

al. Composition and variation of the human milk microbiota are influenced by maternal and early-life factors. *J. Cell. Host. Microbe.* 2019; 25: 324-335.

20. Ho TTB, Groer MW, Kane B, et al. Dichotomous development of the gut microbiome in preterm infants *Microbiome.* 2018; 6:157.

21. Perez-Munoz ME, Arrieta M-C, Ramer-Tait AE, Walter J. A critical assessment of the "sterile womb" and "in utero colonization" hypotheses: Implications for research on the pioneer infant microbiome. *Microbiome.* 2017; 5: 48.

22. Rosenbauer J. Early infant feeding and risk of type 1 diabetes mellitus – a nationwide

population-based case-control study in pre-school children. *Diabetes Metab. Res.Rev.* 2018; 24:211: 222.

23. Sato Y, Sakurai K, Tanabe H, et al. Maternal gut microbiota is associated with newborn anthropometrics in a sex-specific manner. *J. Dev. Orig. Health Dis.* 2019; 10: 659-666.

24. Sila S, Jelic M, Trivic I, et al. Altered gut microbiota is present in newly diagnosed pediatric patients with inflammatory bowel disease. *J. Pediatr. Gastroenterol. Nutr.* 2020; 70: 495-502.

25. Tamburini S, Shen N, Wu HC, et al. The microbiome in early life: implications for health outcomes. *Nat. Med.* 2016; 22:713: 22.

26. Triantis V, Bode L, van Neerven RJJ. Immunological effects of human milk oligosaccharides. *Front. Pediatr.* 2018; 6: 190.

27. Twigger A-J, Kuffer G, Geddes D, et al. Expression of granulysin, perforin and granzymes in human milk over lactation and in the case of maternal infection. *Nutrients.* 2018; 10: 1230.

28. Unger S, Stintzi A, Shah P, et al. Gut microbiota of the very-low-birth-weight infant. *Pediatr. Res.* 2015; 77:205: 213.

29. Yatsunenko T, Rey FE, Manary MJ, et al. Human gut microbiome viewed across age and geography. *Nature.* 2012; 486: 222-227.

A.A. Yashnov, S.L. Lobanov, O.G. Konovalova, M.A. Burtseva, A.N. Nikolaev

PREDICTION OF THE RISK OF DEVELOPING DESTRUCTIVE FORMS OF ACUTE CHOLECYSTITIS

DOI 10.25789/YMJ.2021.76.26

УДК 616.366-089

The number of patients suffering from cholelithiasis continues to grow steadily all over the world. Acute cholecystitis is one of the most dangerous complications of cholelithiasis. The mortality rate in this complication largely depends on the degree of destructive changes in the biliary tract and ranges from 4 to 26%. In addition to the high mortality rate, acute cholecystitis is characterized by a significant percentage of both preoperative and postoperative complications. At the same time, in acute cholecystitis, there are no clear recommendations that would allow making a timely correct decision on the tactics of patient management. Often, clinicians resort to conservative treatment and are late with the operation. Currently, we are looking for methods that would allow us to predict the risk of developing destructive forms of acute cholecystitis in a timely manner. In some cases, on the contrary, there is an underestimation of contraindications, especially in somatically burdened patients, and unjustified surgical activity. Along with this, there is no consensus on the timing of surgical intervention. In this review, the main methods for predicting the development of destructive forms of acute cholecystitis are considered. The new stage of diagnosis of diseases and predicting complications is characterized by the introduction of various mathematical models in an inextricable relationship with the accumulated diagnostic knowledge. Various methods are proposed based on the creation of mathematical models and programs for predicting acute calculous cholecystitis in emergency patients. Numerous studies have been devoted to the development of a point system for predicting destructive processes in the gallbladder. The algorithm of using these methods in patients with acute cholecystitis is presented, as well as the prospects for further search for effective methods for predicting the destruction of the gallbladder, acceptable for use in a wide clinical practice. At the same time, the problem of predicting the risk of developing this complication remains relevant. There is a need to search for new methods that would allow predicting the risk of developing destructive forms of acute cholecystitis at an early stage of the disease and determining the most rational treatment tactics. The number of patients suffering from cholelithiasis continues to grow steadily all over the world. One of the most dangerous complications of cholelithiasis is acute cholecystitis. The mortality rate in this complication largely depends on the degree of destructive changes in the biliary tract and ranges from 4 to 26%. In addition to the high mortality rate, acute cholecystitis is characterized by a significant percentage of both preoperative and postoperative complications. At the same time, in acute cholecystitis, there are no clear recommendations that would allow making a timely correct decision on the tactics of patient management. Often, clinicians resort to conservative treatment and are late with the operation. Currently, we are looking for methods that would allow us to predict the risk of developing destructive forms of acute cholecystitis in a timely manner. In some cases, on the contrary, there is an underestimation of contraindications, especially in somatically burdened patients, and unjustified surgical activity. Along with this, there is no consensus on the timing of surgical intervention. In this review, the main methods for predicting the development of destructive forms of acute cholecystitis are considered. The new stage of diagnosis of diseases and predicting complications is characterized by the introduction of various

