил підготовки статей до «Одеського медичного журналу», експериментальні та клінічні дослідження були виконані відповідно до міжнародних етичних норм наукових досліджень, а також надають редакції право на публікацію статті у журналі, розміщення її та матеріалів щодо неї на сайті журналу і в інших джерелах.

6. Стаття супроводжується направленням до редакції, завізованим підписом керівника та печаткою установи, де виконано роботу, а для вітчизняних авторів також експертним висновком, що дозволяє відкриту публікацію.

7. Якщо у статті використано матеріали, які є інтелектуальною власністю кількох організацій і раніше не публікувалися, автор має одержати дозвіл на їх публікацію кожної з цих організацій і надіслати його разом зі статтею.

8. Текст друкується через півтора інтервалу на стандартному машинописному аркуші (ширина полів: лівого, верхнього та нижнього по 2 см, правого — 1 см) шрифтом Arial (Arial Cyr) або Times (Times Cyr) розміром 14 пунктів. Сторінка тексту повинна містити не більше 30 рядків.

9. Мова статей — українська для вітчизняних авторів, російська й англійська для авторів з інших країн.

10. Матеріал статті має бути викладено за такою схемою:

а) індекс УДК;

б) ініціали та прізвище автора (авторів);

в) назва статті;

г) повна назва установи (установ), де виконано роботу, місто, країна;

д) постановка проблеми у загальному вигляді та її зв'язок із важливими науковими та практичними завданнями;

е) аналіз останніх досліджень і публікацій, в яких започатковано розв'язання даної проблеми і на які спирається автор;

ж) виділення не розв'язаних раніше частин загальної проблеми, яким присвячується стаття;

з) формулювання мети статті (постановка завдання);

и) виклад основного матеріалу дослідження з повним обгрунтуванням отриманих наукових результатів;

к) висновки з даного дослідження і перспективи подальших розробок у цьому напрямі;

л) література;

м) два резюме — російською мовою обсягом до 800 друкованих літер (0,45 сторінки) й англійською обсягом до 1800 друкованих літер (1 сторінка) за такою схемою: індекс УДК, ініціали та прізвище автора (авторів), назва статті, текст резюме, ключові слова (не більше п'яти).

11. Резюме англійською мовою має коротко повторювати структуру статті, включаючи вступ, мету та завдання, методи, результати, висновки, ключові слова. Ініціали та прізвище автора (авторів) подаються у транслітерації, назва статті — у перекладі на англійську. Ключові слова й інші терміни статті мають відповідати загальноприйнятим медичним термінам, наведеним у словниках. Не слід використовувати сленг і скорочення, які не є загальновживаними.

12. Хімічні та математичні формули вдруковують або вписують. Структурні формули оформляють як рисунки. У формулах розмічають: малі та великі літери (великі позначають двома рисками знизу, малі — двома рисками зверху простим олівцем); латинські літери підкреслюють синім олівцем; грецькі — обводять червоним олівцем; підрядкові та надрядкові цифри та літери позначають дугою простим олівцем.

13. У статтях слід використовувати Міжнародну систему одиниць СІ.

14. Рисунки (не більше двох) і підписи до них виконують окремо. На зворотному боці кожного рисунка простим олівцем слід указати його номер і назву статті, а за необхідності позначити верх і низ.

15. Таблиці (не більше трьох) слід друкувати на окремих сторінках, вони повинні мати нумерацію та назву. На полях рукопису необхідно вказати місце розміщення рисунків і таблиць. Інформація, наведена в таблицях і на рисунках, не повинна дублюватися.

16. Список літературних джерел повинен містити перелік праць за останні 5 років і лише в окремих випадках — більш ранні публікації. В оригінальних роботах цитують не більше 10 джерел, в оглядах — до 30. На кожну роботу в списку літератури має бути посилання в тексті рукопису. Література у списку розміщується згідно з порядком посилань на неї у тексті статті, які подають у квадратних дужках, або за алфавітом. Якщо наводяться роботи лише одного автора, вони розміщуються у хронологічному порядку. До списку літературних джерел не слід включати роботи, які ще не надруковані.

17. Список подається у двох примірниках для кожного екземпляра статті, які друкуються окремо один від одного. Перший примірник оформляється відповідно до ДСТУ ГОСТ 7.1:2006. Другий — повністю повторює перший, але латиницею за нижченаведеними схемами.

Для статей:

Author A.A., Author B.B., Author C.C. Title of article. *Title of Journal* 2005; 5(129): 49-53.

