New systems for assessing severity and predicting outcomes of acute pancreatitis

A. A. Litvin[1], A. A. Filatov[2], S. I. Sychev[1], A. S. Prokoptsov[1]

[1]Immanuel Kant Baltic Federal University, Kaliningrad, Russia
[2]Gomel Regional Clinical Hospital, Gomel, Belarus

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Introduction

Acute pancreatitis (AP) is one of the most serious pathologies of the digestive system and lead to significant number of unfavorable outcomes of treatment of gastroenterological pathology [1, 11, 21, 24]. Particularly acute is the problem of timely diagnosis and objectification of severity of acute pancreatitis, as well as predicting its outcomes. The existing "traditional" definition scale Nia severity of acute pancreatitis, such as Ranson [27], Glasgow (Imrie) [26], SIRS [19], APACHE II [8] and the other, though are valuable and diagnostic criteria at the hospital stage, do not fully satisfy the requirements of practical medicine [12, 18]. For example, the scales Ranson, Glasgow, APACHE II require the definition of complex indicators and parameters that go beyond the capacity of the admissions departments of hospitals or small hospitals in general [2, 7, 12]. In turn, the Ranson and Glasgow systems need at least 48 hours to assess the severity of the AP course, which leads to a delay in the provision of intensive therapy (the so-called "break therapy") for patients with severe acute pancreatitis. But the APACHE II scale was created to assess the condition and prognosis of treatment for resuscitation patients in general, and not specifically for acute pancreatitis, which also reduces its diagnostic accuracy and specificity. Note revised classification AP (Atlanta 1992-2012), which is pretty good himself showed in the diagnosis of acute pancreatitis and its complications, however, it has not solved the problem of early (dosutochnogo) identifying severe disease - for the diagnosis of severe AP either CT OCP or multiorgan failure more than 48 hours is required [5, 15].

In addition, with the emergence of new criteria for severity of AP, which are not taken into account in the " traditional " diagnostic systems, the relevance of new scales is predictable povyshat s Xia [2,12]. In this regard, doctors from different countries continue to work on the early detection of severe forms of AP taking into account the emerging opportunities for diagnosis and treatment. And the firstrequirements for developing diagnostic systems are the following: 1) ease of use and interpretation of the results; 2) informative; 3) reliability and reliability, confirmed by clinical studies in the context of practical medicine [3].

The aim of this article was to review the literature on new diagnostic scales for determining severity and predicting acute pancreatitis.

Selection of the literature was conducted over a ten year period of electronic information databases PubMed with the use of IAOD Search lines: Scoring [All Fields] AND acute [All Fields] AND ("pancreatitis " [MeSH Terms] OR " pancreatitis " [All Fields])) AND ("2008/02/20" [PDat]: "2018/02/20" [PDat]; and eLibrary: «scale» AND «acute pancreatitis" in the same publication dates During initial. search was selected 208 publications in the PubMed database and 104 in the eLibrary database.

Based on the results of the processing and analysis of the found articles, a number of modern diagnostic systems for predicting severe acute pancreatitis have been identified.

Brown A. et al. (2007) published an article evaluating the scale of Panc 3, proposed by them for the diagnosis of severity of AP [23]. On the clinical material, consisting of 393 cases of AP, the likelihoodratio ratios for each possible risk factor for severe OD were calculated. As a result, the Panc 3 scale included three most informative criteria: blood serum hematocrit more than 44%, body mass index more than 30 kg/m^2 and the presence of pleural effusion when the ra- phy chest. The authors studied the effectiveness of the proposed scale on a clinical material

consisting of 238 patients with AP. According to them, the scale Panc 3 is simple and convenient for predicting heavy AP. The level of hematocrit from the blood turn was the most informative criterion for severe AP. A combination of these three predictors appeared prognostically the most accurate for the definition of severe forms of acute pancreatitis [23].