mathematical models in an inextricable relationship with the accumulated diagnostic knowledge. Various methods are proposed based on the creation of mathematical models and programs for predicting acute calculous cholecystitis in emergency patients. Numerous studies have been devoted to the development of a point system for predicting destructive processes in the gallbladder. The algorithm of using these methods in patients with acute cholecystitis is presented, as well as the prospects for further search for effective methods for predicting the destruction of the gallbladder, acceptable for use in a wide clinical practice. At the same time, the problem of predicting the risk of developing this complication remains relevant. There is a need to search for new methods that would allow predicting the risk of developing destructive forms of acute cholecystitis at an early stage of the disease and determining the most rational treatment tactics.

Keywords: cholelithiasis, acute cholecystitis, prognosis, destructive forms, cholelithiasis, diagnosis.

Federal State-Funded Educational Institution of Higher Professional Education Chita State Medical Academy: **YASHNOV Alexey Alexandrovich** – Candidate of Medical Sciences, assistant of the Department, alexyashnov@mail.ru, orcid.org/0000-0001-6881-4455; **LOBANOV Sergey Leonidovich** – MD, Professor, head of the Department, orcid.org/0000-0003-1665-3754; **KONOVALOVA Olga Genadiyevna** – Candidate of Medical Sciences, Associate Professor, orcid.org/0000-0002-5601-9558; **BURTSEVA Maria Alexandrovna** – surgeon of the City Clinical Hospital No. 1, Chita, orcid.org/0000-0003-0497-5086; **NIKOLAEV Alexey Nikolaevich** – surgeon of the State Medical Institution "Clinical Medical Center, Chita", orcid.org/0000-0001-5463-5405.

Treatment of acute cholecystitis is a difficult problem for clinicians. This is primarily due to high morbidity and a significant percentage of deaths. In recent years, there has been a steady increase in patients with cholelithiasis all

over the world and reaches 10-15% in the adult population. According to American researchers, 6.3 million men and 14.2 million women aged 20-74 years suffer from cholelithiasis in the USA [29]. In Italy, according to the results of

a multi-centralized study, the frequency of stone formation in the biliary tract reaches 9.5% in men and 18.8% in women [29]. Along with this, it was found that acute cholecystitis occurs in 10-20% of stone carriers, as one of the first manifestations of cholelithiasis [9,37,38]. According to various authors, the mortality rate in acute cholecystitis ranges from 4-26% [9,37,38]. At the same time, with increasing age of the patient, the number of adverse outcomes increases. In addition to high mortality, acute cholecystitis is characterized by a significant percentage of both preoperative and postoperative complications. Thus, in 5-6% of cases, patients develop purulent-inflammatory complications in the postoperative period [9,37,38]. With the increase in the incidence of cholelithiasis, there is a steady increase in the number of cholecystectomies [17,30,32,33]. The latter is considered the gold standard in helping patients with cholelithiasis. At the same time, for various reasons (the age of the patient, the presence of severe concomitant pathology, the equipment of the hospital, the experience of the surgeon, etc.), the tactics of managing patients with cholelithiasis varies markedly [9,32,33]. Surgical activity in cholelithiasis is quite high in world practice, which, according to most clinicians, is a justified measure. Thus, according to American researchers, about 400-500 thousand cholecystectomies are performed annually in the USA, and about 100 thousand in Germany [30, 34,36].