Прізвища авторів і назва журналу подаються латиницею у транслітерації, назва статті — у перекладі на англійську.

Для матеріалів конференцій:

Riabinina, A.A., Berezina, E.V., Usol'tseva, N.V. Surface Tension and Lyotropic Mesomorphism in Systems Consisting of Nonionogenic Surfactant and Water, *Liotropnye zhidkie kristally i nanomaterialy: sbornik statei VII Mezhdunarodnoi nauchnoi konferentsii* (Lyotropic Liquid Crystals and Nanomaterials: Proceedings of the Seventh International Conference), Ivanovo: Ivanovskii Gos. Univ., 2009, p. 73-75.

Прізвища авторів подаються у транслітерації, назва праці — у перекладі на англійську. Головне в описах конференцій — назва конференції мовою оригіналу (подається у транслітерації, якщо немає її англійської назви), виділяється курсивом. У дужках наводиться переклад назви на англійську. Вихідні дані (місце проведення конференції, місце видання, рік, сторінки) — англійською.

Для монографій та інших книжок:

Nenashev M.F. *Poslednee pravitel'stvo SSSR* [Last government of the USSR]. Moscow, KromPubl., 1993. 221 p.

Прізвища авторів подаються у транслітерації, назва книжки — курсивом у транслітерації з пере-

кладом на англійську у квадратних дужках. Місце видання, рік видання, загальна кількість сторінок — англійською, назва видавництва — у транслітерації.

Зауважуємо: у списку латиницею потрібно указувати всіх авторів літературного джерела, на яке Ви посилаєтесь (ДСТУ ГОСТ 7.1:2006 цього не передбачає). Також не слід у ньому застосовувати передбачених ДСТУ ГОСТ 7.1:2006 знаків розділення: // і —. Назву джерела (журнал, конференція, книга) завжди виділяють курсивом.

Дотримання цих правил забезпечить коректне відображення цитованих джерел у переважній більшості реферативних наукометричних баз даних.

18. Скорочення слів і словосполучень подаються відповідно до ДСТУ 3582-97 і ГОСТ 7.12-93.

Для тих, хто не має доступу до повного тексту ДСТУ, на сайті Одеського медуніверситету наведено приклади оформлення бібліографічних записів. Доступ за посиланням http://odmu.edu.ua/index.php?v=1179.

19. До статті на окремому аркуші мовою оригіналу й англійською додаються відомості про авторів, які містять: вчене звання, науковий ступінь, прізвище, ім'я та по батькові (повністю), місце роботи й посаду, яку обіймає автор, адресу для листування, номери телефонів, факсів та адреси електронної пошти.

20. До друкованих матеріалів, виконаних із використанням комп'ютерних технологій, обов'язково додаються матеріали комп'ютерного набору та графіки на дискеті (лазерному диску).

Текст може бути таких форматів: Word for Windows, RTF (Reach Text Format).

Графічний матеріал слід подавати в окремих файлах форматів XLS, TIFF, WMF або CDR. Роздільна здатність штрихових оригіналів (графіки, схеми) форматів TIFF повинна бути 300–600 dpi B&W, напівтонових (фотографії та ін.) — 200–300 dpi Gray Scale (256 градацій сірого). Ширина графічних оригіналів — 5,5, 11,5 і 17,5 см.

21. Статті піддаються науковому рецензуванню, за результатами якого ухвалюється рішення про доцільність публікації роботи. Відхилені статті не повертаються і повторно не розглядаються.

22. Редакція залишає за собою право редакційної правки статей, яка не спотворює їх змісту, або повернення статті автору для виправлення виявлених дефектів. Статті, відіслані авторам на виправлення, слід повернути до редакції не пізніше ніж через три дні після одержання.

23. Датою надходження статті до журналу вважається день отримання редакцією остаточного варіанта тексту.

24. Коректури авторам не висилаються, проте, якщо це не порушує графік виходу журналу, можливе надання препринту, в якому допустиме виправлення лише помилок набору і фактажу.

25. Публікація матеріалів у «Одеському медичному журналі» платна. Оплата здійснюється після рецензування статей і схвалення їх до друку, про що авторів повідомляють додатково.

Реквізити для перерахування коштів за публікацію:

Одержувач платежу: Одеський національний медичний університет.

Банк: ГУДКСУ в Одеській області, МФО 828011, р/р 31258273210481, ідент. код 02010801.