Singh VK et al. (2009), using a regression analysis using "wood and solutions", Ali developm th clinical systems in assessing the severity of acute pancreatitis BISAP (Bedside Index of Severity in AcutePancreatitis) [1]. The scoring system was obtained from data collected from an analysis of 17,992 cases of AP from 212 hospitals in 2000-2001. The new scale was confirmed during processing 18 256 cases of OC, collected from 177 hospitals in 2004-2005. Conducted a nalysis revealed five of the most informative variables to determine the severity of the AP and the prediction of in-hospital mortality:blood urea levels> 25 mmol/l, ie disorders of consciousness, SIRS (SIRS), age> 60 years, the presence of pleural effusion. The indicators were evaluated on the first day of the patient's stay in the hospital.Mortality varied from 20% and more in the group with the highest risk of mortality, up to less than 1% in the group with the lowest risk. The accuracy of determining the severity of acute pancreatitis was comparable to that of APACHE II - AUC BISAP yl composition of 0.82 (95% CI 0.79 to 0,84), AUC APACHE II - 0.83 (95% CI from 0.80 to 0.85) [1].

In 2011, a group of researchers from the University of Carolina (Sweden) published the results of a study of the informativeness of the proposed HAPS (H armless A cute P ancreatitis S core). Authors on the basis of an analysis of the data of all hospitalized patients (531 patients) with acute pancreatitis in the period from 2004 to 2009 revealed the most informative of the following criteria - the severity ofperitonitis, hematocrit, and serum creatinine. Specificity HAPS scale for prediction I of mild acute pancreatitis was 96.3% (95% CI: 81.0-99.9) with a corresponding positive predictive value of 98.7% (95% CI: 93.1-100). In the authors' opinion, the HAPS scale is an informative way to detect non- severe acute pancreatitis and can be an additional tool in the clinical differentiation of various forms AP on earlyterms [32].

Andersson B. et al. (2011) of the 23 potential severity indicators of AP using artificial neural networks (ANNs), which are now widely accepted in Big Data, selected six most informative parameters: duration of a pain attack, blood creatinine level, hemoglobin, alanine aminotransferase (ALT), heart rate (HR) and blood leukocytes. The authors conducted a retrospective analysis of the results of treatment of 208 patients with AP (from 2002 to 2005, n = 139, from 2007 to 2009, n = 69). The severity of AP was determined in accordance with the criteria proposed at the conference on acute pancreatitis in Atlanta. The area under the ROC-curve in a neural network model was 0.92 (95% CI: 0,85-0,99) 0,84 (0,76-0,92) - the logistic regression (P = 0,030, $\chi 2$) and 0.63 (0.50-0.76) - in assessing the severity of acute pancreatitis with APACHE II (P <0.001, $\chi 2$). The authors concluded that the scale developed by them on the basis of the data received when the patient entered the hospital is sufficiently accurate to determine the severity and prognosis of outcomes of the AP [25].

An international research team led by E. de - Madaria is currently studying the informativeness of the PROMISE scale (Patient Reported OutcoMes in the acute pancreatitIS) [28]. This scale is formed on the basis of symptom s -zhalob s own patient with acute pancreatitis. Participants in the PROMISE research study two hypotheses: 1) on the basis of subjective complaints of the patient, it is possible to determine the severity of AP according to the Revised classification of AP (Atlanta 2012): heavy, medium heavy and light AP; 2) for scoring on the scale PROMISE correlates with a subsequent decrease in the quality of life assessed by the EORTC-30 QoL system [28]. Variable for PROMISE Study is the following complaints of patients: 1) tinea in the abdomen; 2) into abdominal distension; 3) indigestion; 4) not the departure of stools, gases; 5) nausea and/or vomiting; 6) each; 7) common with the laboriousness. Each element is assessed on the scale 10 liter ball noy scale within days of hospitalization by: 0- no symptoms, up to 10 - Maximum th severity of the symptom.

