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050004, Алматы қ., Желтоқсан көш. 62,
тел. 7(727) 2795306

http://vhk.kz, e-mail: inkar_sagatov@mail.ru

Әрленім және беттеу:

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Адрес редакции:

050004, г. Алматы, ул. Желтоқсан, 62,
тел. 7 (727) 2795306

http://vhk.kz, e-mail: inkar_sagatov@mail.ru

Дизайн и верстка:

ИП «ДАНИЛЕНКО»,
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ХИРУРГИЯ

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Бүйрек трансплантациясы бар науқастардағы такролимус фармакокинетикасының негізгі реттегіші ретінде СYP3A5 генетикалық полиморфизмі: қазақ популяциясындағы деректер5

Османов О.М., Магомедов М.М.
Түйінді жемсаумен ауыратын науқастарды хирургиялық емдеудің заманауи принциптері 10

Макаров В., Баймухаметов Ә., Есентаева С., Қалматаева Ж., Кадырбаева Р., Семенова А., Балтаев Н., Ирсадиев Р., Оразбаев А.
Кеуде ішілік ісіктерді хирургиялық емдеу көлемін таңдау: жақын нәтижелерді талдау 16

Семенов В.Г., Джульфаев Д.И., Жамашев Д.К., Даврешов А.А., Чачидзе Р.Г.
Өкше (ахилл) сіңірінің ескі зақымдануларын емдеу25

Чупин А.Н., Мамырбекова С.А., Алдангарова Г.А.
Жатыр ішілік патологиясы бар науқастарға гинекологиялық көмек көрсетуді жақсарту мақсатында биполярлық мини-резектоскопты қолданудың тиімділігін бағалау . . 31

Ширтаев Б.К., Сундетов М.М., Ақылбеков С.Д., Құрбанов Д.Р., Халықов Қ.Ұ., Еримова Н.Ж., Кокимбаев Д.А., Алханов Б.А.
Оң негізгі бронхтың жарақаттан кейінгі тыртықты тарылуының клиникалық жағдайы 36

ДИАГНОСТИКА ЖӘНЕ ЕМДЕУ

Тореева Ш.М., Кошербаева Л.К., Алдангарова Г.А.
Түтікті-перитонеальды бедеулік. Емі. (Әдебиет шолуы) 2 Бөлім 40

ХИРУРГИЯ

Баймаханов Б.Б., Чорманов А.Т., Медеубеков У.Ш., Сырымов Ж.М., Мададов И.К., Дабылтаева К.С., Белгібаев Е.Б., Набиев Е.С., Садуақас Н.Т., Байыз А.Ж., Аипов Б.Р.
Генетический полиморфизм СYP3A5 как ключевой регулятор фармакокинетики такролимуса у пациентов с трансплантатом почки: данные в казахской популяции. 5

Османов О.М., Магомедов М.М.
Современные принципы хирургического лечения больных с узловым зобом 10

Макаров В., Баймухаметов Ә., Есентаева С., Қалматаева Ж., Кадырбаева Р., Семенова А., Балтаев Н., Ирсадиев Р., Оразбаев А.
Выбор объема хирургического лечения при опухолях внутригрудной локализации: анализ непосредственных результатов 16

Семенов В.Г., Джульфаев Д.И., Жамашев Д.К., Даврешов А.А., Чачидзе Р.Г.
Лечение застарелых повреждений пяточного (ахиллова) сухожилия . . 25

Чупин А.Н., Мамырбекова С.А., Алдангарова Г.А.
Оценка эффективности применения биполярного мини-резектоскопа для улучшения оказания гинекологической помощи пациенткам с внутриматочной патологией 31

Ширтаев Б.К., Сундетов М.М., Ақылбеков С.Д., Курбанов Д.Р., Халықов Қ.Ұ., Еримова Н.Ж., Кокимбаев Д.А., Алханов Б.А.
Клинический случай посттравматического рубцового стеноза правого главного бронха 36

ДИАГНОСТИКА И ЛЕЧЕНИЕ

Тореева Ш.М., Кошербаева Л.К., Алдангарова Г.А.
Трубно-перитонеальное бесплодие. Лечение. (Обзор литературы) Часть 2 40

SURGERY

Baimakhanov B.B., Chormanov A.T., Medeubekov U.Sh., Syrymov Zh.M., Madadov I.K., Dabyltaeva K.S., Belgibaev E.B., Nabiev E.S., Saduakas N.T., Baiyz A.Zh., Aipov B.R.
Genetic polymorphism of CYP3A5 as a key regulator of pharmacokinetics of tacrolimus in kidney transplant patients: evidence in kazakh population 5

Osmanov O.M., Magomedov M.M.
Modern principles of surgery treatment of patients with nodular goiter 10

Makarov V., Baimukhametov E., Yessentayeva S., Kalmatayeva Zh., Kadyrbayeva R., Semenova A., Baltaev N., Irsaliev R., Orazbaev A.
Choice of pulmonary resections in intrathoracic tumors: short-term outcomes 16

Semenov V.G., Dzhulfaev D.I., Zhamashev D.K., Davreshov A.A., Chachidze R.G.
Treatment of chronic injuries calcaneal (achilles) tendon 25

Chupin A.N., Mamyrbekova S.A., Aldangarova G.A.
Evaluation of the effectiveness of the use of a bipolar mini-resectoscope to improve the provision of gynecological care to patients with intrauterine pathology 31

Shirtaev B.K., Sundetov M.M., Akilbekov S.D., Kurbanov D.R., Khalykov K.U., Yerimova N.Zh., Kokimbayev D.A., Alkhanov B.A.
A clinical case of post-traumatic cicatricial stenosis of the right main bronchus 36

DIAGNOSTIC AND TREATMENT

Toreeva Sh.M., Kosherbayeva L.K., Aldangarova G.A.
Tubal-peritoneal infertility. Treatment. (Review) Part 2 40

Аубакирова А.Т., Абдилова Г.Б., Катаева К., Тәртіпқызы Д., Давенова Н.А., Нургалиева А.Н., Дакенова Г.Б.
Сепсис кезінде Т-реттеуші жасушалар мен миелоидты супрессорлық жасушалардың болжамдық клиникалық мәні (Әдебиет шолуы) 44

Реметова А.А., Калмаханов С.Б.
2 типті қант диабетімен ауыратын науқастарды кешенді шипажайлық емдеуде ішетін минералды суларды қолдану 48

ОРТАЛЫҚ ТЫНЫСЫ

Дәрігер-урологтардың Түркістан облысына іс-сапары 52

МЕРЕЙТОЙ

Әбілбек Игасимұлы Чиныбаевтың 80-жылдық мерейтойына 53

ӘРІПТЕСТІ ЕСКЕ АЛУ

Профессор Қалыбай Дурманұлы Дурмановтың туғанына 80 жыл 54

Аубакирова А.Т., Абдилова Г.Б., Катаева К., Тәртіпқызы Д., Давенова Н.А., Нургалиева А.Н., Дакенова Г.Б.
Прогностическое клиническое значение миелоидных супрессорных клеток и Т регуляторных клеток при сепсисе (Обзор литературы) 44

Реметова А.А., Калмаханов С.Б.
Применение питьевых минеральных вод в комплексном санаторном лечении больных сахарным диабетом 2 типа 48

СОБЫТИЯ ЦЕНТРА

Поездка врачей-урологов в Туркестанскую область 52

ЮБИЛЕЙ

К 80-летию юбилею Чиныбаева Абилябека Игасимовича 53

ПАМЯТИ КОЛЛЕГИ

К 80-летию со дня рождения профессора Дурманова Калыбая Дурмановича 54

Aubakirova A.T., Abdilova G.B., Kataeva K., Tartipkyzy D., Davenova N.A., Nurgalieva A.N., Dakenova G.B.
Prognostic clinical significance of myeloid suppressor cells and T regulatory cells in sepsis (Review). 44

Remetova A.A., Kalmakhanov S.B.
The use of drinking mineral waters in the complex sanatorium treatment of patients with type 2 diabetes mellitus 48

CENTER EVENTS

Visit of urologists to the Turkestan region 52

ANNIVERSARY

To the 80th anniversary of Abilbek Igasimovich Chinybayev 53

IN MEMORY OF COLLEAGUE

To the 80th birthday of Professor Kalybai Durmanovich Durmanov. 54

GENETIC POLYMORPHISM OF CYP3A5 AS A KEY REGULATOR OF PHARMACOKINETICS OF TACROLIMUS IN KIDNEY TRANSPLANT PATIENTS: EVIDENCE IN KAZAKH POPULATION

Baimakhanov B.B., Chormanov A.T., Medeubekov U.Sh., Syrymov Zh.M., Madadov I.K., Dabyltaeva K.S., Belgibaev E.B., Nabiev E.S., Saduakas N.T., Baiyz A.Zh., Aipov B.R.
JSC «National Scientific Center of Surgery named after A.N. Syzganov», Almaty, Kazakhstan

Abstract

Objectives: identification of relationship of CYP3A5 genetic polymorphism with tacrolimus pharmacokinetics in kidney transplant patients in Kazakh population.

Immunosuppressive therapy with the use of tacrolimus is one of the main ones in kidney transplantation. The survival and maintenance of satisfactory graft function in a technically perfect operation depends in most cases on immunological factors. At the same time, there is a question of a personal approach to immunosuppressive therapy of kidney recipients in patients of the Kazakh population before and after surgery. The genetic polymorphism of CYP3A5 is an important link affecting the concentration of tacrolimus and potentially able to predict the optimal dosage of tacrolimus in kidney recipients in the Kazakh population

We examined 80 kidney recipients for the presence of CYP3A5 genetic polymorphism. All the patients studied were selected from the ethnic population. Out of the total number of recipients: 37-men and 43-women. The median age was 37±8 years. All the studied patients underwent a related kidney transplant. The induction was performed using basiliximab or anti-thymocytic globulin (ATG). Immunosuppressive regimen was Tacrolimus + Mycophenolic acid + corticosteroids. Postoperatively tacrolimus concentration was taken at 2, 5, 7, 10 and 14th day after the surgery.

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Baimakhanov B.B.
orcid.org/0000-0002-9839-6853

Chormanov A.T.
orcid.org/0000-0003-3513-1935

Medeubekov U.Sh.
orcid.org/0000-0003-2893-2996

Syrymov Zh.M.
orcid.org/0000-0002-7708-3284

Madadov I.K.
orcid.org/0000-0003-2241-8603

Dabyltaeva K.S.
orcid.org/0000-0003-1226-0005

Belgibaev E.B.
orcid.org/0000-0002-9439-2628

Nabiev E.S.
orcid.org/0000-0002-6167-1962

Saduakas N.T.
orcid.org/0000-0002-5249-1783

Baiyz A.Zh.
orcid.org/0000-0002-6075-2787

Aipov B.R.
orcid.org/0000-0003-2124-0065

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tacrolimus, kidney transplantation, genetic polymorphism, immunosuppression

Бүйрек трансплантациясы бар науқастардағы такролимус фармакокинетикасының негізгі реттегіші ретінде CYP3A5 генетикалық полиморфизмі: қазақ популяциясындағы деректер

Баймаханов Б.Б., Чорманов А.Т., Медеубеков Ұ.Ш., Сырымов Ж.М., Мададов И.К., Дабылтаева Қ.С., Белгібаев Е.Б., Набиев Е.С., Садуақас Н.Т., Байыз А.Ж., Аипов Б.Р.
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Аңдатпа

Мақсаты: қазақ популяциясындағы бүйрек трансплантациясынан кейінгі науқастардағы CYP3A5 генетикалық полиморфизмінің такролимустың фармакокинетикасымен байланысын анықтау.

Такролимус қолдануы иммуносупрессивті терапия бүйрек трансплантациясының негізгі әдістерінің бірі болып табылады. Техникалық тұрғыда жақсы орындалған операция кезінде трансплантаттың қанағаттанарлық функциясының сақталуы және қызмет етуі көп жағдайда иммунологиялық факторларға байланысты. Бұл ретте қазақ популяциясындағы пациенттердің бүйрек реципиенттерін иммуносупрессивті терапиясына отаға дейінгі және отадан кейінгі кезеңдерде дербес көзқарас туралы мәселе туындайды. CYP3A5 генетикалық полиморфизмі такролимус концентрациясына әсер ететін және қазақ популяциясындағы бүйрек реципиенттерінде такролимустың оңтайлы дозасын болжауға ықтимал қабілетті маңызды буын болып табылады.

Біз CYP3A5 генетикалық полиморфизмінің болуына бүйректің 80 реципиенттерін зерттедік. Зерттелген барлық науқастар этникалық популяциялардан таңдалды. Реципиенттердің жалпы санынан: 37-ерлер және 43-әйелдер. Орташа жасы 37±8 жыл болды. Барлық зерттелген науқастарға бүйрек трансплантациясы жасалды. Индукция базиликсамаб немесе анти-тимоцитарлық глобулин (АТГ) қолдану арқылы жүргізілді. Иммуносупрессивті режим такролимус + микофенол қышқылы + стероидтер болды. Отадан кейінгі кезеңде такролимус концентрациясының 2,5,7,10 және 14 күндердегі өзгерісі зерттелді.

Түйін сөздер

такролимус, бүйрек трансплантациясы, генетикалық полиморфизм, иммуносупрессия

Генетический полиморфизм CYP3A5 как ключевой регулятор фармакокинетики такролимуса у пациентов с трансплантацией почки: данные в казахской популяции

Баймаханов Б.Б., Чорманов А.Т., Медеубеков У.Ш., Сырымов Ж.М., Мададов И.К., Дабылтаева К.С., Белгибаев Е.Б., Набиев Е.С., Садуакас Н.Т., Байыз А.Ж., Аипов Б.Р.
АО «Национальный научный центр хирургии им. А. Н. Сызганова», г. Алматы, Казахстан

Аннотация

Цель: выявить взаимосвязь генетического полиморфизма CYP3A5 с фармакокинетикой такролимуса у реципиентов почки в казахской популяции.

Иммуносупрессивная терапия с применением такролимуса является одной из основных при трансплантации почки. Выживаемость и сохранение удовлетворительной функции трансплантата при технически идеально выполненной операции, зависит в большинстве случаев от иммунологических факторов. При этом встает вопрос о персональном подходе в иммуносупрессивной терапии реципиентов почки пациентов казахской популяции до - и в послеоперационном периодах. Генетический полиморфизм CYP3A5 является важным звеном, влияющим на концентрацию такролимуса и потенциально способным предсказать оптимальную дозировку такролимуса у реципиентов почки в казахской популяции

Нами было исследованно 80 реципиентов почки на наличие генетического полиморфизма CYP3A5. Все исследованные пациенты были выбраны из этнической популяции. Из общего числа реципиентов: 37 – мужчины и 43 – женщины. Средний возраст которых составил 37±8 лет. Всем исследуемым пациентам была выполнена родственная трансплантация почки. Индукция была проведена с применением базиликсамаба или анти-тимоцитарного глобулина (АТГ). Иммуносупрессивный режим был по схеме такролимус+микофеноловая кислота+стероиды. В послеоперационном периоде было исследовано изменение концентрации такролимуса на 2, 5, 7, 10 и 14 дни.

Ключевые слова

такролимус, трансплантация почки, генетический полиморфизм, иммуносупрессия

Introduction

Kidney transplantation is the most preferable treatment option of terminal chronic kidney disease. The main advantage of kidney transplantation is that graft totally replaces the function of diseased organ. Improvement of the quality of life of patients and return to their daily activities is another great advantage of this option.

Nowadays in Kazakhstan there is an active development of kidney transplantation. One of the most important objectives is to improve the survival rates of graft. With the improvement of donor selection, surgical technique and rational immunosuppressive treatment rates of short-term graft survival greatly increased. For instance, in Kazakhstan 1-year graft survival from living related donor is 91%. Despite these high indicators of 1-year graft survival, 5-year graft survival rates remain to be low. In USA 5-year graft survival from deceased donor is up to 80%, whereas from living donor is from 82 to 90 %, respectively. So it is of paramount interest to improve the rates of long term graft survival [1].

The calcineurin inhibitor tacrolimus are the most widely used immunosuppressive agent. This drug represents a narrow therapeutic index and high inter-individual pharmacokinetic variability, so monitoring its blood level is required to avoid rejection and reduce toxicity [2].

The calcineurin inhibitors tacrolimus is catalyzed by cytochrome P450 CYP3A enzymes. CYP3A4 and CYP3A5 have been identified as the major enzymes

responsible for the metabolism of calcineurin inhibitors in CYP3A subfamilies [3].

The presence of CYP3A4 and CYP3A5 in the intestinal mucosa and in hepatic cells contributes to a first-pass effect as drug molecules are metabolized prior to reaching the systemic circulation. Genetic polymorphism in these 2 enzymes accounts for a significant part of the interindividual variability observed with tacrolimus bioavailability. The best studied genetic variation is in the CYP3A5 gene [4].

The wild-type CYP3A5 *1 allele is associated with greater production of functional CYP3A5 enzyme, thus leading to higher drug-metabolizing activity by CYP3A overall. The CYP3A45*1/*1 genotype increases tacrolimus clearance by 2-fold, while the heterozygous CYP3A5*1/*3 genotype results in approximately 1.7-fold greater clearance compared to the CYP3A5*3/*3 population [5-7] CYP3A5 *3/*3 has 48% lower oral clearance compared to CYP3A5 expressers [8].

In this way, we investigated the personalization and rationalization of immunosuppressive treatment. In our country as in whole world genetic factors, determining long-term kidney graft survival, represents a great relevancy in transplantation. The determination of genetic polymorphism of CYP3A5 gives us the opportunity to predetermine the changes in blood concentrations of tacrolimus, better control of immunosuppressive therapy and this will positively affect the long-term graft survival.

The study aimed to determine the significance of CYP3A5 genetic polymorphism in regulation of

tacrolimus pharmacokinetics in kidney transplant patients in Kazakh population.

Material and Methods

We retrospectively studied 80 kidney transplant recipients. Of them – 32 were female and 48 male patients. Mean age 36±12 years old. All patients were selected from Kazakh population and were investigated for CYP3A5 genetic polymorphism (single-nucleotide polymorphism, rs776746, also known as 6986A>G). Patients underwent related living donor kidney transplantation. There were no substantial differences in surgical technique or warm/cold ischemic times. Graft function was immediate in all cases.

Immunosuppression

Induction therapy was either with basiliximab or Anti-Tymocit globulin. Immunosuppressive regimen was Tacrolimus + Mycophenolic acid + corticosteroids.

Tacrolimus concentration was measured by chemiluminescence method. Tacrolimus was administered 0.1 mg/kg/ body weight. Tacrolimus concentration level was taken initially at 2 postoperative days and furtherly at 5th, 7th, 10th and 14th, respectively. Dose addition/reduction was by 1.0 mg. Accepted tacrolimus target level was 10-13 ng/ml.

Statistics

Patients were arranged according to the results by Fisher’s test and correlation of graft function and genetic polymorphism of CYP3A5 was assessed Mann-Whitney U test. P < 0.05 was given as significant.

Results

According to the results in our study 61.25% (n=49) of patients were homozygotes, CYP3A5*3*3 carriers (non-expressers) and 38.75% (n=31) were heterozygotes, CYP3A5*1*3 carriers (with one ex-

pressor allele). Patients were arranged by sex/type of polymorphism by Fisher’s test. There were no significant differences in sex/CYP3A5 genetic polymorphism in patients Table 1.

Patients were divided into 2 groups: homozygotes and heterozygotes. Tacrolimus concentration was measured on 2, 5th, 7th, 10th and 14th days after surgery and at discharge. There were significant differences in concentrations on 2nd, 5th, 7th and 10th days in both groups (p = 0.02, 0.01, 0.12 and 0.016, respectively). There were no significant statistical differences in tacrolimus concentration on 14 day after the surgery and at discharge (p = 0.085 and 0.171, respectively). In both groups tacrolimus almost reached target level at the end of 2nd week, but in heterozygotes increase was more gradual and predictable rather than in homozygotes (Fig.1). There were no substantial differences in graft function (Table 2). Creatinine level normalized gradually in both groups and there was not significant differences in both groups at discharge (p = 0.834 (Fig.2)

Discussion

Tacrolimus is a commonly used immunosuppressant after kidney transplantation. It has a narrow therapeutic range and demonstrates wide interindividual variability in pharmacokinetics, leading to potential underimmunosuppression or toxicity. Genetic polymorphism in CYP3A5 enzyme expression contributes to differences in tacrolimus bioavailability between individuals. Individuals carrying one or more copies of the wild-type allele *1 express CYP3A5, which increases tacrolimus clearance. CYP3A5 expressers require 1.5 to 2-fold higher tacrolimus doses compared to usual dosing to achieve therapeutic blood concentrations. Individuals with homozygous *3/*3 genotype are CYP3A5 nonexpressers. CYP3A5 nonexpression is the most frequent phenotype in most ethnic populations,

			CYP3A5*1*3	CYP3A5*3*3	p
Sex	Female	N	13	19	1,000
		%	42,0%	38,7%	
	Male	N	18	30	
		%	58,0%	61,2%	
Total %		N	31	49	
		100,0%	100,0%		

Table 1. Arrangement of patients due to gender-CYP genetic polymorphism relationship

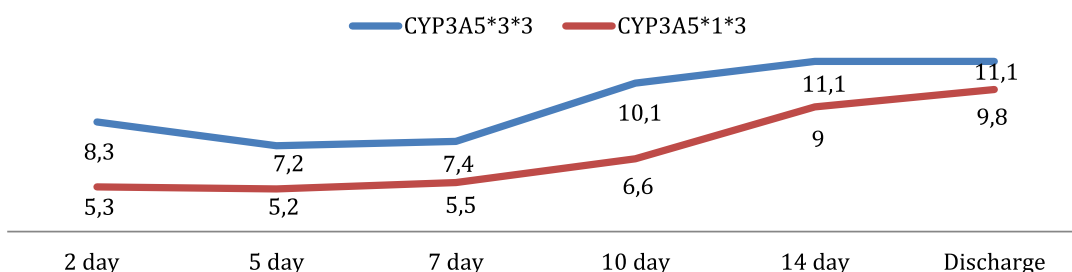


Fig. 1 Changes of tacrolimus concentration (ng/ml) with CYP 3A5 genetic polymorphism

Fig. 2
Changes of creatinine ($\mu\text{mol/l}$) level in kidney patients with CYP3A5 genetic polymorphism
Notes:
B - Time before the operation, and D - time at discharge

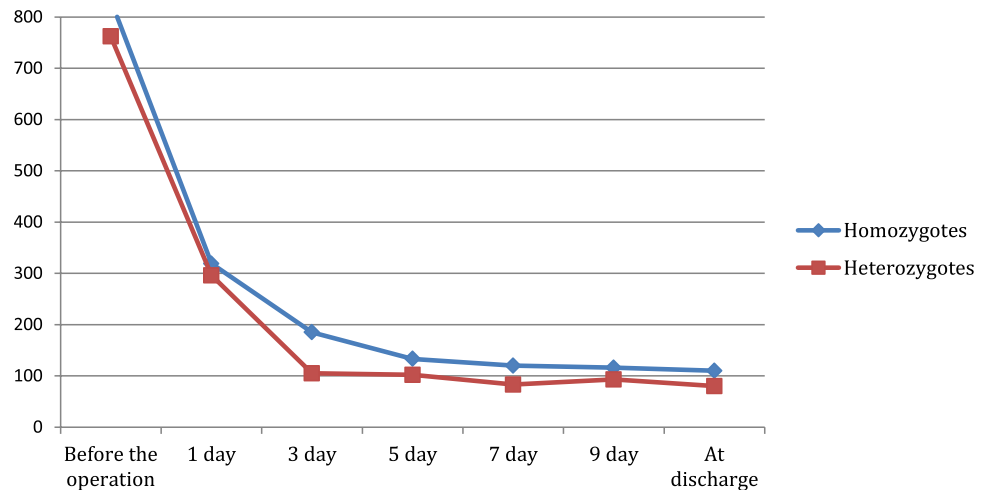


Table 2.
Changes of Tacrolimus concentration in both groups (Mann - Whitney U test)

Type of polymorphism		2 day	5 day	7 day	10 day	14 day	Discharge
CYP3A5*1*3	N	31	31	31	31	31	31
	Average	5,3	5,2	5,5	6,6	9,0	9,8
	Std. Deviation	3,0	2,6	1,7	2,2	2,6	1,9
	Median	4,4	4,6	5,5	6,8	8,3	9,3
	Range	10,2	9,8	6,00	7,90	8,9	5,0
CYP3A5*3*3	N	49	49	49	49	49	49
	Average	8,3	7,2	7,4	10,1	11,1	11,1
	St. D	5,2	2,4	2,2	3,9	4,4	2,9
	Median	7,1	6,5	6,8	10,0	9,9	11,0
	Range	27,0	8,2	8,20	14,10	19,4	13,7
p		0,020	0,010	0,012	0,016	0,085	0,171

except blacks. Differences between CYP3A5 genotypes in tacrolimus disposition have not translated into differences in clinical outcomes, such as acute rejection and graft survival. Therefore, although genotype-based dosing may improve achievement of therapeutic drug concentrations with empiric dosing, its role in clinical practice is unclear [11].