У призначенні платежу обов'язково вказати: код 25010200, за друк статті у журналі (назва журналу).

Копію квитанції про сплату просимо надсилати поштою на адресу: Одеський національний медичний університет, редакція журналу (назва журналу), Валіховський пров., 2, м. Одеса, 65082; факс (048) 723-22-15 для В. Г. Ліхачової; тел. (048) 728-54-58 (р.), (097) 977-23-31 (м.), e-mail: vera@odmu.edu.ua.

26. Статті для публікації направляти за адресою: Одеський національний медичний університет, редакція «Одеського медичного журналу», Валіховський пров., 2, м. Одеса, 65082.

27. Статті, що не відповідають цим правилам, не розглядаються.

Редакційна колегія

Порядок рецензування рукописів наукових статей, які надходять для публікації в редакцію «Одеського медичного журналу»

Наукові статті, які надходять для публікації в редакцію «Одеського медичного журналу», підлягають рецензуванню.

Рецензентами журналу є досвідчені фахівці — доктори наук, члени редколегії журналу та його редакційної ради. Коли є потреба, редакція залучає до рецензування сторонніх фахівців. Допускається публікація наукової статті за письмовим поданням членів редакційної колегії та редакційної ради.

Під час рецензування оцінюються відповідність статті тематиці журналу та її назві, актуальність і науковий рівень, достоїнства й недоліки, відповідність оформлення статті вимогам редакції. Наприкінці робиться висновок про доцільність публікації.

Рецензія надається автору статті на його запит без підпису, вказівки прізвища, посади і місця роботи рецензента.

Якщо рецензент рекомендує виправити або доопрацювати статтю, редакція відправляє автору текст рецензії для внесення в роботу відповідних змін.

Автору, стаття якого не була прийнята до публікації, на його запит відправляється мотивована відмова. Рукопис статті не повертається.

Якщо автор не згоден з думкою рецензента, він може дати мотивовану відповідь.

Коли є потреба, за погодженням з автором може бути проведено додаткове рецензування рукопису іншим фахівцем.

Остаточне рішення про публікацію статті та її терміни приймає редакційна колегія.

В окремих випадках за наявності позитивної рецензії можлива публікація статті за рішенням головного редактора або його заступника.

Після ухвалення рішення про публікацію статті редакція інформує про це автора з указанням терміну публікації.

Оригінали рецензій зберігаються в редакції протягом 1 року.

"ODES'KIJ MEDIČNIJ ŽURNAL"
("The Odessa Medical Journal")

Information about Edition

"Odes'kij medičnij žurnal" ("The Odessa Medical Journal") was founded in 1926. During a few years it was highly appreciated by scientists. The works of the famous scientists had been published there. But then, at the start of 30-s, the publication of the Journal was stopped. It was renewed only in 1997, and very soon the Journal won its authority again and took a proper place among other scientific editions of the country.

The founders of the Journal are the Ministry of Health of Ukraine and the Odessa National Medical University, the publisher — the Odessa National Medical University.

The editor-in-chief of the Journal since the time of its renewal is the academician of the NAMS of Ukraine, the Ukraine State Prize Winner V. M. Zaporozhan. The members of the editorial board and editorial council are the world-known scientists.

By decisions of Presidium of the Higher Attestation Commission of Ukraine N1-05/2 from the 27th of May, 2009 and N 1-05/5 from the 31st of May, 2011 "The Odessa Medical Journal" was included in the list of editions, which publish the basic results of dissertation works on medicine, biology and pharmacy. This fact determines the subject of its publications. About two hundred papers and reports are published in the Journal annually.

The Journal appears bimonthly. It comes to the most known libraries of the country, large scientific centers, some educational establishments. Its release is highly appraised outside of the country.

The Journal is distributed by subscription.

The Journal can be subscribed at any subscription point.

Subscription index — 48717.

THE MANUAL OF ARTICLE STYLE FOR "ODES'KIJ MEDIČNIJ ŽURNAL" ("THE ODESSA MEDICAL JOURNAL") HAS BEEN CHANGED

The articles taken according to the previous rules will be published. New articles are submitted by the new rules, indicated at the end of this issue, will be published in the next issues and on the sites of the Odessa National Medical University **www.odmu.edu.ua** and "The Odessa Medical Journal" **journal.odmu.edu.ua**.