At the same time, in acute cholecystitis, there are no clear recommendations that would make it possible to make a timely correct decision on patient management tactics. Clinicians often resort to conservative treatment and are late with the operation. In some cases, on the contrary, there is an underestimation of contraindications, especially in somatically burdened patients, and unjustified surgical activity. Along with this, there is no consensus on the timing of surgical intervention [15]. This fact is due to the fact that there are no sufficiently reliable methods for predicting destructive forms of acute cholecystitis that would assess the risk of destructive changes in the biliary tract with high sensitivity and specificity [9, 17,33,38,37].

Currently, the main methods of diagnosis of acute cholecystitis are: ultrasound, computer and magnetic resonance imaging. Kiewet et al. [26] presents the results of a meta-analysis in which the sensitivity and specificity of the prognostic significance of different methods are characterized. Thus, according to metanalysis,

ultrasound of the abdominal cavity has a sensitivity of 50 to 100%, and a specificity of 33 to 100% in the diagnosis and prediction of destructive forms of acute cholecystitis. Similar results were obtained in other studies [22,26,39]. It was found that traditional methods of examination of patients with acute cholecystitis have a sensitivity of 26-100%, specificity of 62-88.1%. At the same time, it was revealed that the positive and negative predictive value of traditional methods ranges from 35%-93.7%, while the global accuracy varies from 70,1-79% [18,21, 23,24,25,27].

It should be noted that the sensitivity of computed tomography ranges from 31-95%, and the specificity from 45-100% [1,2,6]. At the same time, it was found that according to various authors, the sensitivity of this method is 85% (95% CI 66-95%), specificity 81% (95% CI 69-90%) [26]. The head to head study indicates that the diagnostic accuracy of magnetic resonance imaging is comparable to the ultrasound method [1,2,6,26].

In addition to the methods described above, for the differential diagnosis of destructive forms of acute cholecystitis, the determination of the plasma absorption coefficient of infrared radiation in the range of 1543-1396 cm⁻¹ is used. This study is carried out using the hardware and software system "Icarus". It was revealed that in all forms of acute cholecystitis, there is a significant decrease in the radiation absorption index in the range of 1543-1396 cm⁻¹. Thus, with an absorption coefficient of $29.7 \pm 1.1\%$, catarrhal cholecystitis is determined, with an absorption coefficient of $26.4 \pm 1.6\%$ - phlegmonous, $21.2 \pm 1.8\%$ - gangrenous, and with an absorption coefficient of $18.6 \pm 0.5\%$ - gangrenous perforative [11].

The diagnosis of destructive cholecystitis in children is difficult. The study by Sushko E.P. describes the use in the diagnosis of acute cholecystitis in children of the determination of antibodies in the reaction of suppression of hemagglutination with gallbladder tissue, it was revealed that during the formulation of the reaction of passive hemagglutination with an antigen from the extract of the tissue of the inflamed gallbladder an antibody titer of 1:32 was obtained. Such a change in the titer of antibodies is regarded as reactive cholecystitis [10].

The new stage of diagnosis of diseases and prediction of complications is characterized by the introduction of various mathematical models in an inextricable relationship with the accumulated diagnostic knowledge. Various methods based on the creation of mathemati-

cal models and programs for predicting acute calculous cholecystitis in emergency patients are proposed. In particular, a program of mathematical prediction of the development of destruction in acute cholecystitis is proposed, based on the study of a number of indicators in peripheral blood. At the same time, the method of support vectors, regression analysis, and the method of a direct non-cyclic graph are used. The following criteria were taken: bilirubin level, AST, leukocyte concentration, a number of indicators of the leukocyte formula (segmented leukocytes, monocytes, lymphocytes), ESR, results of organometry and histometry. The sensitivity of this mathematical program is 79% [7].

Numerous studies have been devoted to the development of a scoring system for predicting destructive processes in the gallbladder. In particular, the use of such parameters as: age more than 45 years (1.5 points); heart rate more than 90 per minute (1 point); male sex (2 points); leukocytosis more than 13 thousand (1.5 points); wall thickness more than 4.5 mm (1 point). Thus, a high probability of gangrenous cholecystitis was determined with a score of more than 4.5 [20,31].