The effect of CYP3A5 *1 and *3 alleles on tacrolimus pharmacokinetics is consistently and extensively documented across a multitude of studies over the past 15 years [9, 10]. The goal of genotype-based dosing is to provide empiric dosing that allows rapid achievement of therapeutic drug concentrations, particularly in the initial days after transplant. In one retrospective study, an empiric weight-based starting dose of 0.1 mg/kg was used to target a therapeutic range of 4-8 mcg/mL [12]. Among CYP3A5 non-expressers (CYP3A5*3/*3), 50% of patients achieved the target range by day 3 of therapy. Among CYP3A5 expressers (CYP3A5*1/*3 or *1/*1), however, only 35.3% of patients achieved through concentrations within the therapeutic range by day 3. Use of therapeutic drug monitoring did allow for rapid dosing correction. By day 7, 64.2% of expressers, compared to 55.4% of non-expressers, achieved therapeutic trough concentrations. These results suggest that CYP3A5 genotyping is likely more useful if available before kidney transplant.

Similar results were received in clinical trial conducted by Quteineh L. and co-authors. In total 136 kidney recipients were studied. As was in previous investigation patients with CYP3A5*1*1 genotype need higher doses of tacrolimus to reach the target concentration. Interestingly the situation remained the same for subsequent 6 and 12 months. CYP3A5 genetic polymorphism was not associated with tacrolimus nephrotoxicity but influenced the dose adjustment. Authors suggest preoperative evaluation of CYP3A5 genetic polymorphism, especially CYP3A5*1 carriers [13].

In kidney recipients with CYP3A5*1*1 and *1*3, tacrolimus concentration remained low even after dose adjustment in contrast to CYP3A5*3*3 carriers. For instance, half of patients with CYP3A5*1 after 7 days from initiation of immunosuppression tacrolimus was less than 5 ng/ml, whereas in CYP3A5*3 carriers – more than 20 ng/ml. Thus this genetic factor is one of most important regulators of rational immunosuppressive treatment [14].

Acute rejection episodes were more frequent in expressers, and they may require higher doses of tacrolimus. Similarly, tacrolimus nephrotoxicity was more frequent in non-expressers. Therefore, CYP3A5 polymorphism analysis before renal transplant may help determine the optimal dose of tacrolimus in this population and prevent acute rejection episodes or tacrolimus toxicity [9, 15].

In our clinical study there were not CYP3A5*1*1 carriers, thus in Kazakh population there are seen only *1*3 and *3*3 genetic polymorphisms. In all cases graft function was immediate. There were not any cases of acute graft rejection in both groups. There was a statistical difference in tacrolimus pharmacokinetics in both groups, but this does not affect graft function and all patients were discharged with good functioning graft. There was also a correlation of tacrolimus concentration with body mass. So in patients with high body mass index tacrolimus had peak rises up to 20 ng/ml soon after the surgery and subsequently gradual decline. In this patients creatinine level normalized slowly. Tacrolimus didn't have any correlation with age and sex.

Conclusion

It is obvious from received results, that genetic polymorphism of CYP3A5 influences tacrolimus blood concentrations, that appear to be key factor

in immunosuppression [16]. Even in rational choice of dose of immunosuppressive agent, genetic factor must be considered as well. In order to improve long-term graft survival rates it is important to maintain therapeutic concentration of tacrolimus in blood. In this way it is important to determine the CYP3A5 genetic polymorphism preoperatively [17], as one of approved genetic determinants of graft survival and for the correct selection of initial dose.

In Kazakh population most patients are non-expressers and this is a national characteristic. Patients reached tacrolimus trough level quickly at low doses. We expect that genotype-based dosing may be the key factor in determination of preferred doses of tacrolimus in each individual. Moreover, genotype-based patterns of dose regimen are now being investigated in order to ease the choice of suitable dose regimen. Rational immunosuppressive treatment leads to prolonged graft function and genetic factors appear to be the key factor in drug dose selection.

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MODERN PRINCIPLES OF SURGERY TREATMENT OF PATIENTS WITH NODULAR GOITER

Magomedov M.M.

orcid.org/0000-0002-3335-525x

Osmanov O.M.

orcid.org/0000-0002-6000-2425

Osmanov O.M.¹, Magomedov M.M.²

¹State Budgetary Institution of Healthcare "Clinical City Hospital №67", Moscow, Russia

²Federal State Budgetary Educational Institution of Higher Education «Dagestan state medical university», Department of surgery, faculty of advanced training and professional retraining of specialists with the course of endoscopic surgery, Makhachkala, Republic of Dagestan, Russia

Abstract

Purpose of the study. To justify and confirm the differentiated approach to choosing the volume of surgical intervention in benign nodular goiter. **Materials and methods.** A prospective analysis of 180 patients who underwent thyroid surgery was performed; 11 (6.1%) were men and 169 (93.9%) were women aged 20-65 years. The duration of the patients' disease was 8 months to 12 years. All patients with benign non-toxic goiter underwent a thorough evaluation of changes in the level of thyroid hormones in serum, ultrasound of the thyroid gland, and aspiration biopsy of the thyroid gland. **Results.** In laboratory studies, a high level of malignancy is observed in patients with higher levels of TSH and antibodies, TG and antibodies, TPO. There were no significant differences in the values of T3 and T4. In the ultrasound study, the average and maximum diameter of malignant nodes were significantly smaller than that of benign ones (1.99 ± 1.88 cm; $p < 0.001$). The difference between surgical procedures described as subtotal, total, and hemi-thyroidectomy was statistically significant. In 128 (71.1%) patients nodes were located in one lobe, 68 (37.8%) patients had multiple nodes, and 52 (28.9%) had solitary nodes in one of the thyroid lobes. Intraoperatively, 68 (37.7%) patients underwent cytomorphological examination of removed thyroid tissue. Hemithyroidectomy was performed in only 57 (31.6%) patients. Subtotal thyroidectomy was performed in 78 (43.3%) patients, and total thyroidectomy was performed in 45 (25%) patients. With the development of hematoma, one patient was re-operated after total thyroidectomy. Hypoparathyroidism was diagnosed in 2 (4.4%) patients after thyroidectomy, and in 1 (1.3%) patient after subtotal thyroidectomy. 3 patients had transient laryngeal paresis after thyroidectomy. Hypothyroidism developed in 14 (24.6%) patients after hemithyroidectomy, in 50 (64.1%) patients after subtotal thyroidectomy and in 45 (100%) after thyroidectomy. **Conclusion.** The decision of surgical intervention should be differentiated with respect to the choice of surgical intervention tactics.

Keywords

thyroidectomy, subtotal thyroidectomy, hemithyroidectomy, hypothyroidism, hypoparathyroidism

Түйінді зобпен аурытын науқастарды хирургиялық емдеудің заманауи принциптері

Османов О.М.¹, Магомедов М.М.²

¹МБДСМ №67 Қалалық клиникалық аурухана, Мәскеу қ., Ресей

²ФМББМ ЖО «Дагестан мемлекеттік медицина университеті», Эндоскопиялық хирургия курсы бар ҚҚД және БАФ хирургия кафедрасы, Махачкала қ., Дағыстан Республикасы, Ресей

Аңдатпа

Зерттеу мақсаты. Қатерсіз түйінді жемсау кезіндегі отаның көлемін анықтауды таңдаудағы дифференциалды тәсілдемені негіздеу және бекіту. **Материалдар мен әдістер.** Қалқанша безіне ота жасатқан 180 науқасқа проспективті талдау жүргізілді. Оның ішінде – 20-65 жас аралығындағы 11 (6,1%) ер адамдар және 169 (93,9%) әйелдер. Науқастардың ауру ұзақтығы – 8 айдан 12 жылға дейін. Қатерсіз токсикалық емес жемсауы бар науқастардың барлығы қан сарысуындағы ҚБ гормондары деңгейінің өзгерістерін мұқият бағалаудан, қалқанша безінің УДЗ-сынан, қалқанша безінің аспирациялық биопсиясынан өтті. **Нәтижелер:** Зертханалық зерттеу кезінде қатерліліктің жоғары деңгейі ТТГ және АТ, ТТ және АТ, ТПО жоғары деңгейі бар науқастарда байқалды. Т3 және Т4 мөңдерінде нақты айырмашылық анықталған жоқ. УДЗ зерттеу кезінде қатерсіз түйіндерге қарағанда, қатерлі түйіндердің орташа және макси-малды диаметрі едәуір аз болды ($1,99 \pm 1,88$ см; $p < 0,001$). Субтоталды, тоталды және гемитиреоидэктомия ретінде сипатталған хирургиялық шаралар арасындағы айырмашылық статистикалық маңызды болды. Науқастардың 128-інде (71,1%) түйіндер бір бөлікте, науқастардың 68-інде (37,8%) көптеген түйіндер болған, ал 52 (28,9%) науқаста қалқанша безінің бір бөлігінде жеке түйіндер болды. Интраоперациялық кезеңде 68 (37,7%) науқастың қалқанша бездерінің жойылған тіндеріне цитоморфологиялық зерттеу жүргізілді. 57 (31,6%) науқасқа гемитиреоидэктомия жасалды. 78 (43,3%) науқасқа субтоталды тиреоидэктомия, ал 45 (25%) науқасқа тоталды тиреоидэктомия орындалды. Гематоманың дамуына байланысты тоталды тиреоидэктомиядан кейін бір науқасқа, гипопаратиреоз тиреоидэктомиядан кейін 2 (4,4%) науқасқа, субтоталды тиреоидэктомиядан кейін 1 (1,3%) науқасқа қайтадан операция жасалды. 3 науқаста тиреоидэктомиядан кейін көмейдің транзиторлық жарасы пайда болды. Гемитиреоидэктомиядан кейін 14 (24,6%), субтоталды тиреоидэктомиядан кейін 50 (64,1%) және тиреоидэктомиядан кейін 45 (100%) науқаста гипотиреоз дамыды. **Қорытынды.** Оталық араласудың шешімі отаның тактикасын таңдауға қатысты саралануы тиіс.

Түйін сөздер

тиреоидэктомия, субтоталды тиреоидэктомия, гемитиреоидэктомия, гипотиреоз, гипопаратиреоз

Современные принципы хирургического лечения больных с узловым зобом

Османов О.М.¹, Магомедов М.М.²

¹ГБУЗ Городская клиническая больница №67, г. Москва, Россия

²ФГБОУ ВО «Дагестанский государственный медицинский университет», кафедра хирургии ФПК и

ППС с курсом эндоскопической хирургии, г. Махачкала, Республика Дагестан, Россия

Аннотация

Цель исследования. Обосновать и подтвердить дифференцированный подход к выбору объема оперативного вмешательства при доброкачественном узловом зобе. **Материалы и методы.** Проведен проспективный анализ 180 пациентов, перенесших операцию на щитовидной железе. Из них – 11 (6,1%) мужчин и 169 (93,9%), женщин в возрасте от 20 до 65 лет. Продолжительность заболевания пациентов от 8 месяцев до 12 лет. Все пациенты с доброкачественным нетоксическим зобом прошли тщательную оценку с изменением уровня гормонов ЩЖ, в сыворотке крови, УЗИ щитовидной железы, аспирационная биопсия щитовидной железы. **Результаты.** При лабораторном исследовании высокий уровень злокачественности наблюдается у пациентов с более высоким уровнем ТТГ и АТ, ТГ и АТ, ТПО. Достоверных различий в значениях Т3 и Т4 не было выявлено. УЗИ исследовании средний и максимальный диаметр злокачественных узлов было достоверно меньше, чем у доброкачественных ($1,99 \pm 1,88$ см; $p < 0,001$). Разница между хирургическими процедурами, описанными как субтотальная, тотальная и гемитиреоидэктомия, была статистически значимой. У 128 (71,1%) пациентов узлы располагались в одной доле, у 68 (37,8%) пациентов узлы были множественные, а 52 (28,9%) – солитарные узлы в одной из долей щитовидной железы. Интраоперационно у 68 (37,7%) проводилась цитоморфологическое исследование удаленной ткани щитовидной железы. Гемитиреоидэктомия была выполнена всего 57 (31,6%) пациентам. Субтотальная тиреоидэктомия выполнена 78 (43,3%) пациентам, а тотальная тиреоидэктомия была выполнена у 45 (25%) пациентов. С развитием гематомы повторно была оперирована одна больная после тотальной тиреоидэктомии, у пациентов после тиреоидэктомии гипопаратиреоз у 2 (4,4%), а после субтотальной тиреоидэктомии 1 (1,3%). У 3 пациентов после тиреоидэктомии транзитный парез гортани. Гипотиреоз развился после гемитиреоидэктомии у 14 (24,6%), субтотальной тиреоидэктомии 50 (64,1%) и тиреоидэктомии 45 (100%). **Заключение.** Решение оперативного вмешательства должно быть дифференцированным относительно выбора тактики оперативного вмешательства.

Ключевые слова

тиреоидэктомия, субтотальная тиреоидэктомия, гемитиреоидэктомия, гипотиреоз, гипопаратиреоз

Introduction

In recent years, there has been an increase in thyroid diseases, including nodular goiter. Dagestan is an endemic region where nodules are detected in most patients with thyroid pathology. The frequency of nodular non-toxic goiter among other thyroid diseases ranges from 25 to 62% [1, 2, 3, 4]. Recently, surgery for a benign goiter has been recognized as an acceptable and safe treatment method that has a low surgical risk and mortality. Despite improvements in the diagnosis and treatment of thyroid diseases over the past two decades, the literature remains controversial as to which method is best for a benign disease [2]. Previously, subtotal thyroidectomy for multiple goiter was considered a gold standard treatment, which was due to a decrease in complications related to the laryngeal nerve and parathyroid gland and a decrease in the need for lifelong hormone replacement therapy [3, 4, 5]. However, it is widely known that with long-term follow-up after subtotal thyroidectomy in multi-nodular goiter an increase in the frequency of relapses to 78% should be expected [5, 7]. Meanwhile, it is well known that repeated surgery for a receding nodular goiter results in increased damage to the laryngeal nerve and parathyroid gland compared to the original approach to the surgery. Although many clinics have changed their surgical strategy in favor of thyroidectomy, sub-

total thyroidectomy still appears to be the preferred option in every-day practice [6].

At the same time, the issue of choosing the volume of surgical intervention in patients with non-toxic goiter has not been completely resolved and requires further study [6, 7, 8, 9, 10].

Purpose of the study

To justify and confirm the differentiated approach to choosing the volume of surgical intervention in benign nodular goiter.

Material and methods

A prospective analysis of 180 patients who underwent thyroid surgery for nodular and multi-nodal non-toxic goiter at the Republican Clinical Hospital and Clinical City Hospital № 67 in Moscow was performed.

11 (6.1%) were men and 169 (93.9%) were women aged 20-65 years. The duration of the patients' disease was 8 months to 12 years.

All clinical and pathological data were prospectively entered into a computer database from medical records. We extracted data on gender, age, the composition of thyroid disease and the frequency of postoperative complications. The ethics Committee of Dagestan State Medical University approved this study, and all patients signed an informed consent.

Criteria for exclusion from the study:

1. a case of a malignant disease diagnosed before surgery;
2. the suspicion of malignancy before surgery;
3. those who have previously had thyroid surgery;
4. patients receiving treatment.

A reasonable criterion for including patients for surgery was ultrasound and fine needle aspiration biopsy with the exception of malignancy. After excluding 8 patients from the study, the main group was formed.

The reason for surgical intervention was tracheal compression syndrome and dysphagia in 108 patients (57.4%). Of these patients, 29 (26.8%) had a cervical and retrosternal arrangement of nodes. Fine needle aspiration biopsy (TAB) is an effective method that should be preferred as first-line diagnostic procedure as it gives the most accurate results for suspicious thyroid nodes detected by ultrasound. In our study, when evaluating thyroid nodes, it showed sensitivity of 65- 88%, specificity of 86% and 5% of false negative results.

Cytological evaluation of patients who underwent a fine needle aspiration biopsy revealed benign cytology in 98 patients, suspicious cytology of thyroid carcinoma in 8 patients, follicular adenoma in 32 patients, and insufficient cytology for diagnosis in 31 patients. 8 patients were excluded from the study as a malignant disease.

In 128 (71.1%) patients, nodes were located in one lobe of the thyroid gland. 68 (37.8%) patients had multiple nodes, and 52 (28.9%) had solitary nodes in one of the thyroid lobes. During the surgical intervention, a cytomorphological assessment was performed in 68 (37.7%) samples of the thyroid tissue. The study of surgery outcome lasted 6 months to 5 years and was conducted on the basis of examination of patients, study of thyroid status by ELISA, thyroid ultrasound was performed using the ultrasound scanner "AlocaSSD-3000" with a linear phased antenna transducer with frequency of 7.5 MHz. Serum (TSH), free triiodothyronine (T3), and free thyroxine (T4) were analyzed in the laboratory and determined using a chemiluminescent analyzer RocheCodashE601 (Switzerland) and a matched set.

The collected data was analyzed using the SPSS software (version 20; SPSS Inc.). Quantitative data were expressed as an average $SD \pm$ standard deviation

and qualitative data were reported by frequency (%). For interference analysis, we used the exact Fischer test and Chi-square to compare qualitative data in the frequency distribution. Based on the results of the Kol-mogorov-Smirnov test, which shows the normality of the data distribution, independent t-test samples were used to compare quantitative data for each gender. Logistic regression was used to assess the association of factors such as gender, age, body mass index (BMI), medical history, type of surgery, indications for surgery, the experience of the surgeon, and the frequency of post-operative early and late complications. Thus, the values for the 95% confidence interval and the odds ratio were obtained. The significance level ($p < 0.05$) was taken into account for all analyses.

Results

Surgical intervention was performed depending on the composition and spread of the pathological process, the results of preoperative (fine needle aspiration biopsy) performed under the control of ultrasound. During the operation thyroid tissue was removed using intraoperative cytophotometry.

At the nodal lesion of one lobe, hemithyroidectomy was carried out with removal of isthmus. Hemithyroidectomy was performed with visual control of the recurrent laryngeal nerve and extracapsular ligation of the thyroid artery tributaries. The thyroid artery was not ligated to preserve blood flow to the parathyroid gland. Only 57 (31.6%) patients underwent such operations. If there were small nodes in the other lobe, the subtotal removal of that lobe was performed. Thyroidectomy was performed for multinodal goiter and adenoma of both lobes.

Subtotal thyroidectomy was performed according to the method of O. V. Nikolaev in 78 (43.3%) patients with the colloid goiter with the preservation of a clinically significant volume of tissue of the thyroid residue (more than 3 cm³), in the absence of clinical and morphological data indicating the presence of thyroid cancer. Thyroidectomy was performed in 45 (25%) patients.

There was a significant difference between the groups of surgical patients ($p < 0.05$).

The composition and volume of surgical intervention for benign thyroid diseases are presented in table 1.

Table 1.
Volume and composition
of surgical intervention in
nodular goiter of benign
origin

№	Volume of surgical intervention	n= 180	
		Quant.	%
1.	Hemithyroidectomy	57	32,0
2.	Subtotal thyroidectomy	78	43,3
3.	Total thyroidectomy	45	25
Total		180	100

Complications of various thyroid operations and the frequency of postoperative complications were compared between patients with different approaches. There was no lethality in the postoperative period. A serious complication requiring re-opening of the operative wound occurred only in a 57 year-old patient who underwent a thyroidectomy with a modified neck dissection with the development of a hematoma. In patients who underwent radical treatment (thyroidectomy) hypocalcemia (levels less than 2.1 mmol/l) was observed in 2 (4.4%), and in 1 (1.2%) after subtotal thyroidectomy.

In 3 patients, the operating period after thyroidectomy was complicated by transient laryngeal paresis with respiratory preservation. Surgical intervention performed for a benign nodular formation of the thyroid gland was confirmed by the results of histological examination of the surgical material. In a laboratory study, as shown in table 2, there were no significant differences in the values of T3 and T4 between the two groups. The prevalence of malignant diseases was 1.6% at a TSH level of less than 0.36 Mme/l, compared to 8.5% at a TSH level of 4.9 Mme/l or more ($p = 0.14$). A relatively high level of malignancy was observed in patients with higher levels of TSH.

Continuous variables are compared using the Mann-Whitney U-criteria, and categorical variables are compared using χ^2 -tests ($p < 0.05$).

Abbreviations: Ab-TG - antibody against thyroglobulin, Ab-TPO - antibody against thyroid peroxidase.

Patients with malignant nodes had positive results of Ab-TG and Ab-TPO testing more often than patients with benign nodes, as can be seen from the table 2. In an ultrasound study, the average maximum diameter of malignant nodes was significantly smaller than that of benign ones (1.99 ± 1.88 cm vs. 2.88 ± 1.91 cm, $p < 0.001$). The distribution of solitary nodes in malignant cases did not differ from that in benign ones (29.1% vs. 25.4%, $p = 0.108$).

There were no differences in eggshell calcification between the benign and malignant groups ($p > 0.05$).

91 (50.5%) patients had follicular adenomas, 5 (2.7%) patients had papillary thyroid cancer, and 3 (1.6%) patients had follicular cancer. Ultrasound examination revealed 8 cases of thyroid cancer, but surgical treatment was not included.

The analysis of postoperative intervention found that characteristic preoperative syndromes disappeared in 45% of patients. Clinical manifestations of laryngeal paresis in 3 patients resolved with conservative treatment within a year.

The results of surgical intervention and their functional results are shown in table 3.

The results of surgery for hemithyroidectomy with the manifestation of hypothyroidism were observed in 14 (24.6%) patients. Statistically significant differences in the frequency of postoperative hypothyroidism after thyroidectomy and subtotal thyroidectomy were found ($p < 0.05$).

In all patients with hypothyroidism, drug-induced euthyroidism was achieved by prescribing L-thyroxine 75 mcg per day. In patients with subtotal removal of the thyroid gland, the need for L-thyroxine was 150 mcg per day.

However, the frequency of relapse largely depended on the duration of the postoperative period. On ultrasound examination, in 8 (14%) patients after hemithyroidectomy nodules with a volume of from 0.6 to 0.9 cm³ were identified. The detection period for these nodes is up to 4 years.

In euthyroid patients after subtotal thyroidectomy, in the tissue of the thyroid residue the nodes in the volume from 0.7 to 2.5 cm³ were detected up to 5 years after surgery. In patients who initially underwent less radical hemithyroidectomy, 6 (3.3%) patients relapsed after 8 years and had to undergo a second operation to remove the remaining thyroid tissue.