The PROMISE scale is a practical application of PROMs principles. PROMs (Patient R eported O utco m es Methods - methods for assessing disease outcomes based on patient responses) is defined as any report on the patient 's complaints and status without interpretation by a research physician. In the PROMs system, the patient is treated as a subject of the medical process. Data on the patient's condition comes directly from him. The essence of this approach is the absence of any kind of intervention in the processing of data on the severity of the patient's condition [22]. In the first stage of the study is, PROMISE was formed list of the main complaints of the patient, in accordance with the principles of PROMs. Study Group symptoms of acute pancreatitis have been taken into account that most disturbed patients. At the second stage of the study, which the authors take part, we study the applicability of the scale on the example of the international cohorts s patients. The study design is a prospect of a prospective international multicenter study. The subject of the study is all patients admitted with acute pancreatitis in uchastvuyuschi e s Center for Research and Eligible. In this case, the set of singularities has a number of variables. In patient sample during the first 24 h x s from the time the hospitalization. After receiving informed consent, an anamnesis and a clinical picture of the disease will be evaluated. PROMISE scale is determined at the admission of the patient to the admission department, during the first 24 hours of hospitalization, then 48 hours later, on the 5th day, on the 7th, 12-15th day, 16-30 days, then after 15 days (± 2- e day) after discharge (along with the EORTC scale QLQ - C 30).

The PROMISE scale has a number of advantages and disadvantages. On the one hand, to the accuracy of the results obtained by using scale PROMISE can affect both unmotivated aggravation andnegation or reducing the severity of any COMPLAINTS. On the other hand, the use of the scale is as simple, requires no special training and additional clinical and laboratory studies. The use of this scale is possible to reduce the duration of determination of severity of AP and can be a good addition to standard diagnostics. When confirmed in the course of the study of the information scale, it can be used to evaluate the effectiveness of the new method in the treatment of acute pancreatitis. In addition, the obvious advantage of this approach to the diagnosis of the disease is the transition of the patient from the object to the subject of the medical process. The patient himself "establishes" the severity of his condition, which in some cases can help establish a stronger and more trustful relationship between the patient and the attending physician, and increase the patient's adherence to treatment [22, 28]. N redvaritelnye results of the study suggest that br feces PROMISE, composed on the basis of complaints of patients with acute pancreatitis, can be used as a quantitative indicator in assessing the severity of AP and its treatment efficiency as well as quality prediction evaluating patients life.

Papachristou GI et al. (2017) created a multi-center international consortium for the full-scale study of acute pancreatitis and developm ki s platform for future randomized clinical trials in patients with AP.In 2014, the district was formed Registers patient s with AP to explore new treatments - APPRENTICE (Acute Pancreatitis Patient Registry to Examine Novel Therapies in Clinical Experience) [6]. Was developed detailed online questionnaire for the prospect of a prospective collection of information on all the key points of diagnosis and treatment of AP. The study involved 20 hospitals (8 in the US, 5 in Europe, 3 in the Americas, 2 in Mexico and 2 in India), prospectively zaregistrirova us 509 patients AP. APPRENTICE study demonstrates the possibility and the need to create a large, etc. of a prospective, multicenter registry of patients for the study of AP. The analysis of the collected data can provide a deeper understanding of the problem of acute pancreatitis and will serve as a good platform for randomized clinical trials [6].

Hungarian Pancreatic Club in 201 5 he initiated a prospective, multicenter cohort EASY study (Early Achievable Severit Y) [20]. The aim of the study was to develop a simple and accurate system of clinical screening and differential diagnosis acute pancreatitis, which can be used even in small hospitals with limited access to diagnostic capabilities. The main feature of the study is an attempt to randomize patients with acute pancreatitis according to available