Mustafin D.G. He described conducted a study aimed at finding patterns of change in clinical, laboratory and instrumental data using a new mathematical method based on modeling network neural substances. In this study, the following indicators were used as a basis: changes in tumor necrosis factor, a-2-glycoprotein, ferritin study in gallbladder tissues, bile microbiology, ultrasound and CT data of the gallbladder. As a result of this study, it was found that different forms of acute cholecystitis are characterized by certain changes in the studied parameters (wall thickening according to ultrasound, wall compaction according to CT, increased C-reactive protein and TNF-alpha) [8].

The study of ferritin in patients with acute cholecystitis as a diagnostic criterion for detecting destructive forms of acute cholecystitis is described in the work of Kchibekov. E. A. This method is based on the study of the level of ferritin in blood serum and gallbladder tissues. At the same time, the concentration of ferritin in the blood serum is 0-10ng / ml and in the tissues of the gallbladder 0-0.25 mg / l is taken as 1 point. At the same time, the level of ferritin in the blood serum of 70 ng / ml corresponds to 7 points, and in the tissues of the gallbladder of 0.75 ng / ml - 3 points. Further, the scores are added up and at a value of 10 points, they do not assume destructive cholecystitis, and at a value of 10 points

or higher, destructive cholecystitis [13].

Sibilev V.N.'s study indicates the effectiveness of computer infrared blood spectrophotometry, which allows confirming the diagnosis of acute cholecystitis and predicting the occurrence of destructive forms [11].

Features of diagnosis and prediction of acute cholecystitis forms according to ultrasound of the gallbladder are presented in a number of works. Polymorphism of ultrasound signs in patients with acute cholecystitis is indicated. A diverse picture is associated with both morphological changes and various microbial flora in the gallbladder. At the same time, the diagnostic significance of ultrasound was revealed in the so-called "erased" forms, when there are no changes from the peripheral blood. The leading ultrasound criterion is considered to be changes in the structure of the gallbladder wall [3]. It was also found that destructive cholecystitis is characterized by the following ultrasound criteria: a "double contour" symptom, the appearance of hyperechoic suspension, a "hanging" symptom, the presence of perivesical effusion [4]. Along with this, the effectiveness of determining ultrasound criteria (length, area and volume of the gallbladder) in conjunction with the assessment of blood flow (the value of the maximum systolic velocity (V_{max}) and resistance indices (RI, PI) in the gallbladder wall in the diagnosis of acute cholecystitis is noted. It was found that as hypertension in the gallbladder increases, there is an increase in the extent and speed of blood flow in venous vessels, recorded by color duplex scanning. At the same time, an increase in the frequency of ultrasound criteria (the ratio of length to its transverse size) and Doppler parameters of blood flow (maximum systolic blood flow velocity and systolic-diastolic ratio of the Doppler spectrum of blood flow) allow us to judge intravesical hypertension [28].

Numerous studies have noted that the traditional use of ultrasound should be combined with other methods to increase the informative value of the study. As an additional method, point shear-wave elastography (pSWE) should be used. The use of this method increases the diagnostic accuracy of ultrasound up to 96.3%, and the specificity up to 95%. In addition to pSWE, microvascular imaging (SMI) can be used to increase the accuracy of ultrasound. This method is used to assess the microcirculatory bed and blood flow rate in liver tissues. It was found that the use of SMI increases the diagnostic accuracy of ultrasound up to 85% [4, 12, 28].

Along with this, a method of rapid diagnosis of destructive changes of the gallbladder in acute cholecystitis is proposed. The following four criteria are taken as a basis: palpable gallbladder; body temperature and heart rate; the level of leukocytosis and rod-shaped shift in the general blood test; the layering of the gallbladder wall and effusion around the gallbladder during ultrasound examination. It was found that in the absence of the listed 4 criteria and the presence of leukocytosis up to 12 thousand, catarrhal cholecystitis can be suspected. And if they are present, including leukocytosis of more than 12 thousand, heart rate values of more than 80 beats / min, phlegmonous cholecystitis is diagnosed [5].