Values	Benign tumor	Malignant tumor	P-value
Free T3, pmol/l	4,11 (3,93 – 5,08)	4,45 (3,98 – 5,01)	0,808
Free T4, pmol/l	14,98 (12,81 – 16,99)	15,51 (13,7 – 18,08)	0,064
TSH, Miu/l	1,19 (0,59 – 2,21)	1,65 (0,80 – 2,70)	< 0,001
Ab-TG	15	231,3	< 0,001
Ab-TPO	18,1	126,8	0,028

Table 2. Laboratory values in patients with nodular formation thyroid

№	Volume of surgical intervention	Functional state		Total, %
		Euthyroidism, %	Hypothyroidism, %	
1.	Hemithyroidectomy	47 (32,8)	14(24,6)	57
2.	Subtotal thyroidectomy	28 (35,9)	50 (64,1)	78
3.	Total thyroidectomy	–	45(100)	45
Total		75 (41,7%)	109 (60,5)	180

Table 3. The results of surgical intervention

Discussion

There are several types of surgical interventions used in the treatment of benign thyroid diseases. However, in recent years there has been an increase in the use of radical operations, such as total thyroidectomy, and a decrease in the number of less radical operations like subtotal thyroidectomy and hemithyroidectomy. In our study, the percentage of radical thyroidectomy operations increased from 12% in 2001 to 25% in 2018. Some authors have recommended a more radical operation for a non-toxic multi-node goiter [5]. They emphasized that since the entire thyroid gland is affected, leaving behind even a small amount of tissue, the risk of pathological changes, such as a relapse that requires repeated surgery, increases. Other authors consider a high risk of relapse and a significantly higher risk of postoperative complications a similar disadvantage of non-radical treatment [16, 17].

Some studies have found that the frequency of relapses after non-radical surgery of a multi-node non-toxic goiter is very high, up to 20% [7]. However, the frequency of relapses described by various authors largely depended on the duration of the postoperative period. According to these authors, the problem of recovery after surgery is more complex. Relapse is not a problem in itself. The problem occurs when a second operation is required. Repeated operation on the thyroid gland is technically much more difficult and is associated with a higher risk of complications than the previous operation. According to the literature, repeated surgery is associated with a greater risk of damage to the laryngeal nerve and hypoparathyroidism [8]. Hormonal treatment is often discussed by opponents of radical surgery [4]. Subtotal thyroidectomy does not require hormonal treatment. Opponents of a less radical operation quickly disproved this claim [6]. They proved that the left-over thyroid tissue does not protect against hypothyroidism.

According to their research, 100% of patients after subtotal thyroidectomy require high doses of levothyroxine, up to 150 mcg per day. In our study, all patients after subtotal thyroidectomy received hormonal support in daily doses from 75 mcg to 100 mcg.

The main goal of surgical treatment of thyroid diseases should always be the most effective performance with minimal complications and frequency of relapses. The authors of less radical thyroid

surgery oppose total thyroidectomy in the treatment of benign diseases, and emphasize increased morbidity, including damage to the laryngeal nerve and parathyroid gland. They emphasize that these patients are also sentenced to life-long hormone replacement therapy [7]. Recent studies concerning relapse in benign thyroid diseases show that young age, nodular and multi-nodular goiter, family history, and inadequate surgery are the main risk factors for relapse [1, 10]. To prevent the recurrence of benign thyroid disease, a detailed preoperative assessment is required to decide on the appropriate surgical intervention. Studies have shown that l-thyroxine therapy protects against relapses and repeated operations by reducing TSH stimulation on residual tissue. Thus, there is an opinion that the addition of thyroid hormones after surgery can effectively protect patients from recurrence [11, 12]. On the other hand, according to other researchers, despite substitution therapy, long-term postoperative follow-up showed a high rate of relapses after subtotal thyroidectomy [8].

Recent studies show that the protective effect of hormone therapy is controversial [7,8].

Thus, the rate of relapses after surgery for benign thyroid diseases was 11.1%. Inadequate surgical interventions, lack of substitution therapy, presence of a multi-node goiter, young age and family history should be taken into account as predictors of relapse. The need for repeated surgery for recurrent benign nodular diseases of the thyroid gland is a serious clinical problem due to the high frequency of post-operative complications.

Conclusion

Analysis of the results of surgical treatment of benign thyroid diseases confirmed the validity of the differential approach to the choice of the volume of surgical intervention, taking into account the detection of pathology and according to ultrasound, fine needle aspiration biopsy and intraoperative cytomorphometry of the damaged thyroid tissue. Therefore, each decision regarding the choice of thyroidectomy should be made individually. In addition to absolute medical indications for more radical treatment, such as compression symptoms, goiter progression, or suspected cancer, other factors should also be considered, such as young age, concomitant diseases, and an iodine-deficient region.

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CHOICE OF PULMONARY RESECTIONS IN INTRATHORACIC TUMORS: SHORT-TERM OUTCOMES

Makarov V.

orcid.org/0000-0003-2120-5323

Baimukhametov E.

orcid.org/0000-0002-4023-5985

Yessentayeva S.

orcid.org/0000-0001-7087-1440

Kalmatayeva Zh.

orcid.org/0000-0002-5562-1969

Semenova A.

orcid.org/0000-0003-2944-1400

Baltaev N.

orcid.org/0000-0003-3022-7372

Kadyrbayeva R.

orcid.org/0000-0001-8254-8675

Irsaliev R.

orcid.org/0000-0002-0988-0417

Orazbaev A.

orcid.org/0000-0001-9001-7321

Makarov V.^{1,2}, Baimukhametov E.³, Yessentayeva S.⁴, Kalmatayeva Zh.¹, Kadyrbayeva R.⁵, Semenova A.², Baltaev N.², Irsaliev R.², Orazbaev A.²

¹Al-Farabi Kazakh National University, Almaty, Kazakhstan;

²Almaty Oncology Center, Almaty, Kazakhstan;

³Kazakh Medical University of Continuing Education, Almaty, Kazakhstan;

⁴Kazakh-Russian Medical University, Almaty, Kazakhstan;

⁵Kazakh Institute of Oncology and Radiology, Almaty, Kazakhstan

Abstract

Relevance: Lung cancer still leads in morbidity and mortality among other cancers. In 2018, 2.094 million new lung cancer cases and 1.8 million deaths from lung cancer were registered globally. The study aimed to evaluate the effectiveness of surgical treatment for lung cancer depending on the extent of surgery. **Material and Methods:** The article provides a retrospective analysis of 137 patients operated for lung cancer at Almaty Oncology Center in 2014-2018. The database was created in Microsoft Excel. IBM SPSS Statistics, package 19 (trial version) mathematical data processing software was used for statistical processing. The survival rate was measured from the commencement of treatment till the patient's death for any reason or to the last observation date. The cut-off date was January 1, 2019. **Results:** Most of the patients (91/137, 69.3%) had a locally advanced Stage IIb-IIIb process. Localized forms of the disease were diagnosed in 21.1% of cases. R0 resection was achieved in 83.9%, R1 – 13.1%, R2 – 2.9% of patients. The post-surgery mortality amounted to 5.8%. One-year survival amounted to 70% SE4 for lobectomy, 87% SE9 for segmental resections, 79% SE8 for bronchoplastic, lobar resections, and 67% SE10 for pneumonectomy. The difference in median survival was statistically significant: $\chi^2 = 9.7$, $p = 0.045$. **Conclusion:** We consider the extent of surgery a risk factor. The organ ectomies should be minimized since our data and the literature report high one-year mortality and low 5-year survival after such surgeries.

Keywords

lung cancer, lung cancer surgery, lobectomy, pneumonectomy, sleeve lobectomy, segmentectomy.

Кеуде ішілік ісіктерді хирургиялық емдеу көлемін таңдау: жақын нәтижелерді талдау

Макаров В.^{1,2}, Баймухаметов Э.³, Есентаева С.⁴, Қалматаева Ж.¹, Кадырбаева Р.⁵, Семенова А.², Балтаев Н.², Ирсадиев Р.², Оразбаев А.²

¹Әл-Фараби атындағы Қазақ Ұлттық университеті, Алматы қ., Қазақстан;

²Алматы онкологиялық орталығы, Алматы қ., Қазақстан;

³Қазақ медициналық үздіксіз білім беру университеті, Алматы қ., Қазақстан;

⁴Қазақ-Ресей Медицина Университеті, Алматы қ., Қазақстан;

⁵Қазақ онкология және радиология ғылыми-зерттеу институты, Алматы қ., Қазақстан

Аңдатпа

Өзектілігі: Өкпенің қатерлі ісігі барлық онкологиялық аурулардың арасында өлім-жітім және аурушаңдық бойынша көш бастап тұр. 2018 жылы әлемде ӨҚІ-нің 2,094 млн жаңа жағдайы тіркелді, осы патологиядан көз жұмғандардың саны 1,8 млн-ға жетті. **Зерттеудің мақсаты:** хирургиялық араласу көлеміне байланысты өкпенің қатерлі ісігін хирургиялық емдеудің тиімділігін бағалау. **Материалдар және әдістер:** Мақалада 2014-2018 жылдар аралығында Алматы Онкология орталығының хирургия бөлімшесінде өкпенің қатерлі ісігі бойынша ота жасалған 137 науқасқа ретроспективтік талдау жасалғаны туралы ақпарат қамтылған. Мәліметтер базасы Microsoft Excel бағдарламасы арқылы жасалды. Материалды статистикалық өңдеу IBM SPSS Statistics 19 (trial-нұсқа) мәліметтерді математикалық өңдеу пакетінің көмегімен жүзеге асырылды. Өмір сүру деңгейі емдеу басталған күннен бастап кез келген себеп бойынша орын алған өлімге дейін немесе науқасты соңғы бақылау күніне дейін есептелді. Ақпарат жинау 2019 жылғы 1 қаңтарда аяқталды. **Нәтижелер:** Науқастардың көпшілігінде (137-нің 91, 69,3%) IIb-IIIb сатылары деп бағаланған жергілікті кең таралған процесс болды. 21,1% жағдайда аурудың локализацияланған формалары деген диагноз қойылды. R0 резекцияға науқастардың 83,9%-

ы, R1 – 13,1%, R2 – 2,9% жетті. Ота жасалған науқастар арасындағы өлім-жітім 5.8%-ды құрады. Бір жылдық өміршеңдік: лобэктомия – 70% SE4, сегментарлық резекция – 87% SE9, бронхопластикалық, лобарлық резекция – 79% SE8, пневмонэктомиядан кейін – 67% SE10. Өмір сүру медианасындағы статистикалық сенімді айырмашылық: $\chi^2 = 9,7$, $p = 0,045$. **Қорытынды:** Осылайша, біз ота көлемі қауіп-қатер факторы деп санаймыз. Ағзаны сақтау оталары барынша азайтылуы керек, өйткені біз біз алған мәліметтер мен әдеби деректер осындай оталар кезіндегі бір жылдық өлім-жітімнің жоғары деңгейін және бес жылдық өміршеңдіктің төмен деңгейін көрсетеді.

Түйін сөздер

өкпе обыры, өкпе обырын хирургиялық емдеу, лобэктомия, пневмонэктомия, sleeve лобэктомия, сегментэктомия

Выбор объема хирургического лечения при опухолях внутригрудной локализации: анализ непосредственных результатов

Макаров В.^{1,2}, Баймухаметов Э.³, Есентаева С.⁴, Калматаева Ж.¹,
Кадырбаева Р.⁵, Семенова А.², Балтаев Н.², Ирсалиев Р.², Оразбаев А.²

¹Казахский национальный университет им. Аль-Фараби, г. Алматы, Казахстан;

²Алматинский онкологический диспансер, г. Алматы, Казахстан;

³Казахский медицинский университет непрерывного образования, г. Алматы, Казахстан;

⁴Казахстанско-Российский медицинский университет, г. Алматы, Казахстан;

⁵Казахский научно-исследовательский институт онкологии и радиологии, г. Алматы, Казахстан

Аннотация

Актуальность: Рак легкого занимает лидирующие позиции по заболеваемости и смертности среди всех онкологических заболеваний. В 2018 году в мире было зарегистрировано 2,094 млн. новых случаев РЛ, число умерших от этой патологии достигло 1,8 млн. **Цель исследования:** оценка эффективности оперативного лечения рака легкого в зависимости от объема оперативного вмешательства. **Материалы и методы:** Статья содержит ретроспективный анализ 137 пациентов, прооперированных по поводу рака легкого в хирургическом отделении Алматинского Онкологического Центра с 2014 по 2018 годы. База данных была создана с использованием программы Microsoft Excel. Статистическая обработка материала производилась с помощью пакета математической обработки данных IBM SPSS Statistics 19 (trial-версия). Выживаемость рассчитывалась от даты начала лечения до смерти от любой причины или до даты последнего наблюдения пациента. Сбор информации был завершён 1 января 2019 года. **Результаты:** Большинство пациентов (91 из 137, 69,3%) имели местно-распространенный процесс, который оценивался IIb-IIIb стадиями. Локализованные формы заболевания были диагностированы в 21,1% случаев. R0 резекция достигнута у 83,9% больных, R1 – у 13,1%, R2 – у 2,9%. Летальность среди прооперированных пациентов составила 5,8%. Одногодичная выживаемость составила: для лобэктомии – 70% SE4, для сегментарных резекций – 87% SE9, при выполнении бронхопластических, лобарных резекций – 79% SE8, после пневмонэктомии – 67% SE10. Статистически достоверная разница в медиане выживаемости составила: $\chi^2 = 9,7$, $p = 0,045$. **Заключение:** Таким образом, мы считаем, что объем операции является фактором риска. Выполнение органо-уносящих операций следует минимизировать, так как полученные нами и литературные данные свидетельствуют о высоком уровне одногодичной летальности и низком уровне пятилетней выживаемости при таких операциях.

Ключевые слова

рак легкого, хирургическое лечение рака легких, лобэктомия, пневмонэктомия, циркулярная резекция бронха, сегментэктомия

Relevance

Lung cancer still leads in morbidity and mortality among other cancers despite active prevention, new diagnostic methods, and advances in anesthesiology and surgical treatment. In 2018, 2.094 million new lung cancer cases (11.6% of all new cancer cases) and 1.8 million deaths from lung cancer (18.4% of all deaths from cancer) were registered globally [1]. Five-year overall survival with non-small cell lung cancer (NSCLC) has not exceeded 23% [2].

In the Republic of Kazakhstan, in 2018, lung cancer ranked second in cancer incidence (20.5 per 100,000) and first in cancer mortality (13.7 per 100,000). One-year mortality remained high: 49.4% died within a year after diagnosis. Five-year overall

survival varied by regions from 2.5% to 11.5%[3].

Surgery is a generally accepted standard of resectable lung cancer treatment providing real healing prospects [4]. Surgical techniques are constantly improved thanks to high-tech dissection instruments, atraumatic suture material, parenchymal and bronchial stapling devices. Anesthetic support is also improving. The use of separate pulmonary ventilation, the widespread introduction of inhalation (combined) anesthesia, and modern means of cardiac support provide a chance for surgery in a functionally difficult group of patients.

The study aimed to evaluate the effectiveness of surgical treatment for lung cancer depending on the extent of surgery.

Material and Methods

The article provides a retrospective analysis of 225 patients operated for lung cancer at Almaty Oncology Center in 2014-2018. Thoracotomy was performed in 137 of 225 (53.7%) operations.

The patients for surgery were thoroughly selected by contrast-enhanced CT modeling with 3D imaging. According to ICH guidelines, all the patients signed informed consent for surgery and medical data processing upon approval of a multi-disciplinary team [5].

Profile of the patients enrolled in the study: the average age of lung cancer patients – 63.42 (40 to 83) years of age; SE 0.689, SD 8.063, dispersion – 65.01. Most of the patients enrolled (45.3%) belonged to the age group of 61-70 years; least of the operated patients (4.4%) were below 50 years. Men were more often affected by lung malignancies, with the men-to-women ratio of 3:1 (Table 1).

Cardiovascular comorbidity was presented in 96 (70.1%) cases, more often in men – 78.4% (80/102) vs. 45.7% (16/35) in women. Chronic obstructive pulmonary disease was registered in 86 (62.8%) patients, again more often in men – 65.7% (67/102) vs. 54.3% (19/35) in women. In 11 (8%) cases, NSCLC was diagnosed as a second metachronous cancer since those patients have been previously treated for cancer. Those patients had neither relapse nor progression of the primary malignant disease. A history of cancer was confirmed in 8/102 (7.8%) male and 3/35 (8.6%) female patients. 56 (40.9%) patients had combined cardiovascular and respiratory comorbidity, with a clear prevalence among male patients: 51.0% vs. 8.6% of females. Thus, men had a reliably higher frequency of comorbidity (Table 2).

By the prevalence of the disease and the topical localization of the primary tumor, patients taken for surgical treatment most often had an upper lobe tumor – 59 (43.1%) cases, with the same frequency

to the right and left – 31 (22.6%) and 28 (20.4%), respectively. Lower lobe lung cancer was detected in 17.5% (24) cases, more often to the left – 15 (10.9%) vs. 9 (6.6%) to the right. Bilobar involvement has been reported in 13 (9.5%) patients, with a predominant lesion of the right lung – 12 (8.8%) vs. 1 (0.7%) lesion of the left lung. Centralized tumor was found in 29 (21.2%) cases: 16 (11.7%) cases to the right and 13 (9.5%) to the left.

The choice of extent of surgery depended on the disease prevalence and the patient's cardio-pulmonary reserve. The surgical technique was selected according to the generally accepted NCCN criteria [6]. The intervention was performed under total intravenous and inhalation anesthesia. The lungs were intubated and ventilated separately, through axillary access of 8-12 cm in the 5th intercostal space, with maximum preservation of the muscle layer and separate lung roots treatment. All patients with primary lung cancer underwent a systemic ipsilateral lymph node dissection on the surgery side, regardless of the lymph nodes macroscopical lesion [7]. The bronchus stump was treated with a mechanical endostepler, with an individual selection of cassettes. A. at v. bronchialis were preserved for sleeve lobectomy.

Standard contraindications for surgery included: the patient's inability to endure anesthetic support; inconsistency of the functional lungs reserve with the planned resection; tumor (T4) with spread to the trachea, heart, spine, esophagus [4, 8, 9].

The main pulmonary trunk was discharged and fixed by a tourniquet-guidewire to prevent massive pulmonary bleeding. In case of vessel damage and/or bleeding development, the Satinsky clamp was turned down along the conductor to block the blood flow.

Early postoperative activation of patients was one of the factors to reduce postoperative compli-

Table 1.
Lung cancer patients' distribution by demographic indicators (age, gender) (n=137)

Gender	Number of patients				Total
	Below 50 years	51-60 years	61-70 years	Over 71 years	
Female	3 (2.2%)	10 (7.3%)	15 (10.9%)	7 (5.1%)	35 (25.5%)
Male	3 (2.2%)	32 (23.4%)	47 (34.3%)	20 (14.6%)	102 (74.5%)
Total	6 (4.4%)	42 (30.7%)	62 (45.3%)	27 (19.7%)	137 (100%)

Table 2.
Lung cancer patients' distribution by comorbidity (n=137)

Gender	Ischaemic Heart Disease	Chronic obstructive pulmonary disease	Metachronous cancer	Total
Female	16(45.7%)	19(54.3%)	3(8.6%)	35 (100%)
Male	80(78.4%)	67(65.7%)	8(7.8%)	102 (100%)
Log-rank (Mantel-cox) P(value)	0.023	0.018	0.018	0.018
Chi-Square	5.186	5.564	5.576	5.645
Total	96 (70.1%)	86(62.8%)	11(8.0%)	137 (100%)

cations. 82% of operated patients were activated on Day 1-2 after surgery. The ICU patients were transferred to the wards with functional beds and central oxygen supply. Blood pressure, heart rate, respiratory rate, SpO₂ were monitored to get the patient out of bed for further controlled walking in the ward. The "Threeball" device maximizing the inspiratory volume was used for respiratory gymnastics. The intensity of physical activity depended on the volume of air discharged through the drainage tubes. The remaining 18% of patients were bedridden until the massive air discharge through the drainage tubes ceased and cardiopulmonary insufficiency was compensated. Despite the active drainage, those patients were sited and did exercises using the "Threeball" device. All patients used drainage box systems with adjustable aspiration within the range of 0-30 mm w.g. The drain was removed on Day 1 after pneumonectomy.

The database was created in Microsoft Excel. IBM SPSS Statistics, package 19 (trial version) mathematical data processing software was used for statistical processing. The survival rate was measured in intervals using Lifetables recommended by the International Union Against Cancer (UICC) and the World Health Organization (1979) from the

commencement of treatment till the patient's death for any reason or to the last observation date. The cut-off date was January 1, 2019.

Results

Most of the patients (91/137, 69.3%) had a locally advanced Stage IIb-IIIb process. Localized forms of the disease were diagnosed in 21.1% of cases: Ia – 1 (0.7%), Ib – 18 (13.1%), and IIa – 10 (7.3%) cases. Only two (1.5%) patients had a primary-advanced process. Four patients with a morphologically confirmed benign process and three patients with secondary, metastatic lung disease were excluded from the analysis.

More than half of operated patients (76/137) underwent lobectomy (Table 3).

Only in one (0.7%) case of expository thoracotomy with the right-side tumor localization, the tumor involved the venous sinus, right pulmonary artery, and right heart auricle. Such involvement could not be diagnosed preoperatively (Table 3).

Postoperative histology confirmed the radicality of performed surgical interventions. R0 resection was achieved in 115 (83.9%) patients, R1 (microscopically positive edge) – in (13.1%) patients, R2 – in 4 (2.9%) patients (Figure 1).

Surgical intervention	No. of operations				Total
	Right side		Left side		
	Abs.	%	Abs.	%	
Lobectomy	43	31.4	33	24.1	76 (55.5%)
- upper	24	17.5	23	16.8	47 (34.3%)
- middle	3	2.2	-	-	3 (2.2%)
- lower	5	3.6	10	7.3	13 (10.9%)
Bilobectomy	11	8.0	-	-	11 (8.0%)
Pneumonectomy	11	8.0	10	7.3	21 (15.3%)
Anatomical lung resection (sub-lobe):	7	5.1	8	5.8	15 (10.9%)
- upper lobe	2	1.5	5	3.6	7 (5.1%)
- middle lobe	2	1.5	-	-	2 (1.5%)
- lower lobe	3	2.2	3	2.2	6 (4.4%)
Reconstructive plastic (sleeve) lobectomy:	16	11.7	8	5.8	24 (17.5%)
- upper	7	5.1	4	2.9	11 (8.0%)
- middle	4	2.9	-	-	4 (2.9%)
- lower	2	1.5	4	2.9	6 (4.4%)
bilobectomy	3	2.2			3 (2.2%)
Explorativethoracotomy	1	0.7	-	-	1 (0.7%)
Total	78	56.9	59	43.1	137 (100%)

Table 3.

The volume of surgery in lung cancer patients (n=137)

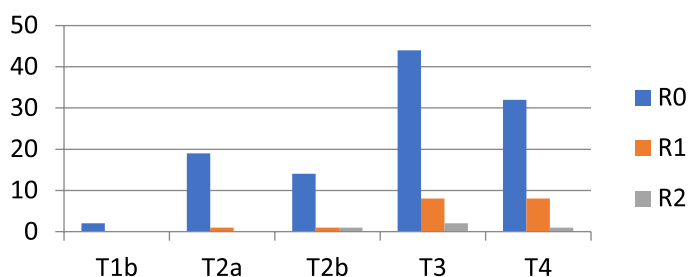


Figure 1.