The change of previous rules is caused by a necessity in deep integration of our edition into the world scientific space with its developed scientometrical tool, which allows to define precisely the role of any scientist, any edition in the scientific process. The time, when gaining a scientific degree without consideration of the world rating of a scientist will be impossible, is not so far.

The abstract scientometrical databasis Scopus is the greatest in the world. It determines a so-called Hirsch index (h-index), which, despite all criticism, is considered to be enough objective and reliable parameter of scientist's contribution to the science and his recognition in the scientific world.

So, our requirements to the articles remained basically the same. They changed only in the aspects, which directly concern their usage in the scientometrical databases. We draw authors' special attention to this fact, because Hirsh index, calculated by the system, mainly depends on strict observance by the author of the requirements given below.

THE MANUAL OF ARTICLE STYLE FOR "ODES'KIJ MEDIČNIJ ŽURNAL" ("THE ODESSA MEDICAL JOURNAL")

1. "Odes'kij medičnij žurnal" ("The Odessa Medical Journal") publishes theoretical and review articles, which cover important achievements of science, results of completed original clinical and experimental researches, basic results of dissertations on medicine, biology and pharmacy, and also memorial materials.

2. Problem articles with total volume of up to 8 pages, reviews — up to 10 pages, original and other types of articles — up to 6 pages, short reports — up to 2 pages are submitted.

3. Articles, which have been already published in other editions or were submitted for publication to some editions at the same time, as well as the works which are a remake of the articles published before and do not contain new scientific material or new scientific comprehension of already known material are not submitted.

4. The following materials are published in the Journal:

a) results of original researches concerning main directions of development of medical, biological and pharmaceutical sciences;

b) works on fundamental problems in biology, medicine, pharmacology and pharmacy:

— genetics and applied aspects of medical genetics;

— biophysical and morphofunctional analysis of cells of an organism at different types of pathology;

— works on modern cellular technologies;

— the modern elaborations in the field of general and clinical pharmacology and pharmacy;

— achievements in the field of study of etiology, pathogenesis and diagnostics of modern diseases;

— prophylaxis of diseases, inoculation, prevention of especially dangerous diseases;

c) reviews on the modern actual problems of biology, medicine and pharmacy;

d) information, chronicle, anniversaries.

5. An article should be submitted to editorial in two copies, signed by all the authors. By their signatures the authors guarantee that the article meets all the requirements of the manual of the article style for "The Odessa Medical Journal", experimental and clinical researches have been executed according to the international ethical norms of scientific researches, and also they give the publisher a right for publication of the article in the Journal, placing it and its materials on the Journal's site and in other sources.

6. An article is accompanied with a letter to the editorial staff, vised signature of the chief and the seal of the establishment where the work was done, and for the home authors also by the expert inference, that authorizes the open publication.

7. If used in the article materials are intellectual property of some organizations and have not been published before, an author should get permission for their publication from each of these organizations and send it together with the article.

8. The text is printed with 1.5-spacing throughout the text on a standard paper (width of fields: on the left, above and below by 2 cm, on the right — 1 cm) in Arial (Arial Cyr) or Times (Times Cyr) 14 points. The page of the text should contain no more than 30 lines.

9. The language of the articles is Ukrainian for home authors, Russian and English for foreign authors.

10. The material of the article should be placed in the following order:

a) UDC index;

b) initials and the last name of the author (authors);

c) title of the article;

d) a complete name of the establishment (establishments) where the work was done, city, country;

e) statement of a problem in general and its connection with important scientific and practical tasks;

f) analysis of the modern researches and publications, in which the given problem was initiated and which the author is guided by;

g) pointing out the parts of general problem which were not resolved before;

h) formulation of the aim of the article (raising a task);

i) statement of the basic material with complete substantiation of obtained scientific results;

j) conclusions from the given research and perspectives of subsequent works in this direction;

k) references;

l) two abstracts — in Russian up to 800 printing letters (0.45 page) and in English up to 1800 printing letters (1 page) after the following scheme: UDC index, initials and the last name of author (authors), title of the article, text of the abstract, key words (no more than five).

11. The abstract in English should shortly reproduce the structure of the article, including introduction, purpose and task, methods, results, conclusions, key words. Initials and the last name of author (authors) are given in transliteration, the title of the article must be translated into English. The key words and other terms of the article should correspond to generally used medical terms cited in dictionaries. One should not use slang and abbreviations which are not in general use.