Of particular importance for surgeons is the diagnosis and prognosis of clinically asymptomatic forms of acute cholecystitis. Among the works devoted to this problem, the use of immunochemical methods is of interest. Shikhragimov M.I. studied the concentration of lactoferrin in blood serum and saliva by enzyme immunoassay to diagnose and predict the latent form of acute cholecystitis. As a result of this study, an increase in the concentration of lactoferrin was found in patients with a latent course of destructive cholecystitis. It is noted that the assessment of lactoferrin concentration makes it possible to predict destructive forms and complications of acute cholecystitis [16]. The significance of the lactoferrin study is described by E.A. Kchibekov [13]. The invention of the latter evaluates the level of lactoferrin in the blood serum of patients with acute cholecystitis during hospital treatment. To clarify the diagnosis, it is proposed to rank the obtained concentrations of lactoferrin, take the value of 200 ng/ml as 1 point, with a value of 8-10 points, catarrhal cholecystitis is predicted, and with a value above 10 points, a destructive form [14].

Thus, it can be concluded that at the present stage, the diagnosis of destructive forms of acute cholecystitis is not difficult. At the same time, the problem of predicting the risk of developing this complication remains relevant. There is a need to search for new methods that would make it possible to predict the risk of developing destructive forms of acute cholecystitis at an early stage of the disease and determine the most rational treatment tactics.

Reference

Абдурахманов А.М. Особенности течения, диагностика и выбор лечения острого холецистита при метаболическом синдроме: автореф.

дис. ...канд. мед. наук: 14.01.17 / А.М. Абдурахманов. – М., 2011. – 29 с. [Abdurakhmanov A.M. Features of the course, diagnosis and choice of treatment of acute cholecystitis in the metabolic syndrome: abstract. dis. ...candidate of medical sciences. 14.01.17 / A.M. Abdurakhmanov. Moscow, 2011: 29 (In Russ.).]

2. Артемов А.А. Лучевые и эндоскопические исследования в дифференциальной диагностике заболеваний органов гепато-панкреато-дуоденальной зоны: автореф. дис. ...канд. мед. наук: 14.01.13 / А.А. Артемов. – М., 2010. – 24 с. [Artemov A.A. Radiation and endoscopic studies in the differential diagnosis of diseases of the hepato-pancreato-duodenal zone: abstract. dis. ...candidate of medical sciences: 14.01.13. Moscow, 2010: 24 (In Russ.).]

3. Беловолова Е.В. Особенности ультразвуковой диагностики различных форм острого калькулёзного холецистита, микробной контаминации и реакции периферической крови / Е.В. Беловолова // Медицинский вестник Юга России. – 2012. – №3. – С. 19-24. [Belovolova E.V. Features of ultrasound diagnostics of various forms of acute calculous cholecystitis, microbial contamination and peripheral blood reactions. Meditsinskii vestnik Yuga Rossii. 2012; 3: 19-24.]

4. Боровский В.В. Роль эхографии в диагностике деструктивного холецистита / В.В. Боровский // Вестник экстренной медицины. – 2010. – 4. – С. 60-64. [Borovsky V.V. The role of echography in the diagnosis of destructive cholecystitis. Vestnik ekstreynoi meditsiny. 2010; 4: 60-64.]

5. Верзакова О.В. Обоснование ультразвуковых и доплерографических критериев в дифференциальной диагностике различных форм острого холецистита: дис. ... канд. мед. наук: 14.01.13: защищена 19.12.2017 / Верзакова Ольга Владимировна. – Уфа, 2017. – 111с. [Verzakova O.V. Substantiation of ultrasound and Dopplerographic criteria in the differential diagnosis of various forms of acute cholecystitis. : dis. ... candidate of medical sciences: 14.01.13: defended 19.12.2017. Ufa, 2017; 111 (In Russ.).]

6. Иванова И.В. Комплексная лучевая и дифференциальная диагностика при obstructивных заболеваниях желчевыводящих путей и ее влияние на хирургическую тактику: автореф. дис. ...канд. мед. наук: 14.00.19 / И.В. Иванова. – М., 2009. – 24 с. [Ivanova I.V. Complex radiation and differential diagnostics in obstructive diseases of the biliary tract and its effect on surgical tactics: abstract. dis. ...candidate of Medical Sciences. Sciences: 14.00.19. M. 2009; 24 (In Russ.).]