Radicality of resection and tumor size as per TNM 7 (n=137)

Figure 2.
Distribution of the morphological forms of the disease in NSCLC patients (n=137)

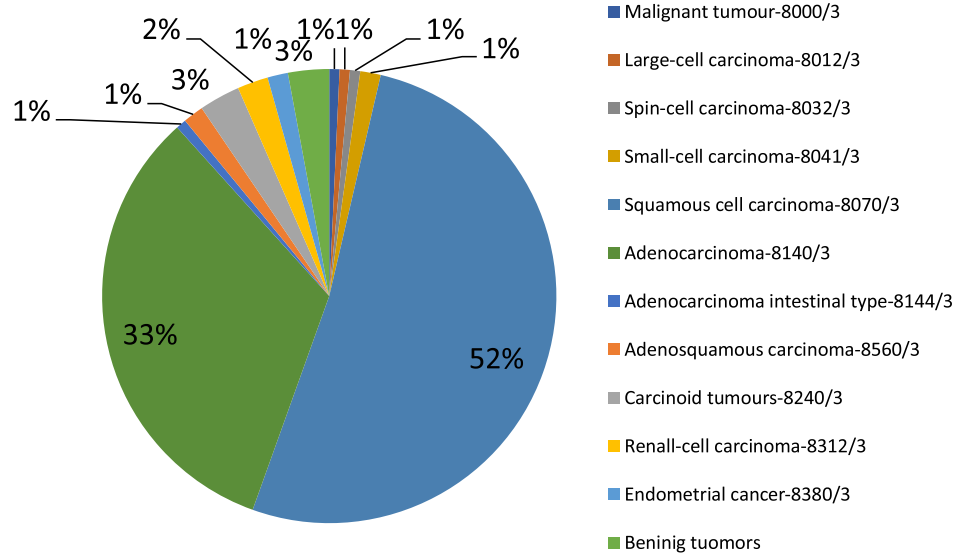


Table 4.
The incidence of lymph node involvement depending on the main histological forms of lung cancer (n=137)

	Large cell carcinoma - 8012/3	Spindle cell carcinoma - 8032/3	Small cell carcinoma - 8041/3	Squamous cell carcinoma - 8070/3	Adenocarcinoma - 8140/3	Adenosquamous carcinoma - 8560/3	Carcinoid tumor - 8240/3
n1	0	0	1	13	5	0	0
n2	0	0	0	16	13	0	1
n3	0	0	0	0	3	0	0

Postoperative histology revealed: squamous cell cancer – 51.8%, adenocarcinoma – 32.8%, adenosquamous carcinoma – 1.5%, carcinoid tumor – 2.9%, and other cancers - in single cases. Thus, smallcell carcinoma was found in 1.5%, non-differentiated carcinoma – 0.7%, large cell carcinoma – 0.7%, spindle cell carcinoma – 0.7%. Three (2.2%) patients had secondary tumor lesions of the lungs, another 4 (2.9%) had no malignant cells detected (Figure 2).

The histological examination of the surgical material revealed no lesion to the lymph nodes (N0) in 79 (57.7%) patients, first-order lymph node metastasis (N1)– in19 (13.9%), second-order (N2)– in 31 (22.6%), third-order (contralateral side) (N3)– in 3 (2.2%) patients. In 5 (3.6%) cases, the postoperative status of regional lymph nodes remained unknown (NX) due to the operation’s palliative purpose. It was decided to abstain from systematic lymph node dissection not to burden the patient’s condition. Another reason was the spread of tumor metastasis outside the lymph node to adjacent structures (so-called «bulky») (Table 4).

Table 4 shows that the first and second-order lymph nodes were most often affected by metastases in squamous cell carcinoma and adenocarcinoma of the lung: 29 (21.2%) and 18 (13.1%) cases, respectively. Third-order or contralateral side lymph

nodes were affected in 3(2.1%) patients with adenocarcinoma of the lung.

Pain intensity was another criterion of postoperative cure quality. The pain was assessed on a digital scale from 0 to 10: Grade 1 (1-3 points) – minor, Grade 2 (4-6 points) – moderate, Grade 3 (7-9 points) – expressed[10]. Twenty-two (16.1%) patients assessed postoperative pain as minor, 93 (67.9%) – moderate, and another 22 (16.1%) – expressed.

At that, women tolerated pain better than men (Figure 3).

According to Thoracic Morbidity and Mortality System classification of complications [11,12], 14(10.2%) of patients had grade 3-5 early postoperative complications (Table 5).

Most patients, 123 (89.8%), had no complications of such grade.

During lung surgery with separate pulmonary ventilation using double-lumen endotracheal tubes, a rare intraoperative anesthesia-related complication [13] is possible in the form of iatrogenic perforation of the lower third of the trachea membranous part and right main bronchus by the endotracheal tube. This pathology was detected in one patient (0.7%) and managed intraoperatively, without changing the extent of surgery. The complication developed on the background of the patient’s ana-

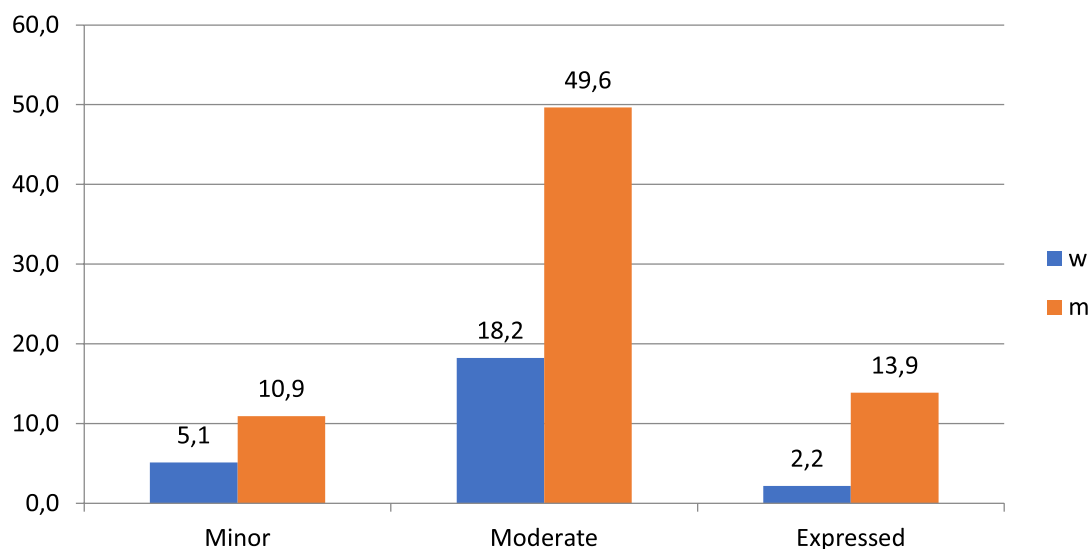


Figure 3.
Postoperative pain intensity distribution in lung cancer patients, by gender, % (n = 137)

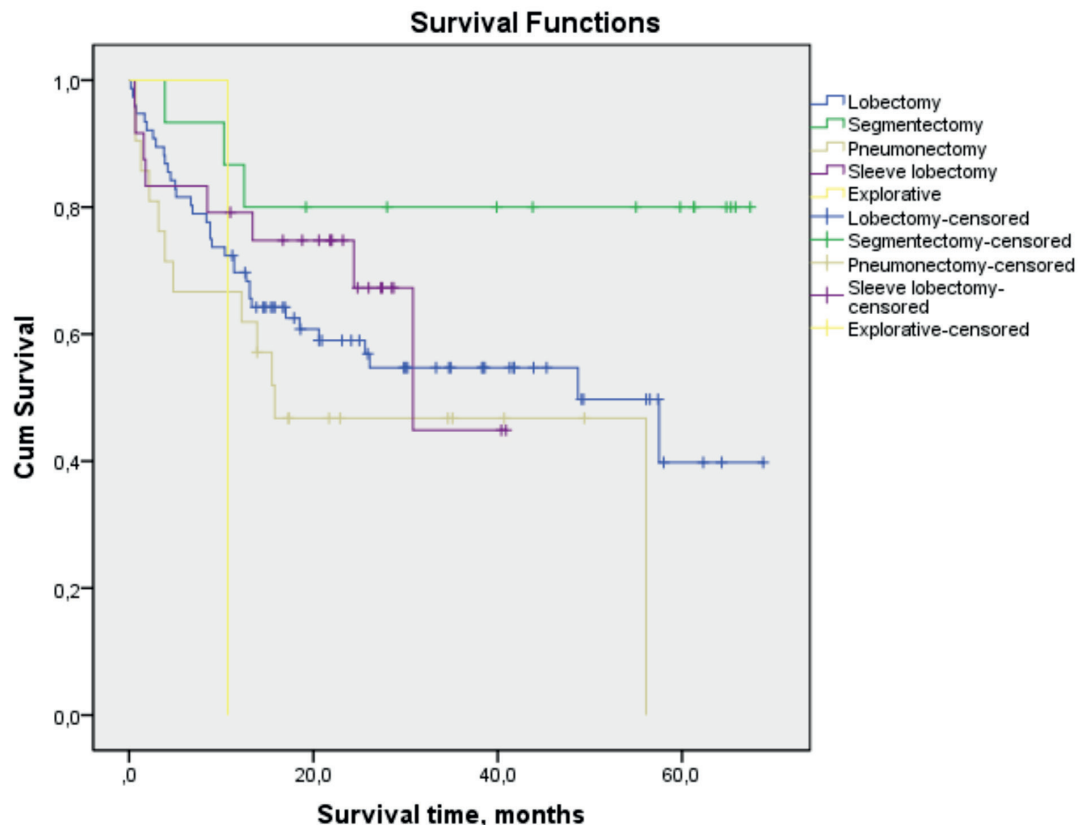
Complication	Grade	Frequency, abs.	%
Intrapleural bleeding	IIIB	3	2.2
Bronchial fistula	IVB-V	5	3.6
Parenchymal fistula	IIIA	3	2.2
Iatrogenic perforation of the lower third of the trachea membranous part and the right main bronchus	IIIB	1	0.7
Chronic renal insufficiency	IVB	1	0.7
Interbronchial anastomosis leak	V	1	0.7
Total		14	10.2

Table 5.
Grade 3-5 postoperative complications' distribution after lung cancer surgery (n=137)

No.	Age, years	Complication	Outcome	
1	63	Bronchial fistula	Death	Rhetoracotomy, suturing of stump, thoracostomy
2	71	Alveolar fistula	Death	Drainage
3	66	Erosive-purulent endobronchitis. Postoperative deformity of the left main bronchus with partial obstruction.	Death, AMI	Non-surgical
4	66	Alveolar fistula	Death within a month	Drainage
5	63	Chronic renal insufficiency (CRI)	Death due to CRI progression within a month	Non-surgical
6	67	Bronchial fistula (the upper lobar bronchus stump membranous wall necrosis) on 02.05.2018	Death	Rhetoracotomy. para-pericardial timus pacefollower transposition, plastics of the upper lobar bronchus stump defect
7	68	Anastomotic leakage after sleeve surgery	Death	Rhetoracotomy leftward (06.03.2018) – left lung pneumonectomy. Bronchial fistula. Left pleural cavity empyema. Mediastinitis.
8	72	Bronchial fistula	Death	Tracheal stenting of the right main bronchus, mediastinitis.

Table 6.
Complications with fatal outcome after lung cancer surgery (n = 137)

Figure 4.
Survival rate by Kaplan-Meier depending on the extent of surgery



tomical features associated with the hypersthenic constitution and cervical osteochondrosis.

The intrapleural bleeding occurred in 3 cases (2.1%). Two cases required re-thoracotomy for surgical hemostasis; one case was managed conservatively. Intraoperative bleeding after re-thoracotomy originated from the lower pulmonary vein due to a suture failure.

After surgery, five (3.6%) patients developed a bronchial fistula due to the main bronchus stump insolvency – four (2.9%), or a lobar bronchus stump insolvency – one (0.7%). Interbronchial anastomosis failure occurred in one (0.7%) case. These complications required three re-thoracotomies. Two cases of suture failure were caused by the bronchial wall necrotic changes. In one patient, the suture cut out after a pronounced cough reflex. One patient (0.7%) developed chronic renal failure.

The mortality among operated patients of 5.8% (8/137 cases) was mainly caused by the bronchus or parenchyma seam integrity failure. The performed re-thoracotomies using various sealing techniques were not successful. Therefore, the timing of fistula detection and its early abolition are extremely important risk factors (Table 6).

Survival was calculated using SPSS tables. Postoperative mortality up to one month after surgery amounted to 5.8% SE2. One-year survival was 72% SE 4 (median survival time (MST) – 57.5 months).

One-year survival was dependent on the extent of surgery and amounted to 70% SE4 (MST – 51.6 months) for lobectomy, 87% SE9 (MST – 60 months) for segmental resections, 79% SE8 (MST – 36 months) for bronchoplastic, lobar resections. Pneumonectomy was associated with the lowest one-year survival of 67% SE10 (MST – 20.6 months). Exploratory thoracotomy was associated with the survival of 10.7 months (n=1) (Figure 4). The difference in median survival was statistically significant: $\chi^2 = 9.7$, $p = 0.045$.

Discussion

The presented surgical technique was adapted for anatomical lung resections (also sleeve lobectomy, segmentectomy). Its introduction and improvement at Almaty Oncology Center allow expanding indications for invasive operations without increasing the frequency of intra- and postoperative complications and mortality. The use of contrast-enhanced CT-modeling with 3D image reconstruction reduced the frequency of trial thoracotomies to 0.7%. The pulmonary artery blood flow control allows a safe vascular resection and vascular suture. A systemic ipsilateral lymph node dissection ensures correct staging of the case and a better long-term disease prognosis [14-16]. Oncological radicality was not compromised since R0 resections in 83.9% of cases, and R1 in 13.1% of cases totaled to 97%. Unresectable tumor invasion R2 was detected in 2.9% of cases.

In our study, the lung parenchyma integrity was maintained in 83.8% of cases. Pneumonectomies amounted to 15.3%. The one-year survival was highest in segmental resections and amounted to 87% SE9 (MST – 60 months). In most leading thoracic clinics performing complex surgical interventions for lung cancer, the frequency of postoperative complications still ranges from 9 to 26.4% of the number of operations. Postoperative mortality also persists at the level of 6-9% on average [17]. A bronchial stump suture failure with the development of bronchopleural fistula and pleural empyema is one of the most severe and dangerous postoperative complications. Over the past decades, its frequency after pneumonectomy has notably decreased from 28% to 10% [18-20]. However, it remains the cause of high mortality from 16% up to 71% [21]. In our study, bronchopleural fistula developed in 3.6% of cases, but the mortality in that group of patients was rather high (60%). Anastomotic leak is a specific threatful complication of bronchial sleeve surgery, which amounts to 1.9% to 14.3% of cases [20,22]. We observed

that complication in one (4.1%) of 24 cases. Urgent surgical intervention in the amount of pneumonectomy did not save the patient's life. These figures correspond to Corinna Ludwig et al., who reported anastomotic leak during bronchoplastic lobectomy in eight (6.9%) of 116 patients, with postoperative mortality of 4.3%. The main bronchus stump failure occurred in seven (3.6%) of 194 patients, with postoperative mortality of 4.6%. 5-year survival amounted to 39% after bronchoplastic lobectomy and 27% after pneumonectomy [24].

Conclusion

The lowest one-year survival of 67% SE10 (MST – 20.6 months) was registered after pneumonectomy, while after bronchoplastic, lobar resections, it amounted to 79% SE8 (MST – 36 months). The difference in median survival was statistically significant: $\chi^2 = 9.7$, $p = 0.045$. Thus, we consider the extent of surgery a risk factor. The organ ectomies should be minimized since our data and the literature report high one-year mortality and low 5-year survival after such surgeries.

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TREATMENT OF CHRONIC INJURIES CALCANEAL (ACHILLES) TENDON

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Semenov V.G., Dzhulfaev D.I., Zhamashev D.K., Davreshov A.A., Chachidze R.G.
The hospital of a fast emergency aid, Almaty, Kazakhstan

Semenov V.G.
orcid.org/0000-0002-4468-3793

Dzhulfaev D.I.
orcid.org/0000-0002-4436-3490

Zhamashev D.K.
orcid.org/0000-0002-1887-3665

Davreshov A.A.
orcid.org/0000-0002-7822-1351

Chachidze R.G.
orcid.org/0000-0002-3289-8252

Abstract

From 2015 to 2019 32 patients (14 men, 18 women), aged 15-65 years, underwent surgical treatment for old Achilles tendon rupture. In all cases correct diagnosis was made not earlier than 1 month after injury and sonographic examination for diagnosis of Achilles tendon rupture is underlined. For the restoration of Achilles tendon V-Y plasty was used. Surgery was performed in a period of 1 to 13 months in patients with subcutaneous Achilles tendon ruptures. Follow-up results of patients in the postoperative period ranged from 6 months to 10 years (mean follow-up 1 year 7 months). Date of observation in the postoperative period ranged from 6 months to 19 years. Marginal necrosis wound occurred in 3 (10%) patients, re-rupture of the Achilles tendon to tendon suture zone - in one patient, even in one patient on day 14 became infected. Violations of the foot innervation were no detected.

Keywords

rupture of the Achilles tendon,
ultrasound examination, V-Y plasty

Өкше (Ахилл) сіңірінің ескі зақымдануларын емдеу

Семенов В.Г., Джульфаев Д.И., Жамашев Д.К., Даврешов А.А., Чачидзе Р.Г.
Жедел шұғыл көмек көрсету ауруханасы, травматология бөлімшесі, Алматы қ., Қазақстан

Аңдатпа

2015-2019 жж. аралығында 32 науқасқа операция жасалды: ахилл сіңіріндегі ескі зақымдануларға байланысты 15-65 жас аралығындағы 14 ер адамға және 18 әйелге. Барлық жағдайда дұрыс диагноз жарақаттан кейінгі бір айдан ерте емес мерзімде қойылған және барлық жағдайда ультрасонография әдісі арқылы нақтыланған. Ұшын-ұшына тігу арқылы ахилл сіңірін V-Y-ұзарту хирургиялық техникасы қолданылды. Ахилл сіңірінің тері астындағы үзілулері бар науқастарға 1 айдан 3 айға дейінгі мерзімде операциялық араласу жүргізілді. Отадан кейінгі кезеңде науқастарды бақылау мерзімі 6 айдан 10 жылға дейінгі мерзімді қамтыды (орташа бақылау мерзімі 1 жыл 7 ай). Отадан кейінгі кезеңде бақылау мерзімі 6 айдан 19 жылға дейінгі мерзімді құрады. 3 (10%) науқаста операциядан кейінгі жараның шеткі некрозы дамыды, бір науқаста сіңір тігісінің аймағында ахилл сіңірінің қайталама үзілуі орын алды, тағы бір науқаста 14 тәулікте инфекциялық асқину дамыды. Табан иннервациясының бұзылысы анықталған жоқ.

Түйін сөздер

ахилл сіңірінің үзілуі,
ультрадыбыстық зерттеу,
V-Y-пластика

Лечение застарелых повреждений пяточного (Ахиллова) сухожилия

Семенов В.Г., Джульфаев Д.И., Жамашев Д.К., Даврешов А.А., Чачидзе Р.Г.
Больница скорой неотложной помощи, отделение травматологии, г. Алматы, Казахстан

Аннотация

С 2015 по 2019 г. прооперировано 32 пациента: 14 мужчин и 18 женщин в возрасте от 15 до 65 лет по поводу застарелого повреждения ахиллова сухожилия. Правильный диагноз во всех случаях был поставлен не ранее чем через месяц после травмы и всех случаях был подтвержден методом ультрасонографии. Применялась хирургическая техника V-Y-удлинения ахиллова сухожилия со сшиванием конец-в-конец. Оперативное вмешательство выполнялось в сроки от 1 до 13 месяцев у больных с подкожными разрывами ахиллова сухожилия. Сроки наблюдения за пациентами в послеоперационном периоде составили от 6 месяцев до 10 лет (средний срок наблюдения 1 год 7 месяцев). Сроки наблюдения в послеоперационном периоде составили от 6 месяцев до 19 лет. Краевой некроз послеоперационной раны развился у 3 (10%) пациентов, повторный разрыв ахиллова сухожилия в зоне шва сухожилия - у одной пациентки, еще у одного больного на 14-е сутки развилось инфекционное осложнение. Нарушений иннервации стопы выявлено не было выявлено.

Ключевые слова

разрыв ахиллова сухожилия,
ультразвуковое исследование,
V-Y-пластика.

Introduction

Calcaneal (Achilles) tendon ruptures account for 19-32% of the total number of musculoskeletal system large tendon injuries [8, 18].

Recovery after a rupture of the calcaneal (Achilles) tendon with extreme loads, for example, while playing sports, is an intractable and exclusively surgical task. The relevance of its solution increases in connection with the noted increase in injuries caused, in particular, by sports activities [5].

At the outpatient stage, 20 to 58% of calcaneal tendon injuries are not diagnosed [7]. In this regard, it becomes necessary to perform traumatic and time-consuming surgeries aimed at restoring old damage to this localization. Closed and open suture surgeries of the Achilles tendon in the acute period are not difficult, since there are no problems with eliminating the diastasis of the stumps. The ratio of patients operated on for fresh Achilles tendon injuries (up to 10 days) and chronic injuries, according to our data, is 5: 1 [9].

The low level of diagnosis of Achilles tendon ruptures is associated with the lack of doctors's special skills of the outpatient network. It is not difficult to make a correct diagnosis in the vast majority of cases. It is possible to assume an Achilles tendon rupture from the patient's typical complaints. Some compare their sensations with the blow of a whip from behind on the lower third of the lower leg, others note the crunch of a crushed nut, and still others try to find the one who struck them on the leg. In the first hours after the injury, in many victims of the asthenic and normosthenic body type, it is possible to visually and by palpation determine the retraction of the Achilles tendon in the damaged area. In addition, a simple diagnostic test, the Thompson test, helps to establish the diagnosis of "damage to the Achilles tendon" [22]. The patient kneels on the couch, the legs are horizontal, the feet hang freely from the edge of the couch. The doctor alternately on each of the legs sharply compresses the triceps muscle in the transverse direction in its widest part. In response to a healthy limb, plantar flexion of the foot occurs; on the side of the injury, flexion of the foot does not occur. In this case, positive test and tendon rupture should be discussed.

The most accessible method for diagnosing tendon injuries and diseases is considered to be ultrasound examination [2, 20]. Sonography not only helps the clinician to make a diagnosis in a timely manner, but also allows to assess the effectiveness and correctness of the surgical intervention. In addition, with the help of the ultrasound method, it is possible to assess the stages of tendon recovery and timely identify complications that have arisen in the postoperative period. Paying tribute to the

informative value of ultrasound research, it should be noted that there is a rather high frequency of erroneous interpretations of data obtained in the process of echolocation by specialists in ultrasound diagnostics. This leads to an underestimation of the tendon rupture degree and, as a consequence, to the wrong choice of treatment method and an increase in the number of patients seeking help at a later date. Sufficient experience of the researcher and the high class of the equipment used allows avoiding mistakes.

To restore the Achilles tendon anatomical integrity, a number of surgical methods are used, such as cutting out various flaps of the calcaneal tendon proximal stump, transposition of the peroneal muscle tendons, moving the long flexor tendon of the first toe, cutting out flaps from the thigh wide fascia.

One of the methods of Achilles tendon old injuries surgical treatment of is V-Y lengthening with end-to-end stitching. This method was first proposed and used in 1975 and is still widely used abroad [10, 19]. In Russia, the popularity of this method is low. In our country, the plastic of the heel tendon according to A.V. Chernavsky [8], despite a number of described negative parameters and proposed new methods [6].

The aim of the study was to evaluate the effectiveness of using Achilles tendon V-Y plastics with end-to-end stitching in case of its chronic injuries.

Material and methods

From 2015 to 2019, 32 patients were operated on: 14 men and 18 women aged 15 to 65 years. The average age was 46.6 for men and 50.4 for women. The diagnosis in all cases was confirmed by ultrasonography. The study was carried out on ultrasound scanners iU22 (PHILIPS MEDICAL SYSTEMS) and ALOKA ProSound Alpha 10 (Aloka) using sensors with a frequency of 5-12 MG.

The operative technique of Achilles tendon V-Y lengthening with end-to-end stitching is as follows. A large S-shaped incision of the skin and subcutaneous tissue penetrates to the fascia of the triceps muscle of the leg (m. triceps surae) and opens the distal third of this muscle, areas of the small saphenous vein (v. saphena parva) and the sural nerve (n. suralis). This wide access makes it possible to fully verify the anatomical structures and to visually determine the state of the damaged heel tendon ends.

In the zone of gastrocnemius muscle transition (m. Gastrocnemius) into the tendon extension, from the fibers of which the posterior portion of the calcaneal tendon is formed distally, a dissection is made along the edge of this formation (Fig. 1) and parts of individual strands that go into the depth of the muscle. We call this action V-mobilization and we perform it against the background of constant

traction for the proximal end of the tendon towards the calcaneus.