12. The chemical and mathematical formulas are inprinted or put down. The structural formulas are designed as figures. In formulas there are marked out: small and large letters (large ones by two hyphens from below, small ones — by two hyphens from above by a lead pencil); the Latin letters are underlined with a dark blue pencil; Greek ones — with a red pencil; subscript and superscript letters — by an arc line with a lead pencil.

13. The International System of Units (SI) should be used in the articles.

14. Figures (no more than two) and signatures to them are made separately. On the back side of every figure by a lead pencil one should indicate its number and title of the articles, and if necessary to note a top and bottom.

15. The tables (no more than three) should be placed on separate pages, be numbered and titled. The marginal notes should indicate the place of figures and tables. The information given in tables and figures must not be duplicated.

16. The references must contain the list of works for the last 5 years and only sometimes — more early publications. In the original works they quote no more than 10 sources, in the reviews — about 30. Every work in the literature list should be referred in the manuscript. The literature in the list is ordered according to reference to it in the text of the article, which is given in the square brackets, or after the alphabet. If the works of one and the same author are presented, they take place after the chronological order. The references shouldn't contain works, which have not been published yet.

17. The list is given in duplicate for every copy of the article, which are published separately one from another. The first copy is designed according to DSTU GOST 7.1:2006. The other one — fully duplicates the first one, but by the Roman alphabet after the schemes given below.

For articles:

Author A.A., Author B.B., Author C.C. Title of article. *Title of Journal* 2005; 5(129): 49-53.

The last names of authors and title of the Journal are given by the Roman alphabet in transliteration, title of the article — in translation into English.

For materials of conferences:

Riabinina, A.A., Berezina, E.V., Usol'tseva, N.V. Surface Tension and Lyotropic Mesomorphism in Systems Consisting of Nonionogenic Surfactant and Water, *Liotropnye zhidkie kristally and nanomaterialy: sbornik statei VII Mezhdunarodnoi nauchnoi konferentsii* (Lyotropic Liquid Crystals and Nanomaterials: Proceedings of the Seventh International Conference), Ivanovo: Ivanovskii Gos. Univ., 2009, 73-75.

The last names of authors are given in transliteration, title of the work — in translation into English. The main thing in descriptions of conferences is the name of conference in the language of original (is given in transliteration if there is not its English name), indicated by italic. Translation of the name into English is given in brackets. Imprint (place of holding a conference, place of publication, year, pages) — in English.

For monographs and other books:

Nenashev M.F. *Poslednee pravitel'stvo SSSR* [Last government of the USSR]. Moscow, KromPubl., 1993. 221 p.

The last names of authors are given in transliteration, title of the book — in italic in transliteration with

translated into English in the square brackets. Place of publication, year of publication, total number of pages — English, name of publishing house — in transliteration.

Please, note: in the references in the Roman alphabet it is necessary to indicate all the authors of the literary source, which you refer to (DSTU GOST of 7.1:2006 does not provide it). Also one should not use the signs of division: // and — , which are provided by DSTU GOST of 7.1:2006. The name of the source (Journal, conference, book) is always indicated by italic.

The observance of these rules will provide the true representation of quoted sources in the majority of abstract scientometrical databases.

18. Abbreviations of words and word combinations are given according to DSTU 3582-97 and GOST 7.12-93.

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The reviews should estimate if the article corresponds to the subject of the Journal and its title, actuality and scientific level, advantages and disadvantages, correspondance of the article design to the editorial requirements. The conclusion about advisability of publication is drawn in the end.

A review is given to the author of the article on his demand without signature, pointing the last name, occupation and places of the work of a reviewer.

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Чт	3 10 17 24 31	7 14 21 28	7 14 21 28
Пт	4 11 18 25	1 8 15 22	1 8 15 22 29
Сб	5 12 19 26	2 9 16 23	2 9 16 23 30
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Вт	2 9 16 23 30	6 13 20 27	3 10 17 24
Ср	3 10 17 24 31	7 14 21 28	4 11 18 25
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Сб	6 13 20 27	3 10 17 24 31	7 14 21 28
Нд	7 14 21 28	4 11 18 25	1 8 15 22 29

	Жовтень	Листопад	Грудень
Пн	7 14 21 28	4 11 18 25	2 9 16 23 30
Вт	1 8 15 22 29	5 12 19 26	3 10 17 24 31
Ср	2 9 16 23 30	6 13 20 27	4 11 18 25
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Пт	4 11 18 25	1 8 15 22 29	6 13 20 27
Сб	5 12 19 26	2 9 16 23 30	7 14 21 28
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