7. Марупов Б.А. Математическая модель и программа прогнозирования формы калькулёзного холецистита у экстренных больных / Б.А. Марупов // Инновации в науке. – 2016. – Т.8, №57. – С.28-35. [Magrupov B.A. Mathematical model and program for predicting the form of calculous cholecystitis in emergency patients. Innovatsionnye v nauke. 2016; 8(57): 28-35 (In Russ.).]

8. Мустафин Д.Г. Современные технологии диагностики, прогнозирования вариантов течения острого obstructивного холецистита / Д.Г. Мустафин // Бюлл. Волгоградского научного центра РАМН. – 2006. – №2. – С. 47. [Mustafin D.G. Modern technologies of diagnostics, forecasting of variants of the course of acute obstructive cholecystitis. Byull. Volgogradskogo nauchnogo centra RAMN. 2006; 2: 47 (In Russ.).]

9. Натрошвили И.Г. Насколько активной должна быть хирургическая тактика у больных острым холециститом (по результатам проспективного многоцентрового исследования) / И.Г. Натрошвили, М.И. Прудков // Вестн.Росс.

ун-та дружбы народов. Серия: Медицина. – 2019. – Т. 23, №2. – С.156-167. [Natroshvili I.G., Prudkov M.I. How active should surgical tactics be in patients with acute cholecystitis (according to the results of a prospective multicenter study). *Vestn.Ross. un-ta friendship of peoples. Series: Medicina.* 2019; 23 (2): 156-167 (In Russ.).]

10. Патент 2011201 РФ, МПК G01N33/53. Способ диагностики холецистита у детей / Е.П. Сушко, Л.И. Жукова; заявитель и патентообладатель Витебский медицинский институт. – № 4732774/14; заявл. 28.08.89; опубл. 15.04.1994. [Patent 2011201 Russian Federation IPC G01N33/53. Method for the diagnosis of cholecystitis in children. E.P. Sushko, L.I. Zhukov; applicant and patentee of the Vitebsk medical Institute. No. 4732774/14; application 28.08.89; publ. 15.04.1994 (In Russ.).]

11. Патент 2247379 РФ МПК G01N33/52. Способ дифференциальной диагностики деструктивных изменений при различных формах острого холецистита / В.Н. Сибилев, Е.М. Мохов, А.В. Каргаполов; заявитель и патентообладатель Тверская ГМА. – № 2003120838; заявл. 07.07.03; опубл. 27.02.05. Бюл. №6. [Patent 2247379 Russian Federation IPC G01N33/52. Method of differential diagnosis of destructive changes in various forms of acute cholecystitis / V.N. Sibilev, E.M. Mokhov, A.V. Kargaplov; applicant and patent holder Tver State Medical Academy. – No. 2003120838; application 07.07.03; publ. 27.02.05. Byul. No. 6. (In Russ.).]

12. Патент 2269299 РФ МПК A61B 8/00. Способ экспресс-диагностики деструктивных изменений желчного пузыря при остром холецистите / А.М. Машкин, С.А. Клиндюк, Р.В. Зиганшин, А.Г. Синяков, А.А. Хойрыш, Е.Ю. Зайцев, Л.А. Тарасенко; заявитель и патентообладатель Машкин Андрей Михайлович. – № 2269299; заявл. 10.02.06; опубл. 10.02.10. Бюл. №4. [Patent 2269299 Russian Federation IPC A61B 8/00. Method of express diagnostics of destructive changes of the gallbladder in acute cholecystitis. A.M. Mashkin, S.A. Klindyuk, R.V. Ziganshin, A.G. Sinyakov, A.A. Khoirys, E.Yu. Zaitsev, L.A. Tarasenko; applicant and patent holder Mashkin Andrey Mikhailovich. – No. 2269299; application 10.02.06; publ. 10.02.10. Byul. No. 4 (In Russ.).]

13. Патент 2407017 РФ МПК G01N33/68. Способ диагностики деструктивных форм острого холецистита / Э.А. Кчибеков, М.В. Рамазанов; заявитель и патентообладатель Астраханская ГМА. – № 2009114533; заявл. 16.04.09; опубл. 20.12.10. Бюл. №35. [Patent 2407017 Russian Federation IPC G01N33/68. Method of diagnosis of destructive forms of acute cholecystitis / E.A. Kchibekov, M.V. Ramazanov; applicant and patent holder Astrakhan State Medical Academy. – No. 2009114533; application No. 16.04.09; publ. 20.12.10. Byul. No.35 (In Russ.).]