In the anterior part of the calcaneal tendon, as we conventionally believe, fibers coming from the perimysium of the soleus muscle (m. soleus), which does not have such a tendon extension as the digastric muscle, are interwoven, which allows the formation of a "retractable" flap. Sometimes this reduction can be significant (up to 6-7 cm) and extend to the calcaneal tubercle. In four clinical observations of our study (1 man and 3 women), this retraction ended with a transosseous suture. Bearing in mind that the tendon breaks during traction violence and looks morphologically the same as a rope or cable (Fig. 2), which requires the obligatory excision of the fiber ends, the tendon proximal end is cut off transversely until the capillary bleeding, the so-called "bloody dew" (Fig. 3). This is a reliable sign of reaching the blood supply part of the tendon. The distal end is cut off according to the plane of the proximal incision. With transosseous fixation, it is desirable to obtain capillary bleeding from the abrasively destroyed area of the calcaneal tubercle. Measurement of diastasis between the resected tendon ends is performed when the limb is bent at the knee joint to an angle of 160-170 ° (the position of the maximum weakening the triceps of the lower leg). To connect the tendon ends end-to-end, a Kuno or Kessler suture is used with additional separate U-shaped sutures. The area of the sending incision of the tendon stretch is sutured with separate sutures to form a Y-joint (Fig. 4). Such a seam is considered the most optimal for restoring the subsequent function [11]. Additional strengthening by means of tendon transposition was not used. The surgery was completed by closing the skin access using Donati-Algoveri sutures.

Neuraxial anesthesia (SMA) in combination with local anesthesia was used in the operation area, to anesthetize patients during the surgery.

The follow-up period for patients in the post-operative period ranged from 6 months to 10 years (average follow-up period 1 year 7 months).

Results and discussion

Surgical intervention was performed within 1 to 13 months in patients with subcutaneous Achilles tendon ruptures. Attention is drawn to the high average age of the observed patients. As mentioned above, it was 46.6 years for men and 50.4 for women. This, in our opinion, can be explained by the more common chronic degenerative changes in the Achilles tendon in the age group over 45, for which many patients underwent local injections of hormonal drugs (dipropan, kenalog). In addition, in patients over 55 years of age, motor activity is usually low, as a result of which the requirements for



Figure 1. Scheme of a V-shaped incision at the border of the tendon-muscular junction and excision of the tendon stumps

the range of physiological capabilities of the lower leg and foot are reduced. In young active people, the diagnosis of damage to the calcaneus is carried out in a timely manner, the suture is performed in the acute period, and there is no need to use special techniques to eliminate diastasis.

In our study, an ultrasound study was used to diagnose the Achilles tendon injury. This method was used in all patients. The diagnosis of "chronic rupture of the Achilles tendon" was correctly established in all cases. The difference in the size of diastasis of the damaged tendon ends revealed during sonography and surgical intervention, amounted to 1 cm. Thus, we can confidently state that ultrasound



Figure 2. Determination of the tendon defect after damaged part excision; the tendon of the plantar muscle and the Achilles tendon stump is visible



Figure 3. Tendon stumps are excised to bleeding tissue

Figure 4.
Scheme of the state after
the tendon lengthening
and suturing its ends

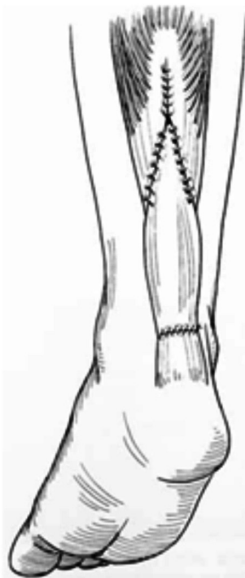


Figure 5.
Sonogram: Achilles tendon
chronic damage. In the
diastasis area (diastasis is
about 4 cm), scar tissue is
visualized in the form of a
heterogeneous hypoechoic
structure (arrows)



examination is a high-precision diagnostic method for Achilles tendon injuries, and it can be successfully applied at the prehospital stage in patients with suspicion of this type trauma. We admit that in non-specialized clinics, the indicators of ultrasound diagnostics of Achilles tendon injuries may not be so accurate, so we will share our experience.

In order to avoid possible errors in chronic Achilles tendon injuries, the researcher should pay attention to the following features. The tendon ends are degeneratively changed, often thinned, the damaged tendon loses its characteristic fibrillar striation, its echogenicity is reduced, which determines poor differentiation from the surrounding tissues (Fig. 5). In addition, in the zone of injured Achilles tendon diastasis, the intact tendon of the plantar muscle is often visualized, which is mistaken for an intact portion of the Achilles tendon, and sometimes for the tendon itself. To avoid misinterpretation of the received ultrasound image, it is imperative to perform a test with passive plantar flexion of the foot. Even with old injuries, despite the cicatricial process in the diastasis zone and around the tendon ends, the damaged ends will

diverge during the test, the distance between them will increase, and it will be easier for the researcher to understand the ultrasound picture. In addition, it is useful to conduct a sonography with a transverse location of the transducer from the point of attachment of the Achilles tendon to the calcaneal tuberosity to the tendon-muscle junction. In this projection, the difference between the structure of the damaged tendon ends and the structure of the scar tissue located in the diastasis zone is more clearly visible. The plantar tendon is always located along the medial edge of the tendon and must also be traced proximally in a transverse view. The Achilles tendon in the lower third of the leg passes into the gastrocnemius muscle, the tendon-muscular junction of the plantar muscle is located much higher - at the level of the upper third of the leg. In addition, the researcher should alert the revealed unchanged tendon structure with clinical symptoms of the Achilles tendon pathology.

For successful surgical treatment, let us note some of the features of the anesthesiological aid used by us during the surgery. Traditionally, spinal anesthesia (SA) is used to anesthetize patients during surgery using isotonic anesthetic solutions. A significant drawback of this technique, in our opinion, is an unreasonably extensive and unclaimed sympathetic and motor block of the lower extremities from the pelvic level. In addition, SA has a short period of effective postoperative pain relief. To reduce the area of anesthesia and increase its effectiveness, we use SA with the use of Marcaine Spinalheavy 0.5% at a dose of 12.5 ± 2.5 mg. The position of the patient is on the side of the operated limb with an exposure of 5 minutes.

Modern postoperative anesthesia of patients is carried out multimodal, which makes it possible to influence the blockade of pain impulses at different levels [4, 23].

To potentiate and prolong the analgesic effect in the postoperative period, local infiltration of the wound edges should be performed after the end of the operation [12]. For this purpose, ropivacaine 0.75% was used at a dose of 30 ± 10 ml or markain 0.5% 25 ± 5 ml. Infiltration was performed with the obligatory aspiration test. Dexamethasone 4–8 mg was added to the anesthetic solution to relieve postoperative edema. Immediately after the end of the operation, NSAIDs (ketoprofen 200 mg / day) were used in the absence of individual contraindications. Narcotic analgesics (promedol) were prescribed at the request of the patient. Our experience shows that the need for narcotic analgesics is more than halved, which demonstrates the opioid-saving effect and a decrease in the toxicity of opioid use [1, 3].

In the postoperative period, we used immobilization with an anterior longitudinal bandage "foot - lower leg" for 6 weeks with physical therapy from the 4th week. In some patients, S.V. Russkich functional splint was used for the same purpose, which allows you to gradually bring the foot to the right angle position [7]. The knee joint was not fixed, allowing movement in it from the 2-3 day after the operation. Upon reaching a dorsal flexion of 90 °, the patient began to load the foot.

The follow-up period in the postoperative period ranged from 6 months to 10 years. In the early postoperative period, the marginal necrosis of the postoperative wound should be noted, which developed in 3 (10%) patients, which required free skin grafting in 2 patients. We associate this with the errors of the previously used access, which led to overstrain and disruption of the blood supply to the suture zone after restoration of the tendon. It should be noted that the development of marginal necrosis in the early postoperative period is one of the most common complications in reconstructive operations on the Achilles tendon. In the articles devoted to various methods of restoring the anatomical integrity of this tendon in chronic injuries, information on the incidence of postoperative complications is extremely scarce. However, the authors note that marginal necrosis is often found during reconstructive surgery on the Achilles tendon, and plantar flexion of the foot up to 20 ° is necessary as a preventive measure in the postoperative period, since in this position the vascularization of the surrounding soft tissues is maximal [19]. We also consider this position of the foot to be neutral, not leading to the appearance of areas of tension in the skin and, accordingly, vascular spasm.

Another complication often encountered during reconstructive operations is the repeated rupture of the Achilles tendon in the tendon suture zone in the postoperative period. During the entire observation period, this type of complication was encountered in one patient. Re-injury occurred at the time of a sharp load on the foot, when the patient fell on the operated leg a month after the operation, accidentally slipping. Secondary surgical debridement of the postoperative wound edges was performed with restoration of the integrity of the tendon and skin. Later, the rehabilitation period was successful. The observation period for the patient was 6 months. In our opinion, in order to avoid repeated rupture of the Achilles tendon in the stitching zone, it is necessary to carry out the rehabilitation period with great care and not to rush to move the foot to the position of dorsiflexion up to 90 °. Rehabilitation of operated patients in our study began 1-1.5 months after surgery.

M.R. Carmont [14] reports about 9% of infectious complications after reconstructive operations on the Achilles tendon. In our study, we noted only one such case (3% of the total number of patients), the complication developed on the 14th day after the operation. The patient was operated on 13 months after receiving a subcutaneous rupture of the Achilles tendon. While performing V-Y plasty, an almost complete absence of muscle tissue extensibility was found due to significant fibrous degeneration of the triceps muscle of the leg, which did not have such a long term of contractile function and adequate blood supply. The intervention was performed with technical difficulties, the postoperative scar was formed initially, after the removal of the stitches, the patient was discharged for outpatient treatment. The doctor of the polyclinic during dressing, removing the crust over the skin scar, revised the epithelialization zone using a hemostatic clamp. A month after the first operation, the patient was hospitalized with a developing fistula in the area of the postoperative scar. After a secondary surgical debridement, the wound closed.

In the postoperative period, none of the patients we operated on had any disturbances in the innervation of the foot.

As an example, we give the following clinical observation.

Patient R., 67 years old, was injured 4 months before going to the clinic. She stumbled on the street, felt a sharp pain in the lower leg. I compared it with an electric shock to the leg. In the clinic, the diagnosis was made: a partial rupture of the left Achilles tendon. Was treated functionally in an elastic bandage with limited load for 6 weeks. 2 months after the injury, she stumbled again, felt pain in the same leg. The next day, a massive bruise appeared in the lower third of the lower leg. The clinic again diagnosed a partial rupture of the Achilles tendon, prescribed physiotherapy, there was no immobilization. Then, for two months, periodically, against the background of a constant pain syndrome, smaller bruises appeared, which was accompanied by swelling of the lower leg and lameness. I applied for a consultation on my own. On examination, the strength of the injured leg is reduced, there is moderate edema and retraction in the zone of rupture of the calcaneal tendon. Thompson's symptom is positive. Active movements in the ankle joint are reduced. Operated 4.5 months after injury. The tendon defect after excision of scar tissue was 5 cm. Under conditions of adequate anesthesia and muscle relaxation, V-Y plasty of the left Achilles tendon was performed with an end-to-end suture. The anterior plaster cast was applied in the equinus position of the foot. Primary wound healing, the sutures were removed on the 14th day after

the operation. Classes with an instructor began 5 weeks after the operation, the immobilization was finally removed 2 weeks after the start of exercise therapy. She was discharged for work 2 months after the operation. Control examination 13 months

after the intervention: there is no edema, the zone of the tendon regenerate is thickened, painless, the range of motion in the ankle joint is comparable to the intact limb, as well as muscle strength. Able to stand on toes, no limp.

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EVALUATION OF THE EFFECTIVENESS OF THE USE OF A BIPOLAR MINI-RESECTOSCOPE TO IMPROVE THE PROVISION OF GYNECOLOGICAL CARE TO PATIENTS WITH INTRAUTERINE PATHOLOGY

Chupin A.N.^{1,2}, Mamyrbekova S.A.², Aldangarova G.A.¹

¹JSC "National Scientific Center of Surgery named after A.N.Syzganov", Almaty, Kazakhstan

²Al-Farabi Kazakh National University, Almaty, Kazakhstan

Chupin A. N.

orcid.org/0000-0001-6592-2755

Mamyrbekova S. A.

orcid.org/0000-0002-3840-4284

Aldangarova G. A.

orcid.org/0000-0001-5927-0687

Abstract

The analysis of the results of a comprehensive clinical and instrumental examination of 104 women who were treated in the day hospital of the Department of Gynecology in JSC "National Scientific Center of Surgery of A. N. Syzganov" in the period from September 2019 to December 2020 was carried out. In order to evaluate the effectiveness of the technology of bipolar "mini" resectoscopy in intrauterine pathology in women with various forms of infertility, 104 patients were examined, which were divided into two groups:

Group 1 – patients with primary infertility (41);

Group 2 – patients with secondary infertility (63).

The study included women aged 21 to 45 years, the average age of patients was 31.5 years. The main complaint of all patients was the absence of pregnancy with regular sexual activity for 1-10 years. Menstrual disorders were observed in 61 women, which was 59%. The analysis of clinical and anamnestic data of 104 women showed the presence of primary infertility in 40.0% of patients, and secondary infertility in 59%. In women with primary and secondary infertility after mini-hystero resectoscopy (GDS), the lowest percentage of intrauterine pathology was endometrial hyperplasia (0.9%) and frequent or complete intrauterine septa (0.9%). Submycous uterine fibroids were diagnosed in 3.2% of patients, and in 12% of cases there were intrauterine synechiae. The largest number of patients encountered pathologies - chronic endometritis (45%), endometrial polyp (38%). Thus, in the study groups, we determined and established the frequency of intrauterine pathology in women with various forms of infertility after mini-GDS. All surgical manipulations of bipolar mini-hysteroscopy with resection were performed without anesthesia in 43.2% of cases and under local anesthesia in 56.8%.

Keywords

mini hystero resectoscopy, intra-uterine pathology, various forms of infertility

Жатырішілік патологиясы бар науқастарға гинекологиялық көмек көрсетуді жақсарту мақсатында биполярлық мини-резектоскопты қолданудың тиімділігін бағалау

Чупин А.Н.^{1,2}, Мамырбекова С.А.², Алдангарова Г.А.¹

¹«А.Н.Сызғанов атындағы Ұлттық ғылыми хирургия орталығы» АҚ, Алматы қ., Қазақстан

²Әл-Фараби атындағы Қазақ ұлттық университеті, Алматы қ., Қазақстан

Аңдатпа

2019 жылғы қыркүйек және 2020 жылғы желтоқсан аралығында «А.Н. Сызғанов атындағы Ұлттық ғылыми хирургия орталығы» АҚ-да гинекология бөлімшесінің күндізгі стационарында емделіп жатқан 104 әйелдің кешенді клиникалық-аспаптық тексеру нәтижелеріне талдау жүргізілді. Бедеуліктің түрлі формалары бар әйелдердегі жатырішілік патология кезінде биполярлы «мини» резектоскопия технологиясының тиімділігін бағалау мақсатында 104 науқас тексерілді, олар екі топқа бөлінді:

1 топ – бастапқы бедеулігі бар науқастар (41);

2 топ – қайталама бедеулігі бар науқастар (63).

Зерттеуге 21 жастан 45 жасқа дейінгі әйелдер қатысты, науқастардың орташа жасы 31,5 жасты құрады. Барлық науқастардың негізгі шағымы – 1-10 жыл бойы тұрақты жыныстық қатынаста жүктіліктің болмауы. 61 әйелде менструальдық циклдің бұзылуы байқалды, бұл 59%-ды құрады. 104 әйелдің клиникалық-анамнестикалық деректерін талдау науқастардың 40,0%-ында бастапқы бедеуліктің, ал 59% -ында қайталама бедеуліктің бар екенін көрсетті. Мини гистерорезектоскопияны (ГТС) жүргізгеннен кейін бастапқы және қайталама бедеулігі бар әйелдерде жатырішілік патологияның ең төменгі пайызы эндометриялық гиперплазия (0,9%) және жиі немесе толық жатырішілік септумдар (0,9%) болды. Науқастардың 3,2%-ына субмикозды жатыр миомасы диагнозы қойылған, ал 12% жағдайда жатыр ішілік синехия болған. Науқастардың басым бөлігінде созылмалы эндометрит (45%), эндометрия полипі (38%) патологиялары кездесті. Осылайша, зерттелген топтарда біз мини ГТС-тен кейін бедеуліктің түрлі формалары бар әйелдердегі жатырішілік патологияның жиілігін анықтадық. Резекциясы бар биполярлы мини гистероскопияның барлық хирургиялық манипуляциясы 43,2% жағдайда анестезиясыз және 56,8% жағдайда жергілікті анестезия арқылы жүргізілді.

Түйін сөздер

мини гистерорезектоскопия, жатырішілік патология, бедеуліктің түрлі формалары

Оценка эффективности применения биполярного мини-резектоскопа для улучшения оказания гинекологической помощи пациенткам с внутриматочной патологией

Чупин А.Н.^{1,2}, Мамырбекова С.А.², Алдангарова Г.А.¹

¹АО «Национальный научный центр хирургии им. А.Н.Сызганова», г. Алматы, Казахстан

²Казахский Национальный Университет им.Аль-Фараби, г. Алматы, Казахстан

Аннотация

Проведен анализ результатов комплексного клинико-инструментального обследования 104 женщин находившиеся на лечении в дневном стационаре отделения гинекологии в АО «Национальный научный центр хирургии А.Н. Сызганова» в период с сентября 2019 г. по декабрь 2020 г. С целью оценки эффективности технологии биполярной «мини» резектоскопии при внутриматочной патологии у женщин с различными формами бесплодия было обследовано 104 пациенток, которые были распределены по двум группам:

1 группа – пациентки с первичным бесплодием (41);

2 группа – пациентки с вторичным бесплодием (63).

В исследование вошли женщины в возрасте от 21 лет до 45 лет, средний возраст пациенток составил 31,5 лет.

Основной жалобой всех пациенток было отсутствие беременности при регулярной половой жизни в течение 1-10 лет. Нарушения менструального цикла отмечали 61 женщин, что составила 59%. Анализ клинико – анамнестических данных 104 женщин показал наличие первичного бесплодия у 40,0% пациенток, а вторичного – у 59%. У женщин с первичным и вторичным бесплодием после проведения мини гистерорезектоскопии (ГРС) самый низкий процент внутриматочной патологии составил гиперплазия эндометрия (0,9%) и частые или полные внутриматочные перегородки (0,9%). Субмукозная миома матки диагностирована у 3,2% пациенток, а в 12% случаях была внутриматочные синехии. Наибольшее число пациенток встречались с патологиями - хронический эндометрит (45%), полип эндометрия (38%). Таким образом, в исследуемых группах мы определили и установили после мини ГРС частоту внутриматочной патологии у женщин с различными формами бесплодия. Все хирургические манипуляции биполярной мини гистероскопии с резекцией производили без обезболивания в 43,2% случаев и в 56,8% - под местной анестезией.

Ключевые слова

мини гистерорезектоскопия, внутриматочная патология, различные формы бесплодия

Introduction

The basis for the development of modern healthcare remains the improvement of the organization of medical care. In the difficult conditions of economic transformations and deterioration of the health status of the population, improving the organization and improving the quality of gynecological care occupies one of the important places in the reform of the health system of the Republic of Kazakhstan [1].

One of the possible factors of infertility is intrauterine pathology. The frequency of detection of intrauterine pathology in the clinic of female infertility varies quite widely - from 8.5% to 62% according to various authors, which indicates the lack of systematic studies in the group of women with various forms of infertility and the need for further study [2, 3].

According to Boivin et al., 2007, it is shown that 72.4 million couples are infertile worldwide and that 40.5 million of them are currently seeking infertility treatment [4].

According to Maximova T. A. (2019), one of the leading causes of female infertility in the last decade is called intrauterine pathology. Diseases such as hyperplastic processes, endometrial polyps, endocervix pathology, intrauterine synechiae, submucous uterine fibroids, and adenomyosis are an urgent problem of gynecology - in 53.2% of women of reproductive age, including patients us-

ing assisted reproductive technologies [5, 6].

In the available literature, there are works concerning the frequency and structure of intrauterine pathology in patients with infertility of various origins. Thus, in patients with peritoneal factors of infertility, endometrial pathology was detected in 44.3% of cases. The most common pathology is endometrial polyp (20.3%). Submucous uterine fibroids were found in this group in 1.7%, chronic endometritis – 0,9% [7, 8, 9].

Another author also revealed a high incidence of intrauterine pathology in women with infertility of unknown origin - 37%. In this study group, the most common pathology was also endometrial polyp and endometrial hyperplasia (15.5% and 9.5%, respectively) [10, 11].

Objective: To evaluate the effectiveness of the introduction of a bipolar mini-resectoscope based on the study of the frequency of intrauterine pathology in women of reproductive age.

Material and methods

The volume of the material was used by patients aged 21 to 45 years (average age 31.5 years) who were treated in the Department of Gynecology of JSC "National Scientific Center of Surgery of A. N. Syzganov" in the period from September 2019 to December 2020.

The study included 104 patients with intrauterine pathology of reproductive age.

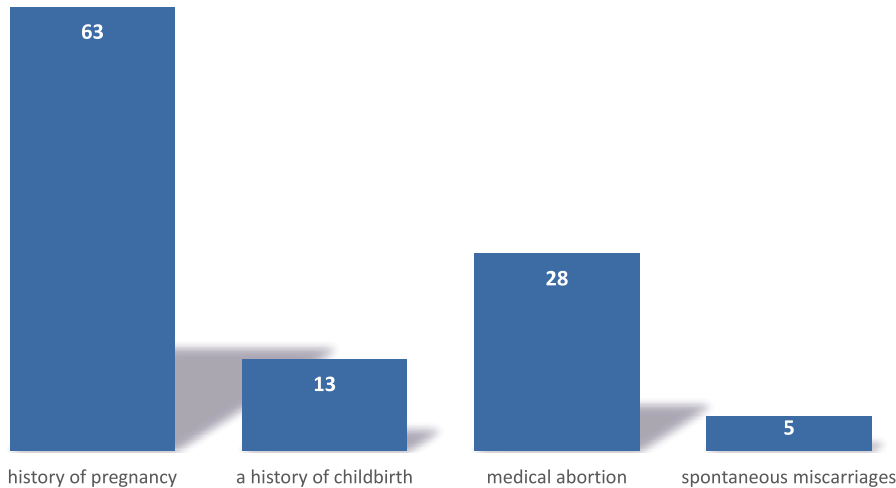


Figure 1.
Frequency of reproductive function of the women studied

The duration of infertility in the patients was from 1 to 10 years (6.5 ± 0.5).

Depending on the factors of infertility, the patients were divided into groups:

Group 1 – patients with primary infertility (41);

Group 2 – patients with secondary infertility (63).

When including patients in the present study, absolute and relative indications and contraindications to bipolar "mini" resectoscopy were taken into account.

According to these indications and contraindications, the criteria for inclusion and exclusion of patients in the study were developed.

Clinical research methods: analysis of complaints, collection of anamnesis, objective examination, description of gynecological status.

When conducting clinical and laboratory research methods, the main material was venous blood, urine sediment, and vaginal smears in 104 examined women.

Pelvic ultrasound examinations were mandatory methods of examination of patients before and in the postoperative period, both in the hospital and in

the outpatient setting during the period of dynamic observation.

Statistical method of data processing using a program in Excel, calculating the average, standard deviation, the indicator of the reliability of differences in two groups, conducting a correlation analysis.

Results

The main complaint of all patients was the absence of pregnancy with regular sexual activity for 1-10 years. Menstrual disorders were observed in 61 women, which was 59%.

The analysis of clinical and anamnestic data of 104 women showed the presence of primary infertility in 40.0% of patients, and secondary infertility in 59%.

Figure 1 shows data on the distribution of patients with intrauterine pathologies by reproductive function.

As can be seen from Figure 1, the frequency of reproductive function of the studied women prevailed in the second group. In 63 cases, the women had a history of pregnancy, 13 births, 28 abortions, and 5 miscarriages.

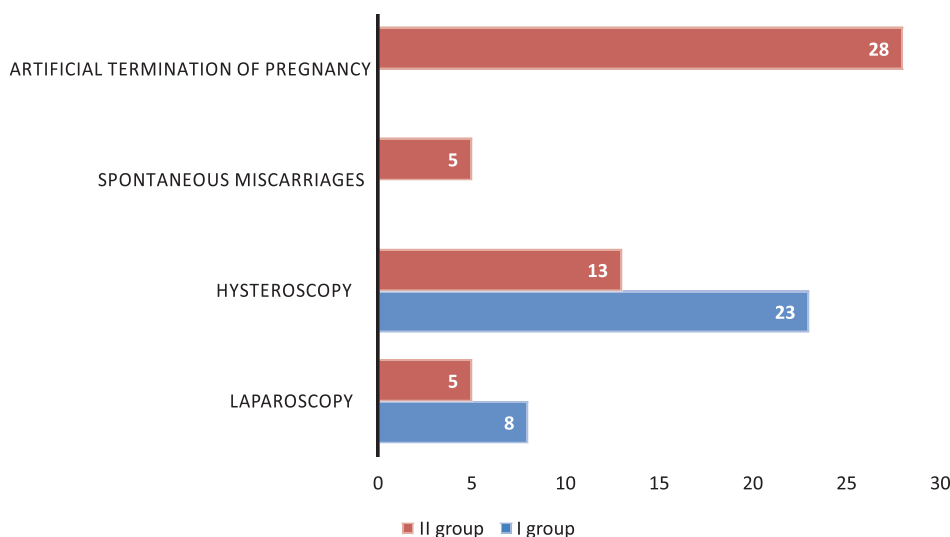
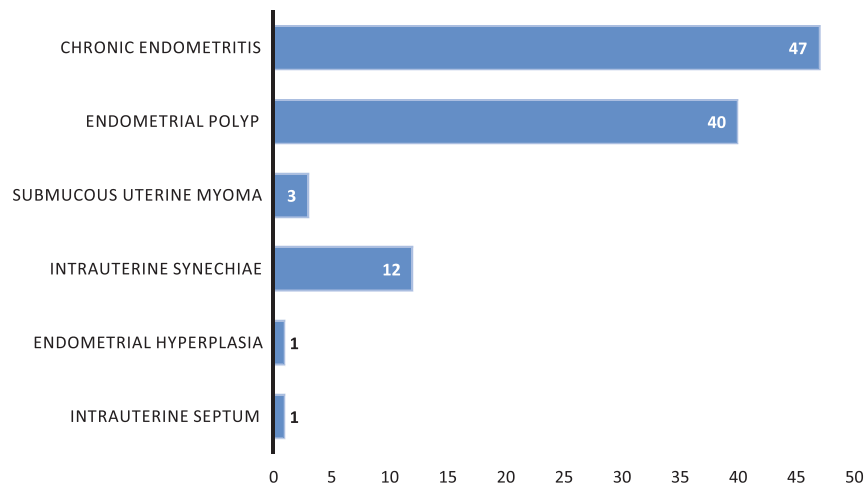


Figure 2
The frequency of therapeutic and diagnostic intrauterine surgical interventions

Figure 3.
Frequency of intrauterine pathology in women with various forms of infertility after mini-HRS



51 women had various medical and diagnostic intrauterine surgeries before applying to our clinic.

The given Figure demonstrates that no woman mentioned artificial termination of pregnancy in the first group, whereas 28 (45%) women had surgical procedures in the second. In addition only 5 women in group 2 suffered from spontaneous miscarriage (followed by curettage), which is 8%. Also, hysteroscopy prevails in 23 cases (56%) in group 1 and in 13 cases (21%) in group 2. If we talk about laparoscopy, there were 5 cases (12%) in the first group and 8 cases (13%) in the second.

Most of the women in the studied groups suffered from previous and concomitant gynecological diseases. With concomitant inflammatory diseases of the pelvic organs such as: vulvovaginitis, colpitis, cervicitis, chronic endometritis, chronic salpingo-oophoritis, endometrial hyperplasia, endometrial polyp, synechiae of the uterine cavity, uterine myoma, septum - there were 94 (91%) women.

In the studied groups, after mini-resectoscopy, intrauterine pathology was confirmed by a clinical diagnosis with biopsy.

All 104 patients with intrauterine pathology underwent mini-hysteroscopy (mini-HRS) with mandatory histological examination.

According to the figure, in women with primary and secondary infertility after mini-HRS, the lowest percentage of intrauterine pathology was endometrial hyperplasia (0.9%) and frequent or complete intrauterine septa (0.9%). Submucous uterine myoma was diagnosed in 3.2% of patients, and in 12% of cases there was intrauterine synechiae. The

largest number of patients met with pathologies - chronic endometritis (45%), endometrial polyp (38%). The incidence of intrauterine pathology according to clinical data among women with various forms of infertility was 74%.

Thus, after carrying out mini-HRS, we identified and established the frequency of intrauterine pathology in women with various forms of infertility - 74%

We have developed and successfully introduced into practice a fundamentally new method of surgical diagnosis and treatment of intrauterine pathology using bipolar mini-resectoscopy.

We removed all endometrial polyps up to 2 cm by the operative mini-hysteroscopy without anesthesia. If the polyp was larger than 2 cm, just by the method of mini-hysteroscopy. With intrauterine synechiae, all patients undergo dissection using the operative mini hysteroscopy. With a thin septum of the uterine cavity and habitual miscarriage, the dissection is performed using the method of operational mini hysteroscopy without anesthesia. In case of a thin septum of the uterine cavity in combination with infertility, dissection was performed using the method of operational mini-hysteroscopy.

As can be seen from the table, the efficiency of bipolar mini-hysteroscopy technology in women with intrauterine pathologies is 100%.

The degree of pain was determined according to the classification of the European Association of Hysteroscopists. All surgical manipulations of bipolar mini hysteroscopy with resection were per-

Table 1.
Efficiency of bipolar mini-hysteroscopy technology in the studied groups

Evaluation parameters	I group (n=41)	II group (n=63)	P
Pain level (VAS)	2,8±1,3	2,4±1,6	<0,01
Duration of surgery	12,52±1,8 min.	13,21±1,7 min.	< 0,01
Duration of incapacity for work	1 day	1 day	<0,01
Complications	no	no	
Relapse after surgery	no	no	

formed without anesthesia in 43.2% of cases and in 56.8% of cases under local anesthesia.

Only local anesthesia was used in our study. The choice of this method depended on the volume of the operation and the general health of the patient (increased anxiety, the presence of allergies or other concomitant diseases). We mainly used local anesthesia (cervical injections).

The duration of anesthesia in our manipulations ranged from 10 minutes to 30 minutes. All patients were admitted to the day hospital. The duration of surgery in group 1 ranged from 10 minutes to 15 minutes (an average of 12.52 ± 1.8 minutes), and in group 2, an average of 13.21 ± 1.7 minutes. The difference between the groups is statistically reliable ($p < 0.01$). The average duration of the opera-

tion for bipolar mini-hysteroscopy was 9.1 ± 1.3 minutes, and for mini-hysteroresectoscopy - 12.52 ± 1.8 minutes ($p < 0.01$). The difference is statistically authentic. There were no intra/postoperative complications in both groups. The recurrence rate after surgery was not observed during the year.

Conclusions

Thus, bipolar mini-resectoscopy technology is an effective outpatient procedure with better long-term results than traditional hysteroresectoscopy. The technology of bipolar mini-hysteroresectoscopy allows intrauterine operations to be performed at the day hospital level, therefore, the cost of treating women with intrauterine pathology is reduced in comparison with inpatient treatment.

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A CLINICAL CASE OF POST-TRAUMATIC CICATRICIAL STENOSIS OF THE RIGHT MAIN BRONCHUS

Shirtaev B.K. –
orcid.org/0000-0002-0773-3878

Sundetov M.M. –
orcid.org/0000-0002-0387-5422

Akilbekov S.D. –
orcid.org/0000-0003-4613-1658

Kurbanov D.R. –
orcid.org/0000-0002-0426-9387

Khalykov K.U. –
orcid.org/0000-0003-1266-697X

Yerimova N.Zh. –
orcid.org/0000-0002-0565-5327

Kokimbayev D.A. –
orcid.org/0000-0001-7879-3328

Alkhanov B.A. –
orcid.org/0000-0001-6543-0712

**Shirtaev B.K.¹, Sundetov M.M.¹, Akilbekov S.D.², Kurbanov D.R.¹,
Khalykov K.U.¹, Yerimova N.Zh.¹, Kokimbayev D.A.¹, Alkhanov B.A.¹**

¹JSC “National Scientific Center of Surgery named after A. N. Syzganov”, Almaty, Kazakhstan

²Al-Farabi Kazakh National University, Almaty, Kazakhstan

Keywords
cicatricial stenosis,
resection of the bronchus

Abstract

Damage to the tracheobronchial tree often occurs due to severe bruising or crushing of the chest. We describe a case of surgical treatment of a rare and complex surgical pathology-post-traumatic scar stenosis of the right main bronchus. This article presents the course of the patient's treatment and diagnosis, describes the stages of the operation and gives recommendations to surgeons.

Оң негізгі бронхтың жарақаттан кейінгі тыртықты тарылуының клиникалық жағдайы

**Ширтаев Б.К.¹, Сундетов М.М.¹, Ақылбеков С.Д.², Құрбанов Д.Р.¹,
Халықов Қ.Ұ.¹, Еримова Н.Ж.¹, Кокимбаев Д.А.¹, Алханов Б.А.¹**

¹«А.Н. Сызғанов атындағы Ұлттық ғылыми хирургия орталығы» АҚ, Алматы қ., Қазақстан

²Әл-Фараби атындағы Қазақ ұлттық университеті, Алматы қ., Қазақстан

Түйін сөздер
тыртықты тарылу,
бронхтың резекциясы

Аңдатпа

Кеңірдек және бронхтардың зақымдануы көбінесе ауыр жарақат немесе кеуде қуысының қысылуы нәтижесінде пайда болады. Біз күрделі және сирек кездесетін оң жақ бронхтың жарақаттан кейінгі тыртықты тарылуының хирургиялық емдеу жолын сипаттаймыз. Бұл мақалада науқасты жүргізу және диагноз қою барысы, ота кезеңдері сипатталған және хирургтарға ұсыныстар берілген.

Клинический случай посттравматического рубцового стеноза правого главного бронха

**Ширтаев Б.К.¹, Сундетов М.М.¹, Акильбеков С.Д.², Курбанов Д.Р.¹,
Халыков К.У.¹, Еримова Н.Ж.¹, Кокимбаев Д.А.¹, Алханов Б.А.¹**

¹АО «Национальный научный центр хирургии им. А.Н. Сызганова», г. Алматы, Казахстан

²Казахский национальный университет им. Аль-Фараби, г. Алматы, Казахстан

Ключевые слова
рубцовый стеноз,
резекция бронха

Аннотация

Повреждения трахеобронхиального дерева часто возникает вследствие тяжелого ушиба или раздавливания грудной клетки. Мы описываем случай хирургического лечения редкой и сложной хирургической патологии - посттравматического рубцового стеноза правого главного бронха. В данной статье представлена ход введения больного и диагностики, описана этапы операции и даны рекомендации хирургам.

Introduction

The cause of post-traumatic cicatricial stenosis of the main bronchi is often ruptures of the main bronchi with a closed chest injury. The main symptoms of bronchial stenosis: paroxysmal cough, shortness of breath, hypoventilation/emphysema of the lungs, inflammatory changes below the site of narrowing. The frequency of tracheal ruptures in closed chest trauma is from 0.5 to 0.9 %, and the main and lobar bronchi—from 2 to 5 % (Figure 1). The main methods of treatment for bronchial rupture are suturing the site of the rupture, and resection of the bronchus with end-to-end anastomosis during the formation of scar stenoses. Given the rarity of such patients, the description of individual clinical cases of the disease is useful.

Clinical case

Patient Kh., 18 years old, was admitted to the A. N. Syzganov national scientific center of surgery on 04.12.19 with complaints of severe shortness of breath, cough with difficult-to-separate sputum, pain in the chest. From the anamnesis: 02.11.19, he was injured in an accident. The scene of the accident were taken by ambulance in the hospital with polytrauma: spontaneous right pneumothorax, subcutaneous emphysema, fracture of the right scapula, fractured ribs III – X on the right, fracture of the pelvis. He was urgently hospitalized in the intensive care unit, and the pleural cavity was drained on the right side. The next day, the patient was transferred to the city hospital. Fibrobronchoscopy revealed a partial rupture of the main bronchus on the right. In dynamics, scar stenosis was formed at the site of the rupture, and therefore balloon dilation was performed twice. Given the lack of effect, the patient was transferred to our center. Chest X-ray from 05.12.19: Right (partial) segmental atelectasis of the lower lobe (S7, S9, S10) the lower lobe is reduced in volume, effusion along the main interlobar pleura. The high standing of the diaphragm. Fibrobronchoscopy from 06.12.19 (Figure 2): The mouth of the right bronchus is scarred to 0.3-0.4 cm. The length is about 0.7-0.8 cm. Cicatricial stenosis of the right bronchus. Computed tomography of the chest organs from 01.12.19 (Figure 3): CT-picture of scar stenosis of the right main bronchus.

A preoperative diagnosis was established: posttraumatic scar stenosis of the right main bronchus. It was decided to perform a circular resection of the right main bronchus with an end-to-end anastomosis. Operation was performed on 10.12.19: in the position of the patient on the

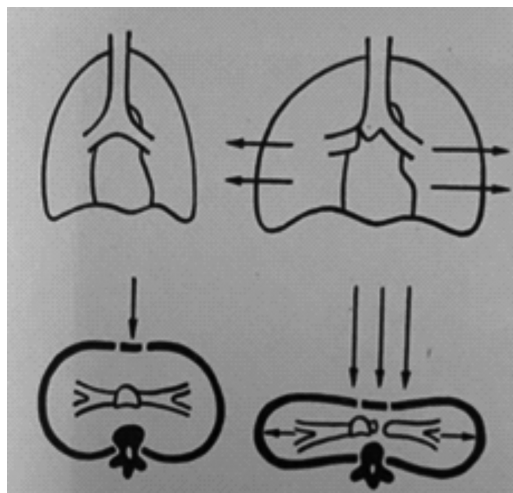


Figure 1.
Scheme of rupture of the main bronchus



Figure 2.
Fibrobronchoscopy on admission



Figure 3.
Computed tomography of the chest organs on admission

left side, a lateral thoracotomy was performed in the 3rd intercostal space on the right. By dissecting the parietal pleura in the projection of the trachea and the posterior edge of the lung root, access to the mediastinum was made. With technical difficulties, the right main bronchus was isolated. Immediately after carina, the right main bronchus is sharply deformed, narrowed, repre-

Figure 4.
Operation diagram

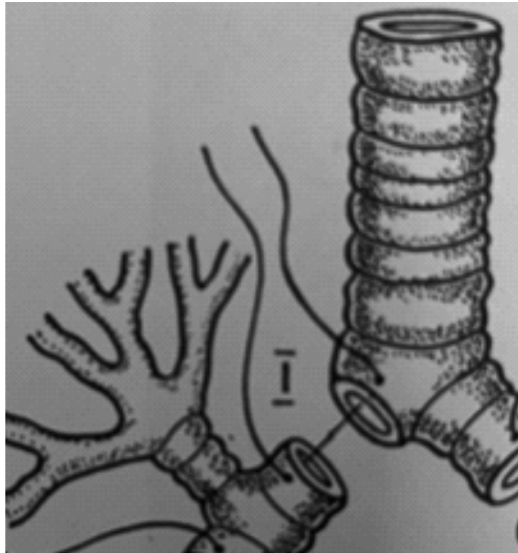


Figure 5.
Fibrobronchoscopy at
discharge



sented by a scar conglomerate up to the level of the upper lobe bronchus. The right vagus nerve and the proximal part of the unpaired vein are involved in the scar. After mobilization of the unpaired vein and n. vagus, a transverse intersection of the right main bronchus was made at the level of deformation. The lumen of the bronchus is obliterated, its wall is scarred. Scar tissue at both ends is excised to healthy tissue. The distal edge is 3 mm to the level of the upper lobe of the bronchus, the proximal edge is directly on the carina. An end-to-end bronchial anastomosis was applied with nodular sutures (PDS 4/00), with

a lumen of 13 mm (Figure 4). The length of the resected bronchus is 18 mm. The operation was completed by draining the pleural cavity.

Over the next few days, the patient received hormonal, antibacterial and inhalation therapy. In the first days after the operation, a pronounced hypoventilation of the right lung, fluid in the pleural cavity was noted on the chest X-ray. The post-operative period was uneventful. The drainage tube was removed on the tenth day after the operation. Fibrobronchoscopy from 23.12.19 (Figure 5): On the right main bronchus at the level of the carina there is an annular narrowing covered with fibrin, with a diameter of up to 0.9 cm. Below immediately begins the mouth of the upper lobar and intermediate bronchi. The patient was discharged in a satisfactory condition on the twenty-fifth day after the operation.

Discussion

An analysis of the literature shows that with active surgical treatment tactics, the majority of patients with tracheobronchial injuries helps to avoid late complications, in the form of cicatricial stenosis of the trachea and main bronchi. In our case, the patient turned in a month after the chest injury. Subsequently, what influenced the course of the operation and the patient's management tactics. One of the key roles in such situations is played by the factor of the time of delivery of the victim to the medical center, the beginning and execution of the operation.

Conclusion

Thus, in the treatment of ruptures of the main bronchi, the method of choice is an emergency thoracotomy and open suturing of the ruptures.

Also, early diagnosis and surgical treatment can avoid cicatricial stenosis of the main bronchi. To establish the rupture of the main bronchi both in the early and late period, a comprehensive study is necessary: CT of the chest organs and endoscopy. Fibrobronchoscopy is the main and main method of diagnosis and control of the effectiveness of the performed operation.

Proper surgical tactics and timely surgery allow you to achieve a good result.

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TUBAL-PERITONEAL INFERTILITY. TREATMENT. (REVIEW) PART 2

Toreeva Sh.M.

orcid.org/0000-0003-1198-8248

Kosherbayeva L.K.

orcid.org/000-0001-8376-4345

Aldangarova G.M.

orcid.org/0000-0001-5927-0687

Toreeva Sh.M.^{1,3}, Kosherbayeva L.K.¹, Aldangarova G.A.^{2,3}

¹Al-Farabi Kazakh National University, Almaty, Kazakhstan

²Kazakh-Russian Medical University, Almaty, Kazakhstan

³JSC "National Scientific Center of Surgery named after A.N.Syzganov", Almaty, Kazakhstan

Abstract

Today, in the age of modern technologies, despite advances in reproductology and improvements in methods of assisted reproductive technologies(ART), the frequency of infertile marriage has not only not stabilized, but also increases from year to year, reaching 25-30% in the population. Tubal-peritoneal infertility is one of the leading places in the frequency of occurrence of various factors leading to the absence of pregnancy.

The female factor in infertile marriage is 40%, the share of the male factor is determined in 40% of cases, and in other cases of infertility there is a combined factor, both female and male. In this regard, the search for new methods and their improvement, as well as reducing the cost of infertility treatment, seem very relevant.

Inflammatory lesions of the fallopian tubes are the leading cause of infertility. As a result of the chronic inflammatory process that occurs with the defeat of the fallopian tubes, the risk of developing tubal-peritoneal infertility is high. Every fifth woman with a history of chronic inflammation of the appendages suffers from infertility, while 70% of them have a fourth degree of adhesion in the pelvis, in which the damage to the fallopian tubes is irreversible even with the help of surgical treatment.

Keywords

infertility, tubal-peritoneal factor, proxy obstruction of the fallopian tubes, selective hysterosalpingography, transcatheter recanalization of the fallopian tubes.

Түтікті-перитонеальды бедеулік. Емі. (Әдебиет шолуы) 2 Бөлім

Тореева Ш.М.^{1,3}, Кошербаева Л.К.¹, Алдангарова Г.А.^{2,3}

¹Әл-Фараби атындағы Қазақ ұлттық университеті, Алматы қ., Қазақстан

²Қазақстан-Ресей медициналық университеті, Алматы қ., Қазақстан

³«А.Н.Сызғанов атындағы Ұлттық ғылыми хирургия орталығы» АҚ, Алматы қ., Қазақстан

Аңдатпа

Бүгінгі таңда, заманауи технологиялар ғасырында репродуктологиядағы жетістіктерге және қосалқы репродуктивтік технологиялар (ҚРТ) әдістерінің жетілдірілуіне қарамастан, бедеулік некенің жиілігі тұрақтанып қана қоймай, популяцияда 25-30%-ға жетіп, жылдан жылға ұлғаяуда. Түтікті-перитонеальды бедеулік жүктіліктің болмауына әкелетін түрлі факторлардың пайда болу жиілігі бойынша жетекші орындардың бірінде орналасқан.

Бедеулік кезіндегі әйел факторы 40%-ды құрайды, еркек факторының үлесі 40% жағдайға байланысты, ал басқа жағдайлардағы бедеулік кезінде әйелде де, еркекте де аралас фактор бар. Осыған байланысты жаңа әдістерді іздеу және оларды жетілдіру, сондай-ақ бедеулікті емдеу құнын төмендету өте өзекті мәселе деп саналады.

Фаллопиялық түтіктердің қабыну зақымдануы - бедеуліктің негізгі себебі. Фаллопиялық түтіктердің зақымдалуымен жүретін созылмалы қабыну процесінің нәтижесінде түтікті-перитонеальды бедеуліктің даму қаупі жоғары. Созылмалы қабынуы бар әрбір бесінші әйел бедеуліктен зардап шегеді, ал олардың 70%-ының жамбас аймағында адгезия процесінің төртінші дәрежесі бар, мұндай жағдайда фаллопиялық түтіктердің зақымдануы тіпті хирургиялық емдеу арқылы да қалпына келмейді.

Түйін сөздер

бедеулік, түтікті-перитонеальды фактор, жатыр түтіктерінің проксимальді кедергісі, селективті гистеросальпингография, жатыр түтіктердің транскатетерді реканализациясы

Трубно-перитонеальное бесплодие. Лечение. (Обзор литературы) Часть 2

Тореева Ш.М.^{1,3}, Кошербаева Л.К.¹, Алдангарова Г.А.^{2,3}

¹Казахский национальный университет им. Аль-Фараби, г. Алматы, Казахстан

²Казахстанско-Российский Медицинский Университет, г. Алматы, Казахстан

³АО «Национальный научный центр хирургии им. А.Н.Сызганова», г. Алматы, Казахстан

Аннотация

На сегодняшний день, в век современных технологий, несмотря на успехи в репродуктологии и усовершенствований методов вспомогательных репродуктивных технологий (ВРТ), частота бесплодного брака, не только не стабилизировалась, но и увеличивается из года в год, достигнув показателей 25-30% в популяции. Трубно-перитонеальное бесплодие находится на одном из ведущих мест по частоте встречаемости различных факторов, приводящих к отсутствию наступления беременности.

Женский фактор при бесплодном браке составляет 40%, доля мужского фактора обусловлено в 40% случаев, а в остальных случаях при бесплодии встречается сочетанный фактор, как женский, так и мужской. В этой связи поиск новых методик и их совершенствование, а также снижение стоимости лечения бесплодия представляются весьма актуальными.

Воспалительное поражение маточных труб – ведущая причина бесплодия. В результате хронического воспалительного процесса, протекающего с поражением маточных труб, высок риск развития трубно-перитонеального бесплодия. Каждая пятая женщина с хроническим воспалением придатков в анамнезе страдает бесплодием, при этом у 70% из них имеет место четвертая степень спаечного процесса в малом тазу, при котором поражение маточных труб является необратимым даже с помощью хирургического лечения.

The prognosis of therapy for tubal-peritoneal infertility depends both on the timeliness of diagnosis and on the usefulness of etiopathogenetic therapy for chronic salpingoophoritis.