14. Патент 2423706 РФ МПК G01N33/53. Способ диагностики острого холецистита / Э.А. Кчибеков, М.В. Рамазанов; заявитель и патентообладатель Астраханская ГМА. – № 2009114533; заявл. 10.12.09; опубл. 10.07.11. Бюл. №19. (Patent 2423706 Russian Federation IPC G01N33/53. Method of diagnosis of acute cholecystitis / E.A. Kchibekov, M.V. Ramazanov; applicant and patent holder Astrakhan State Medical Academy. – No. 2009114533; application No.

10.12.09; publ. 10.07.11. Byul. No. 19 (In Russ.).]

15. Размахнин Е.В. Нестандартные подходы к лечению желчнокаменной болезни: монография / Е.В. Размахнин, С.Л. Лобанов, Б.С. Хышиктеев. – Чита: ПолиграфРесурс, 2017. – 176с. [Razmakhnin E.V., Lobanov S.L., Khyshiktuev B.S. Non-standard approaches to the treatment of cholelithiasis: monograph. Chita: Polygraph Resource. 2017: 176 (In Russ.).]

16. Шахрагимов М.И. Лактоферрин в диагностике латентных форм / М.И. Шахрагимов // Авицена. – 2017. – №4(4). – С3. [Shakhragimov M.I. Lactoferrin in the diagnosis of latent forms. *Avicenna.* 2017; 4(4): 3 (In Russ.).]

17. Ansaloni L., Pisano M., Cocolini F. WSES 2016 Guide to acute calculous cholecystitis. *World surgery.* 2016; 11(1): 1–23. <https://doi.org/10.1186/1749-7922-9-58> <https://doi.org/10.1186/1749-7922-9-58>

18. Bargellini P., Orlandi R., Paloni S. Evaluation of ultrasound with contrast enhancement as a method for detecting necrosis or rupture of the gallbladder in dogs. *Veterinary radiology and ultrasound.* 2016; 57(6): 611-620. <https://doi.org/10.1111/vru.12404>

19. Changfaysarnkul P., Saengruang-Orn S., Bunya-Asadorn T. Diagnosis of acute cholecystitis: sensitivity of sonography, cholecintigraphy and computed tomography/ P.Changfaysarnkul, S.Saengruang-Orn, T.Bunya-Asadorn// *J Med Assoc Thailand.* – 2015. – №98 (8). – P.812-9.

20. Dollhopf M., Lary A., Will U. Controlled EUS drainage of the gallbladder in patients with acute cholecystitis and high surgical risk using a metal stent with enhanced lumen by electrocoagulation / M. Dollhopf, A. Lary, W. Will// *Gastrointest Endoscopy.* 2017; (4): 636-43. <https://doi.org/10.1016/j.gie.2017.02.027>

21. Gerstenmaier J.F., Hoang K.N., Gibson R.N. Contrast ultrasound examination in diseases of the gallbladder: a visual overview. *Abdominal radiology (New York).* – 2016; 41(8): 1640–1652. <https://doi.org/10.1007/s00261-016-0729-4>

22. Irani S., Ngamruengfong S., Teo A. Similar effectiveness of endoscopic ultrasound drainage of the gallbladder with a metal stent covering the lumen Compared with percutaneous transhepatic drainage of the gallbladder in acute cholecystitis. *Clinical gastroenterology and hepatology.* 2017; 15(5): 738-745. <https://doi.org/10.3410/f.727162673.793551534>.