Despite the high percentage of 92% recovery of patency of the fallopian tubes when using endovideosurgery, the frequency of pregnancy on average is about 50%. [13]

The results of the restoration of reproductive function after reconstructive plastic surgery indicate that the problem of endovideoscopic correction of tubal-peritoneal factor of infertility requires further study in terms of determining the maximum therapeutic potential of endoscopic surgery in various manifestations of tubal-peritoneal infertility.

Before the development of endoscopic (laparoscopy and hysteroscopy) and X-ray endovascular technologies, microsurgery and IVF (in vitro fertilization) were the main types of treatment for proximal obstruction. Given the effectiveness of IVF (30-45%), the high frequency (66.3%) of the development of adhesions in the pelvis, as well as the frequent reobstruction (30%) after microsurgical operations, the question arose about the need to find new ways to treat proximal obstruction, given that in 45-47% it is functional, which can be overcome by selective salpingography and transcatheter recanalization of the fallopian tubes. [1, 18].

Surgical treatment of women with tubal infertility is advisable only once. The futility of repeated reconstructive plastic surgery is due to the progres-

sion of the adhesive process in the pelvis and the reocclusion of the fallopian tubes. [24]

Functional obstruction of the fallopian tubes - spasm of the interstitial part or obstruction of the lumen by amorphous mucous plugs. According to the results of HSG (hysterosalpingography), functional occlusion of the fallopian tubes may occur in 45-47% (false-positive result). [2]

Proximal obstruction of the fallopian tubes - obstruction of the interstitial and / or isthmic part of the fallopian tubes. It occurs in 10-25% of women with TPI (tubal peritoneal infertility).

The morphological basis of this condition is most often nodular isthmic salpingitis, chronic salpingitis, tubal endometriosis, "plugs" of amorphous matter or spasm of the intramural part of the tube. [2, 11].

Traditional methods of correction of this condition remain interventions with the use of microsurgical techniques to restore the patency of the proximal parts of the fallopian tubes, as well as the method of in vitro fertilization (IVF). In addition to their invasiveness and high cost, these methods have limited effectiveness [11]

Transcatheter recanalization of the fallopian tubes with their proximal obstruction seems to be a more technological and effective method of treatment, since it is performed on an outpatient basis and in the vast majority of cases does not require anesthesia at all [2, 11]. Catheterization of the fallopian tube, which is an integral compo-

Ключевые слова

бесплодие, трубно-перитонеальный фактор, проксиальная непроходимость маточных труб, селективная гистеросальпингография, чрескатетерная реканализация маточных труб

ment of the intervention, allows to perform selective salpingography and get information about changes of the epithelium of the distal fallopian tube that allows to build a forecast for the onset of spontaneous pregnancy.

Despite the fact that the methodology was proposed in the late 1970s, many aspects of it are not fully covered. Thus, the clinical possibilities of selective salpingography and transcatheter recanalization of the proximal parts of the fallopian tubes with their proximal obstruction have not been determined.

There are no studies comparing different methods of transcatheter recanalization of pipes, in particular, using a coaxial system consisting of a microconduc-

tor and a microcatheter, as well as using a standard hydrophilic conductor. The influence of the state of the distal parts of the fallopian tubes on the probability of spontaneous pregnancy in patients after the restoration of the proximal patency of the fallopian tubes remains virtually unexplored. The question of the influence of the age factor on the effectiveness of the recanalization procedure and the probability of spontaneous pregnancy after the successful restoration of proximal patency is not sufficiently covered. To date, there is no detailed analysis of the side effects and complications that occur during selective salpingography and transcatheter recanalization of the proximal segments of the fallopian tubes. The study of these issues is very relevant.

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PROGNOSTIC CLINICAL SIGNIFICANCE OF MYELOID SUPPRESSOR CELLS AND T REGULATORY CELLS IN SEPSIS (REVIEW)

Aubakirova A. T.

orcid.org/0000-0001-7585-2898

Abdilova G. B.

orcid.org/0000-0002-7587-412X

Kataeva K.

orcid.org/0000-0002-0840-6465

Tartipkyzy D.

orcid.org/0000-0003-5893-6992

Davenova N. A.

orcid.org/0000-0002-1421-0733

Nurgalieva A. N.

orcid.org/0000-0003-2849-3487

Dakenova G. B.

orcid.org/0000-0002-5725-6475

Aubakirova A.T., Abdilova G.B., Kataeva K., Tartipkyzy D., Davenova N.A., Nurgalieva A.N., Dakenova G.B.

National Scientific Center of Surgery named after A.N. Syzganov, Almaty, Kazakhstan

Abstract

Currently in developed countries there is an unsolved problem in medicine, this complication after surgery, in some cases leading to early death.

Modern medicine has made a great stride forward, but despite all the achievements, the problem of finding reliable criteria, concepts, definitions of sepsis remains relevant. Sepsis is potentially fatal in nature. The pronounced biological and clinical heterogeneity of patients with sepsis: age, premonitory background, drugs taken, different sources of infection create a high variability in the onset and course of the pathological process. New definitions of sepsis have refocused the focus on rethinking the clinical manifestations of this syndrome and have emphasized the importance of organ dysfunction as a key diagnostic feature. An unexplained organ failure in a patient should alert the physician to the possibility of sepsis. And the final result will depend on how quickly we can respond to changes, rationally and targeted therapy.

The reasons for the dysregulation of the body's response and delayed return to homeostasis in patients with sepsis are poorly understood. Growing interest is focused on a subpopulation of leukocytes called myeloid suppressor cells (MDSC). MDSC are involved in the regulation of the immune response in many pathological situations, the most studied of which is cancer. A number of comprehensive reviews have discussed MDSC in the context of cancer, autoimmunity, and infectious diseases. Interestingly, recent evidence suggests that MDSC are involved in the immune dysfunctions seen in sepsis.

Keywords

sepsis, myeloid suppressor cells, T regulatory cells

Сепсис кезінде Т-реттеуші жасушалар мен миелоидты супрессорлық жасушалардың болжамдық клиникалық мәні (Әдебиет шолуы)

Аубакирова А.Т., Абдилова Г.Б., Катаева К., Тәртіпқызы Д., Давенова Н.А., Нурғалиева А.Н., Дакенова Г.Б.

«А.Н.Сызғанов атындағы Ұлттық ғылыми хирургия орталығы» АҚ, Алматы қ., Қазақстан

Аңдатпа

Қазіргі таңда дамыған елдерде медицинада шешімін таппаған мәселе бар, бұл – ерте өлімге әкелетін кейбір жағдайлардағы, хирургиялық араласудан кейінгі асқынулар.

Заманауи медицина қарқынды ілгерілеу үстінде, дегенмен осы жетістіктердің барлығына қарамастан, сепсисінің анықтамасын, ұғымдарын, нақты өлшемшарттарын іздеу мәселесі өзектілігін жоймай отыр. Сепсис өз табиғатынан ажал құштыратын сырқат. Сепсисі бар науқастардың айқын көрінетін биологиялық және клиникалық гетерогенділігі: жас, преморбидтік фон, қабылдайтын дәрі-дәрмектер, жұқпалы аурудың түрлі көздері патологиялық процестің басталуы мен ағымының жоғары түрленгіштігін қалыптастырады.

Сепсисінің жаңа анықтамалары бұл құбылыстың клиникалық көріністерін қайта қарауға назар аударылып, негізгі диагностикалық белгі ретінде органдық дисфункцияның маңыздылығын атап өтті. Науқастағы түсініксіз органдық жеткіліксіздік сепсисінің даму мүмкіндігіне қатысты дәрігерді алаңдатуы тиіс. Өзгерістерге біз қаншалықты жылдам әрекет ете алсақ, соңғы нәтижеге әсер ететін терапияны да дұрыс тағайындай аламыз.

Миелоидты супрессорлық жасушалар (МС) деп аталатын лейкоциттердің субпопуляциясына үлкен қызығушылық туындап отыр. МС көптеген патологиялық жағдайлардағы иммундық жауаптың реттелуіне қатысады, олардың ішінде кеңінен зерттелгені – қатерлі ісік. МС-ны жан-жақты шолуларда қатерлі ісік, аутоиммунитет және жұқпалы аурулардың контекстінде талқыланады. Қызығы, соңғы деректер бойынша МС сепсис кезінде бақыланатын иммундық дисфункцияларға қатысады деген болжам бар.

Түйін сөздер

сепсис, миелоидты супрессорлық жасушалар, Т-реттеуші жасушалар

Прогностическое клиническое значение миелоидных супрессорных клеток и T регуляторных клеток при сепсисе (Обзор литературы)

Аубакирова А.Т., Абдилова Г.Б., Катаева К., Тәртiпқызы Д.,
Давенова Н.А., Нургалиева А.Н., Дакенова Г.Б.

АО «Национальный научный центр хирургии им. А.Н.Сызганова», г. Алматы, Казахстан

Аннотация

В настоящее время в развитых странах существует не решенная проблема в медицине, эта осложнения после хирургического вмешательства, в некоторых случаях приводящей к ранней смерти.

Современная медицина далеко шагнула вперед, но, несмотря на все достижения, проблема поиска достоверных критериев, понятий, определений сепсиса остается актуальной. Сепсис потенциально смертелен по своей природе. Выраженная биологическая и клиническая гетерогенность пациентов с сепсисом: возраст, преморбидный фон, принимаемые препараты, разные источники инфекции создают высокую вариабельность начала и течения патологического процесса. Новые определения сепсиса перенастроили фокус на переосмысление клинических проявлений этого синдрома и подчеркнули важность органной дисфункции как ключевого диагностического признака. Необъяснимая органная недостаточность у пациента должна насторожить врача в отношении возможности развития сепсиса. И от того, насколько быстро мы сможем среагировать на изменения, рационально и адресно назначить терапию, будет зависеть конечный результат.

Причины нарушения регуляции ответной реакции организма и задержки возврата к гомеостазу у пациентов с сепсисом мало исследованы. Растущий интерес сфокусирован на субпопуляции лейкоцитов, называемой миелоидными клетками-супрессорами (МС)

Ключевые слова
сепсис, миелоидные супрессорные клетки, T регуляторные клетки

The mortality rate from sepsis is five to six million deaths out of 30 million cases per year worldwide, while in Kazakhstan over the past 5 years about 500 people have died from sepsis.

The incidence of sepsis is increasing due to an aging population, the burden of chronic disease, an increase in the number of immunocompromised patients and microbial resistance to antimicrobial drugs. The World Health Assembly and the World Health Organization made sepsis a global health priority by adopting a resolution on improving the prevention, diagnosis and treatment of sepsis in 2017 [1, 2].

The reasons for the dysregulation of the body's response and delayed return to homeostasis in patients with sepsis are poorly understood. Growing interest is focused on a subpopulation of leukocytes called myeloid suppressor cells (MDSC). MDSC are involved in the regulation of the immune response in many pathological situations, the most studied of which is cancer. A number of comprehensive reviews have discussed MDSC in the context of cancer, autoimmunity, and infectious diseases. Interestingly, recent evidence suggests that MDSC are involved in the immune dysfunctions seen in sepsis [3, 4].

Sepsis is characterized by an early exacerbation of antimicrobial defense mechanisms MDSC, the so-called hyperinflammatory "cytokine storm," mediating tissue damage, organ dysfunction, and early mortality, as well as a concomitant shift towards resolving inflammation and tissue repair. Sepsis-

induced immunoparalysis (or immunosuppression) promotes the development of secondary infections and long-term immune deficiency, which leads to late mortality.

In the Republic of Kazakhstan and the CIS countries, molecular immunological studies on MDSC and T regulatory cells in sepsis have not been carried out until now [5, 6].

A scientific studies review carried out in the world gives the scientific significance of sepsis in clinical trials on MS and T-regulatory cells aimed at identifying the immunosuppression of myeloid cells, which will increase the effectiveness and safety of sepsis treatment.

Clinical trials that have tested adjunctive therapy to alleviate inflammation-related dysfunctions in sepsis have not been conclusive. This can be attributed to several reasons, among which there is a great heterogeneity of sepsis. It is now widely believed that the restoration of immunity with the help of immunostimulants may be more effective than anti-inflammatory therapy. In any case, personalized drugs should be used to determine on an individual level whether they should target inflammatory cytokines, immunoparalysis, or metabolism. From this point of view, significant efforts are directed towards identifying genetic, molecular and cellular biomarkers to stratify patients for clinical research and treatment based on clinical condition and disease stage [7-9].

The reasons for the dysregulation of the body's response and delayed return to homeostasis in pa-

tients with sepsis are poorly understood. Growing interest is focused on a subpopulation of leukocytes called myeloid suppressor cells (MDSC). MDSC are involved in the regulation of the immune response in many pathological situations, the most studied of which is cancer. A number of comprehensive reviews discuss MDSCs in the context of cancer, autoimmunity, and infectious diseases. Interestingly, recent evidence suggests that MDSC are involved in the immune dysfunctions seen in sepsis [10-12].

MDSCs are immature myeloid cells that proliferate in chronic and acute inflammatory conditions. The prerequisites for the discovery of MDSC date back more than a century, when tumor progression was associated with extramedullary hematopoiesis and neutrophilia. In the mid-1960s, Lappat and Cawein reported that subcutaneously transplanted A-280 tumor cells generate factors involved in a leukocytosis response that supports tumor growth. Subsequently, leukocytosis was involved in the multiplication of cells of myeloid origin with immunosuppressive activity. These cells express reduced levels of common markers for mature myeloid and lymphoid cells and have been termed natural suppressor cells, null cells, immature myeloid cells, or myeloid suppressor cells. In 2007, the term "myeloid suppressor cells" was adopted as an umbrella term to minimize confusion in the literature [11, 12, 13].

MDSC are primarily determined by their immunosuppressive functions. In sepsis, MDSC can be predicted to play a dual role depending on the progression of the disease. On the one hand, MDSC may be beneficial by limiting hyperinflammation in the early stages of sepsis, hence protecting against early organ dysfunction. On the other hand, MDSC can be harmful, enhancing long-term immunosuppression. As discussed later, these two aspects were highlighted in experimental models, while all clinical studies indicated a deleterious role for MDSC [13, 14].

Minimal phenotypic characteristics of MDSC have been suggested, but there is no definite consistent phenotyping scheme. Two main subpopulations of MDSC are usually considered: polymorphonuclear MDSC (PMN-MDSC, formerly called granulocytic-MDSC) and monocytic MDSC (M-MDSC), so called because of their morphological and phenotypic homology with PMN and monocytes. In humans, PMN-MDSC is CD11b + CD14- CD33 + (CD15 + or CD66 +) cells and M-MDSC CD11b

+ CD14 + HLA-DR^{low} / - CD15- cells. PMN-MDSC phenotypically overlap with mature neutrophils, but, unlike PMN, MDSC is deposited in the PMN fraction in Ficoll gradients after whole blood density separation. The identification of PMN-MDSC by density gradient is further limited by the growth of not only low density neutrophils, but also high density CD62L^{dim} neutrophils, which suppress T cells in the blood of healthy people infused with endotoxin. Additional markers for the differentiation of MDSC from monocytes or granulocytes have been proposed, for example, high expression of the oxidized LDL-1 receptor of the lectin type (LOX-1) PMN-MDSC compared to granulocytes in whole blood. Other subsets of MDSC have been described, including early stage MDSC and eosinophilic MDSC. In addition, tumor-associated macrophages (TAMMDSC), which, unlike their name, indicate the presence of inflammatory conditions in cancer, can be considered as one of the members making up the MDSC spectrum. Lastly, MDSCs are known very malleable. They can differentiate into osteoclasts and non-suppressing mature myeloid cells, while M-MDSC can differentiate into TAM and PMN-MDSC. In general, to this day, MDSC identification based on cell surface phenotyping usually ends up in a mixed population eventually containing other types of myeloid cells, which does not take into account the characteristic immunosuppressive function of MDSC [15 -18].

Hematopoietic stem cells differentiate into common myeloid progenitors, resulting in the formation of immature myeloid cells. The inflammatory environment observed in sepsis stimulates the release of immature myeloid cells from the bone marrow into the bloodstream and enhances immunosuppressive functions. The identification of mediators and molecular mechanisms underlying the expansion and immunosuppressive functions of MDSC may indicate original therapeutic targets for various diseases [17, 18].

Conclusion

Thus, according to the literature data, it can be seen that myeloid suppressor cells and T regulatory cells study has prognostic value. The level of these cells can be an indicative and prognostic laboratory marker for reducing mortality of patients from sepsis after and before surgery.

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THE USE OF DRINKING MINERAL WATERS IN THE COMPLEX SANATORIUM TREATMENT OF PATIENTS WITH TYPE 2 DIABETES MELLITUS

Remetova A.A.

orcid.org/0000-0003-2296-6378

Kalmakhanov S.B.

orcid.org/0000-0001-5198-5506

Remetova A.A., Kalmakhanov S.B.

Al-Farabi Kazakh National University, Almaty, Kazakhstan

Abstract

The aim of the study is to determine the significance of the use of mineral spring waters in the sanatorium-resort therapy of type 2 diabetes mellitus. The article discusses the main indicators of the prevalence of diabetes in the world and in Kazakhstan. It has been shown that the problem of diabetes mellitus is one of the most pressing world problems of modern medicine. The scientific novelty of the work lies in the approach to the study of macro- and microelements in the composition of mineral waters, their effect on the composition of blood, as well as their ability to control the state of the body through various mechanisms of action. The article focuses on the process of activation of various systems and mechanisms of the body when using mineral waters.

Keywords

type 2 diabetes mellitus, prevalence of diabetes, mineral water, complex treatment

2 типті қант диабетімен ауыратын науқастарды кешенді шипажайлық емдеуде ішетін минералды суларды қолдану

Реметова А. А., Калмаханов С. Б.

Әл-Фараби атындағы Қазақ ұлттық университеті, Алматы қ., Қазақстан

Аңдатпа

Жұмыстың мақсаты- қант диабетінің кешенді шипажайлық емінде минералды судың пайдасын анықтау. Мақалада қант диабетінің әлемде және Қазақстанда таралуы туралы ақпарат берілген. Қант диабетінің қазіргі таңда медицинаның өзекті проблемаларының бірі екені көрсетілген. Жұмыстың ғылыми жаңалығы минералды сулардың құрамындағы макро- және микроэлементтерді, олардың қан құрамына әсерін, сондай-ақ организмнің күйін әр түрлі механизмдер арқылы басқара алу қабілеттерін зерттеу тәсіліне негізделген. Әрекет. Мақалада минералды суларды пайдаланған кезде дененің әртүрлі жүйелері мен механизмдерінің активтену процесіне баса назар аударылған.

Түйін сөздер

2 типті қант диабеті, қант диабетінің таралуы, минералды су, кешенді емдеу

Применение питьевых минеральных вод в комплексном санаторном лечении больных сахарным диабетом 2 типа

Реметова А. А., Калмаханов С. Б.

Казахский национальный университет им. Аль-Фараби, г. Алматы, Казахстан

Аннотация

Цель исследования – определить значение применения вод минеральных источников в санаторно-курортной терапии сахарного диабета второго типа. В статье рассмотрены основные показатели распространенности сахарного диабета в мире и в Казахстане. Показано, что проблема сахарного диабета относится к одной из самых актуальных мировых проблем современной медицины. Научная новизна работы заключается в подходе к изучению макро- и микроэлементов в составе минеральных вод, их воздействия на состав крови, а также их способность контролировать состояние организма через различные механизмы воздействия. В статье акцентируется внимание на процесс активации различных систем и механизмов организма при применении минеральных вод.

Ключевые слова

сахарный диабет 2 типа, распространенность диабета, минеральная вода, комплексное лечение

Diabetes mellitus is one of the most pressing global problems of modern medicine. According to the Federal Target Program "Diabetes mellitus 1996-2005." in terms of its importance, diabetes mellitus is classified as an acute medical and social problem. According to the data of WHO experts in the world, the number of patients with this pathology has reached 150 million and is also continuing to increase, especially due to the increase in the number of people with type 2 diabetes. At a meeting of the III All-Russian Medical Congress on Pharmacoeconomics in 2001, Academician of the Russian Academy of Medical Sciences I.I. Dedov emphasized that about 2 million people are officially registered in the Russian Federation. patients with diabetes mellitus, but the real number of patients is much higher and reaches over 6-8 million people. He also noted that every 15 years the number of patients with diabetes is increasing. The GROWTH of the average life expectancy up to 80 years, according to the calculations of the American researcher C.R. Kahn, in 1995 may lead to an increase in the number of patients with type 2 diabetes in the total population up to 17%. Data from the International Diabetes Federation (IDF) indicate that in 2014 there were 422 million people with diabetes in the world, and its worldwide prevalence was 8.3% of the population. At the same time, according to the prognostic estimate, the number of patients by 2035 will be about 592 million people, of which 77% live in low- and middle-income countries.

Some researchers believe that not all cases of diabetes mellitus are recorded, and that the number of such cases reaches 174.8 million people - among the adult population of the world.

Of course, it is assumed that not all estimates and forecasts are the same. Based on data from the World Health Organization, in 2014 among the population aged 18 and over, the prevalence of diabetes reached 9%. and by 2030 the number of patients may reach more than 360 million people. (The prevalence of diabetes for all age groups worldwide is estimated at 2.8% in 2000 and 4.4% in 2030).

In Kazakhstan, there has been a steady increase in the number of patients with diabetes mellitus over the past 10 years - 2.5 times. In the Republic of Kazakhstan, as of December 31, 2018, patients with type 1 diabetes mellitus were registered - 19021 patients, type 2 diabetes mellitus - 310215 patients.

So, according to the materials of the National Register, the number of patients with diabetes mellitus, at the beginning of 2020, in absolute numbers amounted to 373 183, of which type 1 diabetes is the adult population - 30 611, type 2 - 352 022. Currently, according to the data Of the Ministry of

Health of the Republic of Kazakhstan, 3,994 children are diagnosed with type I diabetes mellitus, 127 children are diagnosed with type II diabetes.

The annual increase in the prevalence of diabetes in Almaty was shown by the analysis of data from the National Register of Diabetes Mellitus of the Republic of Kazakhstan from 2015 to 2019 - from 1.74% to 2.31%, with a trend of 7% average annual growth.

However, the current diabetes mellitus registry in Kazakhstan contains data only on patients who have already been notified of their disease. However, one should not overlook the fact that most of the patients are observed in private medical clinics and are not at all covered by the register. These questions should be studied in depth and clarified.

In Kazakhstan, according to official statistics, the number of people diagnosed with type 2 diabetes of the total number of people is 1.34%. In Kazakhstan, according to the International Diabetes Federation (IDF), the prevalence of this pathology should be 7.5% of the total population, which indicates about 500,000 undiscovered cases. However, some researchers believe that the data obtained from the International Diabetes Federation is significantly exaggerated, as a result of which there is no uniform information on this issue.

Diabetes mellitus is a global problem in society. According to WHO, diabetes will become the seventh leading cause of death by 2030. In the world, the number of patients with diabetes in 2015 at the age of 20-79 was 415 million, with 215.2 million men (2040 - 328.4 million) and 199.5 million women (2040 - 313.3 million). According to the IDF - International Diabetes Federation, the number of people with diabetes will increase to 642 million by 2040. According to the statistics cited in the YR Diabetes Atlas, in 2015 a large number of people living with diabetes mellitus were registered in the Western Pacific - 153.2 million, while this figure in 2040 will reach 215.8 million. In second place - South-East Asia - 78.3 million, and in 2040. an increase is forecasted to 140.2 million. Europe is the third (59.8 million), and in 2040. will reach 71.1 million.

Treatment of diabetes mellitus sets its main goal as a number of indicators, such as maintaining and achieving optimal metabolic control, minimizing acute and chronic complications, and achieving a high level of patient's quality of life.

A high role of sanatorium-resort treatment is assigned in the rehabilitation of patients with diabetes mellitus among the already known methods, labor and medical-social rehabilitation, which are used to prevent the disease. The greatest efficiency of spa treatment is confirmed not only by rich medical practice, but also by the results of clinical and experimental studies. In the process of spa therapy

of diabetes mellitus, an important place is occupied by drinking treatment with mineral waters, it has a beneficial effect on the main pathogenetic links of type 2 diabetes mellitus: impaired insulin secretion, impaired carbohydrate and lipid metabolism, the severity of insulin resistance, overweight, are important factors in prevention of complications in diabetes mellitus. The features of the influence of complex treatment with the use of mineral water with different chemical and gas composition inside and outside, mud therapy, as well as other pre-selected physical factors are revealed.

Sanatorium treatment with mineral waters is indicated for patients with prediabetes, patients with mild and moderate severity of type 1 and 2 diabetes mellitus in a state of stable compensation for impaired glucose tolerance, without a tendency to severe acidosis, the initial stage of microangiopathy, and also indicated for patients with diabetes in combination with diseases of the digestive system, circulatory system, liver and urinary system, biliary tract.

The main methods of sanatorium-resort therapy for type II diabetes mellitus include treatment with drinking waters of mineral springs. Natural mineral water has a positive effect on lipid and carbohydrate metabolism: hyperglycemia and glucosuria decrease, the effect of certain enzymes that promote the passage of glucose into tissues increases, and the lipid X-ray spectrum of blood serum improves. Suddenly, the flow of manufactory metabolism of carbohydrates improves, the organization of adenosine triphosphoric acid (ATP) increases, the breakdown of which produces a tremendous abundance of energy. In addition, natural waters substantially increase the sensitivity of insulin receptors to this hormone, taking into account that in almost all patients the need for insulin hormone and glucose-lowering tablet preparations is lowered. Mineral waters, when used for drinking by patients with type 2 diabetes mellitus, have a positive effect on lipid and carbohydrate metabolism: hyperglycemia and glucosuria decrease, the effect of certain enzymes promoting the passage of glucose into tissues increases, and the lipid X-ray spectrum of blood serum improves. Also, the course of manufacturing metabolism of carbohydrates improves, the organization of adenosine triphosphoric acid (ATP) increases, during the breakdown of which a large abundance of energy is given out. In addition, natural waters fundamentally increase the sensitivity of insulin receptors to this hormone, taking into account that almost all patients have a lower need for the hormone insulin and antihyperglycemic tablet preparations.

The effect of hydrocarbonate and sulphate waters is to affect carbohydrate metabolism, normal-

izing the insulin effectiveness of the blood, exacerbating the effectiveness of the enzyme hexokinase, which promotes the entry of glucose into tissues, which explains the reduction of hyperglycemia and glycosuria.

The bicarbonate cation plays a huge role in maintaining acid balance. In diseases of mild to moderate severity of diabetes, ultimately the use of hydrocarbonate waters improves carbohydrate metabolism. Ultimately, dyspeptic actions are eliminated: heartburn, belching, a feeling of heaviness in the epigastric gland, and others.

Mineral waters containing magnesium occupy a special place in the drinking treatment of a patient with the second type of diabetes mellitus. In the total volume of macro- and microelements, magnesium ions occupy a special place. Like calcium ions, magnesium can determine the activity of more than 300 enzymes. The role of magnesium in maintaining the optimal functionality of cardiomyocytes is also known, and its deficiency can provoke the appearance of various diseases of the cardiovascular system.

Also, magnesium controls blood pressure through various mechanisms of action. Also, to ensure the digestion process, magnesium ions are needed, because, on the one hand, they regulate the intestines, and on the other hand, they contribute to the secretion and formation of bile. The process of reducing the concentration of magnesium ions in the blood by 10-12% in the second type of diabetes mellitus has been established. Therefore, the process of additional intake of magnesium ions with the help of internal drinking of mineral waters can make it possible to quite effectively replenish the reserves of magnesium homeostasis and contribute to the activation of metabolic reactions, which is vital in the second type of diabetes mellitus. The longest and maximum effect can be achieved by combining drinking cure and balneotherapy treatments. If patients with diabetes mellitus of the second type use mineral baths, which will show a good dynamics of the indicator of all types of metabolism, the functional state of the nervous system, metabolism is activated, and a positive reaction to neuroregulatory mechanisms that contribute to the normalization and stabilization of hemodynamics occurs. The use of mineral baths can significantly enhance the special factors of the body's defense and improve the indicators of specific immunity, improve carbohydrate and other types of metabolism and, also, have a pronounced positive reaction to the process of concomitant diseases of the nervous and cardiovascular system, musculoskeletal system, digestive organs, kidneys, skin and genitals, as well as others.

With concomitant diseases of the digestive system in patients with type 2 diabetes mellitus, other methods of internal use of mineral waters are prescribed: duodenal drainage, gastric lavage, microclysters, siphon bowel lavage. Rectal methods of administration of mineral water in patients with type 2 diabetes mellitus contribute to the rapid elimination of ketoacidosis.

The land of Kazakhstan has a variety of tourist resources. According to reliable information from the Committee of the Tourism Industry of the Ministry of Culture and Sports of the Republic of Kazakhstan, 19 resort zones are noted and functioning in the state, a key part of them (more than 10) have medicinal factors and are balneological, mud-healing climatic resorts.

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ДӘРІГЕР-УРОЛОГТАРДЫҢ ТҮРКІСТАН ОБЛЫСЫНА ІС-САПАРЫ

А.Н. Сызғанов атындағы Ұлттық ғылыми хирургия орталығының білікті мамандары, уролог-трансплантолог Ернұр Белгібаев пен Ельшад Набиев Отырар ауданының тұрғындарына дәрігерлік кеңес беріп, екі күн бойы Отырар ауданының тұрғындарын қабылдап, көмек көрсетті.

Қазақстан Республикасының денсаулық сақтау саласын дамытудың 2020 – 2025 жылдарға арналған мемлекеттік бағдарламасын жүзеге асыру аясында А.Н. Сызғанов атындағы Ұлттық ғылыми хирургия орталығының Басқарма Төрағасы, профессор Баймаханов Болатбек Бимендеұлының тікелей қолдауымен келген ақ халатты абзал жандар 2021 жылдың 25-26 ақпан күндері тұрғындарды қабылдады.

Тәжірибелі мамандар несеп-тас ауруы, қуық асты безінің қатерсіз гиперплазиясы, қуық-тас ауруы, бүйрек ісігі, қуық ісігі, бүйрек кистасы, бүйрек жетіспеушілігі секілді аурулар бойынша науқастарды медициналық тексеруден өткізді.

Осылайша Отырар ауданында туып-өскен азаматтар жерлестеріне көмек қолын созып, қамқорлық көрсетілді. Ал, медициналық кеңес беруден түскен қаржыны осы аудандағы әлеуметтік аз қамтылған және көпбалалы отбасыларға табыстауды ниет етіп отыр.



К 80 – летнему юбилею Абильбека Игасимовича Чиныбаева

Абильбек Игасимович Чиныбаев родился 15 марта 1941 года в с. Улгули малши Кокпектинского района Семипалатинской области. После окончания школы в 1958 году он начинает трудовую деятельность в рядах молодежной строительной бригады, где добросовестно трудился по 1960 год. Абильбек Игасимович в 1960 году поступил на лечебный факультет Семипалатинского государственного медицинского института. После окончания института в 1966 году работал районным хирургом, заведующим хирургическим отделением с. Успенка Павлодарской области. С 1969 года по 1976 год работал старшим ординатором, с 1977 года по 2008 год - заведующим хирургического отделения, с 2008 года по 2014г - заведующим операционного блока областной клинической больницы, ныне Университетского Госпиталя Государственного медицинского университета г. Семей. А.И. Чиныбаев прекрасный клиницист, высоко квалифицированный хирург с широким диапазоном знаний. Владеет методикой эндоскопических исследований, хирургической техникой операции на щитовидной железе, легких, желудочно – кишечном тракте, билиарной системе. Является одним из основателей хирургической службы Семипалатинской области. Одним из первых в регионе начал осваивать и активно внедрять различные методики бронхоскопии и бронхографии, а также других эндоскопических исследований, операции при бронхоэктатической болезни, абсцессах легких, эндокринную хирургию, операции на пищеводе, желудке и других отделах ЖКТ. Впервые в 2000 году в регионе Восточно – Казахстанской области им успешно внедрена новая технология малоинвазивной операции с применением аппарата «Мини - ассистент» на желчном пузыре и желчевыводящих протоках. Высокий уровень хирургической техники и диагностики хирургических заболеваний послужил основой присвоения ему высшей квалификационной



категории хирурга в течении многих лет. А.И. Чиныбаев является грамотным организатором. Свою практическую и организаторскую деятельность успешно сочетает с научными исследованиями, являясь соавтором более 50 научных работ, в том числе монографии, атласа органосохраняющих операций при дуоденальных язвах, практикума по госпитальной хирургии, 6 изобретений, 10 рационализаторских предложений. Свой огромный клинический опыт Абильбек Игасимович неустанно передает молодым коллегам, своим ученикам. За добросовестный труд неоднократно награжден почетными грамотами Министерства здравоохранения Республики Казахстан, акима города и области, обкома профсоюза медицинских работников. Награжден медалью «Ветеран труда», нагрудным знаком «Қазақстан Республикасы денсаулық сақтау ісінің үздігі», нагрудным знаком «Адал еңбегі үшін». Абильбек Игасимович прошел большой содержательный путь в медицине: от врача – хирурга районной больницы до заведующего отделением крупной клинической больницы – медицинского центра. Его учителями были видные клиницисты – хирурги Восточно – Казахстанской области, с которыми у него были постоянные творческие связи. Человек высокой культуры и моральных качеств, глубоких профессиональных знаний, необычайной скромности, тонкого чувства юмора и принципиальных жизненных позиций, Абильбек Игасимович пользуется заслуженным уважением среди коллег, многочисленных пациентов. И сегодня он продолжает плодотворно работать как педагог, врач – клиницист. Он прекрасный отец и дед, в нем хорошо сочетаются черты прекрасного хирурга и спортсмена. Абильбек Игасимович за долгие годы практической деятельности неоднократно становился призерами по настольному теннису, лыжным гонкам и волейболу. Он и по настоящее время прекрасно играет в настольный теннис.

**Администрация АО «ННЦХ им. А.Н. Сызганова»,
Редакционный совет журнала «Вестник хирургии Казахстана»,
Казахстанское общество хирургов и коллектив госпитальной хирургии
Государственного медицинского университета г. Семей
сердечно поздравляют Абильбека Игасимовича со славным юбилеем,
желают здоровья и творческого долголетия**

К 80-летию со дня рождения профессора Дурманова К.Д.

25 января 2021 года исполнилось 80 лет со дня рождения академика АПМРК, профессора, Дурманова Калыбая Дурмановича. Дурманов К.Д. родился 25 января 1941 года в посёлке Ак-Арык Джалагашского района Кызыл-Ординской области.

Дурманов К.Д. поступил по конкурсу на лечебный факультет и закончил Алма-Атинский государственный медицинский институт в 1967 году. По направлению института работал хирургом-ординатором, заведующим хирургическим отделением в участковой и районных больницах Кызыл-Ординской области. Работая хирургом ЦРБ Кызыл-Ординской области, получил первую, затем высшую категорию врача-хирурга. Полученные знания, практические навыки позволили молодому хирургу пройти по конкурсу на должность заведующего хирургическим отделением онкодиспансера города Алма-Аты, которым он заведовал в течение 5 лет.

В 1973 году успешно защитил кандидатскую диссертацию на тему: «К вопросу лечения лучами лазера раковых и предраковых заболеваний кожи». В 1975 году прошел по конкурсу на должность ассистента, в 1982 году избран доцентом кафедры общей хирургии АГМИ.

В 1987 году защитил докторскую диссертацию на тему: «Комплексное лечение хронического остеомиелита с применением лазеров» в институте лазерной хирургии в г. Москве под руководством академика АМН Скобелкина О.К. В 1988 году занял должность заведующего кафедрой общей хирургии КазГМУ.

Дурманов К.Д. - хирург высшей категории, академик АПМРК, высококвалифицированный специалист по онкологии и общей хирургии. Профессор выполнил более 5000 различных операций на органах брюшной и грудной полостей, на трубчатых костях и рёбрах при остеомиелите.

Профессор Дурманов К.Д. является одним из пионеров применения лучей лазера при различных операциях на орга-



нах брюшной полости в Республике Казахстан. Является автором приоритетного научно-практического направления по профилактике осложнений при хирургических операциях у больных, проживающих в экологически неблагоприятной зоне Казахстана (Арал и Приаралье) и у людей, занятых на вредных производствах (Шымкент, Тараз).

Дурмановым К.Д. опубликовано свыше 150 научных работ, в том числе 10 методических рекомендаций, получил 5 авторских свидетельств и патентов. Он был редактором 3 изданных сборников научных работ. Под его руководством защищены 18 кандидатских диссертаций, издано 3 учебника на государственном языке, «Жалпы хирургия», «Жалпы хирургия және анестезиология», «Хирургиялық ауруы бар науқастардың күтімі», учебное пособие, 5

учебно-методических рекомендаций. Коллектив кафедры, под его руководством издал «русско-казахско-латинский» словарь хирургических терминов, и толковый словарь по оперативной хирургии и топографической анатомии.

Профессор Дурманов К.Д. создал школу хирургов Казахстана. Его ученики работают заведующим кафедрой (Жумабеков А.Т.), доцентами кафедр хирургии КазНМУ (Курамысов Е.К., Беристемов Г.Т.), заведующим отделения (доцент Бекишев Б.М.).

По стопам отца-профессора пошли и дети, продолжают работу в научно-практическом здравоохранении Республики Казахстана.

В 2009 году в расцвете своих творческих сил профессор Дурманов К.Д. скоропостижно ушел из жизни, оставив кафедру своим ученикам. Дело профессора Дурманова К.Д. продолжают его многочисленные ученики и соратники. Учебники, написанные профессором Дурмановым К.Д. не потеряли свою актуальность и являются настольной книгой студентов и врачей нашей Республики.

**Коллектив Национального научного центра хирургии им. А.Н. Сызганова,
а также профессор Ибадильдин А.С., доцент Кушекбаев М. Н.,
доценты Курамысов Е.А., Рахматуллин Ю.А.**

ТРЕБОВАНИЯ ДЛЯ АВТОРОВ ЖУРНАЛА «ВЕСТНИК ХИРУРГИИ КАЗАХСТАНА»

Уважаемые авторы!

С 1 апреля 2018 года все статьи на публикацию принимаются на государственном или русском языках с обязательным переводом всей статьи на английский язык. Статьи без версии на английском языке будут отклонены.

Также учитывая требования Консультативной Комиссией (CSAB) Scopus об интернационализации авторов и аудиторией редколлегия журналов рекомендуют публиковать статьи в соавторстве с учеными дальнего и ближнего зарубежья.

В журнале публикуются научные статьи и заметки, экспресс-сообщения о результатах исследований в различных областях естественно-технических и общественных наук.

Решение о публикации принимается редакционной коллегией журнала после рецензирования, учитывая научную значимость и актуальность представленных материалов. Статьи, отклоненные редакционной коллегией, повторно не принимаются и не рассматриваются. Рукописи, оформленные не по правилам, возвращаются авторам без рассмотрения.

Рукопись направляется на отзыв члену редколлегии и одному из указанных рецензентов; в спорных случаях по усмотрению редколлегии привлекаются дополнительные рецензенты; на основании экспертных заключений редколлегия определяет дальнейшую судьбу рукописи: принятие к публикации в представленном виде, необходимость доработки или отклонение. В случае необходимости рукопись направляется авторам на доработку по замечаниям рецензентов и редакторов, после чего она повторно рецензируется, и редколлегия вновь решает вопрос о приемлемости рукописи для публикации. Переработанная рукопись должна быть возвращена в редакцию в течение месяца после получения авторами отзывов; в противном случае рукопись рассматривается как вновь поступившая. Рукопись, получившая недостаточно высокие оценки при рецензировании, отклоняется как не соответствующая уровню или профилю публикаций журнала.

Авторы несут ответственность за достоверность и значимость научных результатов и актуальность научного содержания работ. Не допускается **ПЛАГИАТ** – умышленно совершаемое физическим лицом незаконное использование чужого творческого труда, с доведением до других лиц ложных сведений о себе как о действительном авторе.

Редакция принимает на рассмотрение рукописи только на английском языке, присланные через официальный сайт журнала www.vhk.kz.

Материал статьи – абстракт на казахском, русском и английском языках, список литературы, рисунки, подписи к рисункам и таблицы, оформляется одним файлом; дополнительно каждый рисунок оформляется в виде отдельного файла. Если пересылаемый материал велик по объему, следует использовать программы для архивирования. Все страницы рукописи, в том числе таблицы, список литературы, рисунки и подписи к ним, следует пронумеровать.

Представленные для опубликования материалы должны удовлетворять следующим требованиям:

1. Содержать результаты оригинальных научных исследований по актуальным проблемам в области физики, математики, механики, информатики, биологии, медицины, геологии, химии, экологии, общественных и гуманитарных наук, ранее не опубликованные и не предназначенные к публикации в других изданиях. Статья сопровождается разрешением на опубликование от учреждения, в котором выполнено исследование.
2. Размер статьи 7-10 страниц (статьи обзорного характера – 15-20 стр.), включая аннотацию в начале статьи перед основным текстом, которая должна отражать цель работы, метод или методологию проведения работы, результаты работы, область применения результатов, выводы (**аннотация** не менее **20** предложений (150×300 слов) - (на английском языке) через 1 компьютерный интервал), таблицы, рисунки, список литературы (через 1 компьютерный интервал, размер шрифта – 14), напечатанных в редакторе Word, шрифтом Times New Roman, поля – верхнее и нижнее – 2 см, левое – 3 см, правое – 1,5 см. Количество рисунков – 5-10.

Структура должна соответствовать международной формуле IMRAD, где I – introduction (вступление), M – Methods (методы), R – Results (исследование), A – и, D – conclusion+ discussion (заключение, обсуждение результатов и выводы).

Название • Отображает суть работы • Краткое • Без аббревиатур.

Необходимо официально закрепить название организации на английском и сокращение

Резюме • Структурировано • Без аббревиатур • Передает структуру статьи – Зачем (актуальность) – Какими методами? – Что получено – Как это изменило картину знаний. Именно его читают в первую очередь, только хорошее резюме может привлечь внимание!

Вступление • Актуальность работы • Какая задача поставлена • Почему

Методы • Перечисление • Если известные - дать ссылку • Если модифицировали – указать как • Описывать так что бы могли повторить • Статистика!

Результаты • Допускается не хронологическое, а логическое повествование • Основные, а не все что были сделаны •

Иллюстрируются минимально необходимыми сводными данными (исходные могут быть в дополнительных материалах)

Обсуждения • Не повторять результаты • Сопоставить полученные данные с имеющимися • Обсудить возможные причины и следствия

Функции списка литературы: • Аргументировать идею • Сопоставить с существующими аналогами • Обозначить место данного исследования • Избежать плагиата • Для журнала и ученого = признание • Часто указаны только собственные работы или очень старые (самоцитирование допускается только 10-15% от общего списка литературы) • Кочующие ошибки

Различайте • Ссылки • Список литературы • Библиография
Что могут цитировать • Книги, (монографии, главы) • Статьи научных журналов • Материалы конференций • Патенты • Диссертации • Неопубликованные данные • СМИ • Веб ресурсы (протоколы, веб странички) Источник должен быть надежным и легко доступным.

Статья начинается на английском языке. В начале, посередине страницы, идет название статьи прописными жирными буквами, название статьи должно быть коротким и емким, согласно проведенного анализа около 30-40 символов на английском языке.

Далее на следующей строчке – инициалы и фамилии авторов обычным жирным шрифтом, затем на следующей строчке – название организации(ий), в которой выполнена работа, город, страна, затем на новой строчке – адреса E-mail авторов. С красной строки идут ключевые слова (**Key words**), а на новой строчке – сама аннотация (**Abstract** – не менее **150** и более **300** слов).

Далее, после отбивки одной строки, начинается на русском языке. В начале статьи вверху слева следует указать индекс **УДК, МРНТИ**.

Затем, посередине страницы, пишется: 1) название статьи; 2) авторы; 3) название организации; с красной строки – **Ключевые слова**, затем – **Аннотация** (оформление шрифтов, как на английском языке).

Отбиваем одну строку и начинается сама **статья**. Следом за статьей идет список **Литературы**. Ссылки на литературные источники даются цифрами в прямых скобках по мере упоминания (не менее 20).

Для каждой статьи обязателен DOI (Digital Object Identifier) - это цифровой идентификатор документа. DOI выполняет функцию гиперссылки, которая всегда помогает найти нужный документ, даже если сайт, где он находился ранее, был впоследствии изменен. Благодаря этому индексу поиск научной информации в Интернете стал проще и эффективнее. Каждое издание, журнал размещает на своих веб-страницах в интернете, как текущие, так и архивные номера, и материалы. Таким образом, в открытом доступе можно увидеть резюме, которые включают в себя название статьи, фамилию, имя, отчество автора, аннотацию и ключевые слова, место выполнения работы, а также выходные данные опубликованных статей (название журнала, год издания, том, номер, страница).

Список литературы оформляется следующим образом:
В ссылках на книги указывается ISBN (10- или 13-значный). Сокращаются названия только тех журналов, которые указаны: http://images.webofknowledge.com/WOK46/help/WOS/0-9_abrvjt.html.

Для всех ссылок на статьи, опубликованные в международных рецензируемых журналах следует указывать DOI (Digital Object Identifier). DOI указываются в PDF версии статьи и/или на основной интернет-странице статьи, также можно воспользоваться системой поиска CrossRef: <http://www.crossref.org/guestquery/>. Ниже приводятся примеры оформления ссылок:

Статья в международном журнале:

1. Campry TS, Anders T. (1987) SNAP receptors implicated in vesicle targeting and fusion, *Environ Pollut*, 43:195-207. DOI: 10.1016/0269-7491(87)90156-4 (in Eng)

Статья в русскоязычном журнале, не имеющая англоязычной версии:

2. Ivanova TV, Samoilova NF (2009) *Electrochemical Energetics [Elektrohimicheskaya energetika]* 9:188-189. (In Russian)

Книги:

Timrat TA (2008) *Soil pollution: origins, monitoring and remediation*, second edition. Springer, Germany. ISBN: 978-3-540-70777-6

Материалы конференции:

Monin S.A. (2012) Treatment techniques of oil-contaminated soil and water aquifers. *Proceedings of International Conference on Water Resources and Arid Environment*, Riyadh, Saudi Arabia. P.123.

Патенты:

Barin AB, Mukamedzhan NT (2000) A method for determination of 1,1-dimethylhydrazine and nitrosodimethylamine [Metodopredeleniya 1,1-dimetilgidrazina initrosodimetilamina]. Preliminary Patent of the Republic of Kazakhstan [Predvaritelnyi patent Respubliki Kazakhstan]. (In Russian)

Стандарты, ГОСТы:

RMG 61-2003. Indexes of accuracy, precision, validity of the methods of quantitative chemical analysis, methods of evaluation [GSI.Pokazatelitochnosti, pravilnosti, retsizionnosti metodik kolichestvennogo himicheskogo analiza. Metodyotsenki]. Moscow, Russia, 2003. (In Russian)

На сайте <http://www.translit.ru/> можно бесплатно воспользоваться программой транслитерации Русского текста в латиницу, используя различные системы. Программа очень простая, ее легко использовать для готовых ссылок. К примеру, выбрав вариант системы Библиотеки Конгресса США (LC), мы получаем изображение всех буквенных соответствий. Вставляем в специальное поле весь текст библиографии на русском языке и нажимаем кнопку «в транслит».

В конце статьи дается резюме на казахском языке. Оформляется аналогично русскому варианту. Посередине страницы пишется: 1) название статьи; 2) авторы; 3) название организации; с красной строки – **Өзекті сөздер**, после – **Аннотация**.

Последняя страница подписывается всеми авторами, ставится дата.

3. Статьи публикуются только на английском языке.

4. В случае переработки статьи по просьбе редакционной коллегии журнала датой поступления считается дата получения редакцией окончательного варианта. Если статья отклонена, редакция сохраняет за собой право не вести дискуссию по мотивам отклонения.