23. Jain A., Mehta N., Sekko M. Medical history, Physical examination, Laboratory tests and ultrasound examination of the emergency department for the diagnosis of acute cholecystitis. *Academic emergency medicine.* 2017; 24(3): 281-297. <https://doi.org/10.1111/acem.13132>

24. Kania D. Ultrasound measurement of the wall thickness of the gallbladder in assessing the risk of transition from planned laparoscopic cholecystectomy to open surgery - the experience of Olkush county / D.Kania// *Polish Surgical Journal.* 2016; 88 (6): 334-345. <https://doi.org/10.1515/pjs-2016-0073>

25. Kawai R., Hata J., Manabe N. Enlargement of the liver adjacent to the gallbladder during contrast ultrasound examination: comparison of acute cholecystitis and non-cholecystitis. *BMC Med Imaging.* 2016; 10: 16-21. <https://doi.org/10.1186/s12880-016-0115-2>

26. Kim D., Iqbal S.I., Akhari H.K. Expanding

the role of percutaneous cholecystostomy and interventional radiology in the treatment of acute cholecystitis: analysis of 144 patients. *Diagnostic and interventional imaging.* 2017; 12. <https://doi.org/10.1016/j.diii.2017.04.006>.

27. Kim George. E., Choi, D. S., BAE K. Additional value of elastography point shear wave in the diagnosis of acute cholecystitis. *Eur Radiol.* 2017; 27 (4): 17–26. <https://doi.org/10.1007/s00330-016-4509-x> Kimura Yu.,

28. Kiviet JJ, Levenburg MM, Bipat S, Bossite PM, Stocker J, Burmister M.A. Systematic review and meta-analysis of diagnostic efficacy of imaging in acute cholecystitis. *Radiology.* 2012; 264: 708-20. <https://doi.org/10.1148/radiol.12111561>

29. Kimura Y., Takada T., Strasberg S.M. TG13 current terminology, etiology, and epidemiology of acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Sci.* 2013; 20(1): 8–23. <https://doi.org/10.1007/s00534-012-0564-0>

30. Loozen S.S., Van Santvoort H.S., Van Duivendijk P. Laparoscopic cholecystectomy in comparison with percutaneous catheter drainage in acute cholecystitis in high-risk patients (CHOCOLATE): a multicenter randomized clinical trial. *BMJ.* 2018; 363: 3965. https://doi.org/10.4103/sjg.sjg_115_17

31. Mori Yu., Itoi T., Baron T.H. Tokyo Guidelines 2018: strategies for the management of gallbladder drainage in patients with acute cholecystitis (with video). *J Hepatobiliary pancreatic science.* 2018; 25(1): 87-95. <https://doi.org/10.1002/jhbp.526>

32. Oamoto K., Suzuki K., Takada T., Strasberg S.M., Asbun H.J., Endo I. Tokyo Guidelines 2018: a flowchart for the treatment of acute cholecystitis. *J Hepatobiliary pancreatic science.* 2018; 25(1): 55-72. <https://doi.org/10.1002/jhbp.526>

33. Pisano M., Ceresoli M., Kimbanassi S. Recommendations of WSES and SICG 2017 on acute calculous cholecystitis in the elderly. *World surgery.* 2019; 14(1): 1-16. <https://doi.org/10.1186/s13017-019-0224-7>

34. Shigemi D., Aso S., Matsui H. Safety of laparoscopic surgery for benign diseases during pregnancy: A nationwide retrospective cohort study. *J Minimally Invasive Gynecol.* 2019; 26(3): 501–506. <https://doi.org/10.1016/j.jmig.2018.06.008>

35. Singer M., deichman K.S., Seymour, K. the Third international consensus definition for sepsis and septic shock (sepsis-3). *JAMA.* 2016; 315(8): 801-810. <https://doi.org/10.1001/jama.2016.0288>

36. Song G-M., Wei Bian X-TZ. Laparoscopic cholecystectomy for acute cholecystitis: early or delayed? Evidence from a systematic review of discordant meta-analyses. *Medicine (Baltimore).* 2016; 95(23): 801-806 <https://doi.org/10.1097/md.0000000000003835>

37. Stinton L.M., Myers R.P., Shaffer E.A. Epidemiology of gallstones. *Gastroenterol Clin N Am.* 2010; 39(2): 157–169. <https://doi.org/10.1016/j.gtc.2010.02.003>

38. Strasberg SM. Acute calculous cholecystitis. *N Engl J Med.* 2008; 358: 2804-2811. <https://doi.org/10.1056/nejmcp0800929>

39. Villar J., Summers S.M., Minchin M.D. The absence of gallstones during ultrasound examination excludes acute cholecystitis. *J Emerg Med.* 2015; 49 (4): 475-80. <https://doi.org/10.1016/j.jemermed.2015.04.037>