clinical and laboratory parameters in the first hours after admission to the hospital (no later than 6-12 hours). Moreover, a priority is placed just diagnosis of severe acute pancreatitis in which the outcome of the disease and the mortality rate is dependent on properly started the earliest possible intensive care. As initial parameters, 29 clinical and laboratory criteria were taken: anamnestic - acute pancreatitis in history, alcohol consumption, fat metabolism disorders, smoking, concomitant diseases; physical - age, BMI, tenderness or tension of the abdominal wall, heart rate, body temperature, respiratory rate, blood pressure, consciousness level on the Glasgow scale; laboratory - leukocyte blood, hematocrit, blood glucose, urea, cretinin, blood sodium, potassium blood, blood calcium, glomerular filtration rate, C-RB, blood amylase, AST, albumin, LDH; visualization - pleural effusion or infiltration of lung tissue, free fluid in the abdominal cavity. Of these parameters, at the first stage of the study (900 patients) 5-10 most informative and predictive significant indicators will be validated. In the second step using the selected parameters is a bud prospectively stratified 300 new patients with AP, and then compared the predicted results of the course of the disease with EASY and real clinical outcomes. Developed Index EASY has a high potential for practical use and can go and be simple and easy possibility of stratification and patients with AP [20].

Discussion

In the literature, there are many studies comparing the effectiveness of traditional scales for evaluating the severity of AP [10, 14, 16]. In one of the latest publications of Cho J. H. et al (2015) retrospectively analyzed prospectively collected clinical data from 161 patients, and compared with the AP and the accuracy of the following scales: Ranson, APACHE II, BISAP, CTSI, as well as the C-reactive protein level (obtained within 24 hours of hospitalization (CRP24)) [22]. The predictive accuracy of each counting system was measured using AUC ROC - the square and under the ROC-curve.In 21 (13%) patients with AP was defined as severe OD, 3 patients (2%) died. Statistically significant cutoff threshold (cut off) for the diagnosis of severe acute pancreatitis was defined as follows: Ranson$\geq$ 3, BISAP $\geq$ 2, APACHE-II $\geq$ 8, CTSI $\geq$ 3 and CRP24 $\geq$ 21.4. AUC for Ranson was 0.69 (95% CI: 0.62-0.76), for BISAP - 0,74 (95% CI: 0,66-0,80) for APACHE-II - 0,78 (95% CI: 0,70-0,84) for CTSI -0,69 (95% CI: 0,61-0,76) for CRP24 - 0,68 (95% CI: 0,57-0,78). Scale APACHE-II, according to the authors, and demonstrated the highest accuracy for the prediction of heavy AP, but no statistically significant paired differences were observed between APACHE-II and other assessment systems, including CRP24. Thus, different severity scales demonstrated similar predictive accuracy for determining theseverity of acute pancreatitis. In the authors' opinion, in order to improve the accuracy of predicting the severity of AP, it is necessary to develop a scale model based on new principles [17].

The task of determining the severity of acute pancreatitis is particularly acute at the level of the admission department. Kuo D. C. et al. (2015) evaluated the effectiveness of traditional and some new systems for predicting the severity of OD in the admission department [7]. The authors compared the scales of Ranson, Glasgow, APACHE II, CTSI, BISAP, Panc 3, HAPS, Japan Severity Score (JSS),as well as some possible predikt s op as a single variable. These parameters can be used to stratify patients with the OC, arrived at the reception. According to the authors, new systems for assessing the severity of AP, such as BISAP, Panc 3, HAPS and JSS can effectively be used to predict severity and OD, and even slightly exceed the previously proposed "traditional" scales Ranson, Glasgow, APACHE II. Single-factor predictors, such as blood serum hematocrit, blood urea, signs of pulmonary infiltration according to X-ray, C-reactive protein and procalcitonin correlate well with the severity of AP. According to the authors require further research on the identified th informative combinations of various predictors of the severity of AP, especially needed at the front desk to solve tactical issues - patient treatment for some patients with mild AP, hospitalization of patients with OD of medium gravity, the direction in the NICU patients with severe AP [7]. Evaluation system BISAP, HAPS

and predikt op s with one variable, can help in decision making because of their ease of use and applicability within the first 24 hours.

Thus, at the present time there is an intensive search for new ways of stratifying AP. Connected capabilities of artificial intelligence [2, 4, 9, 30], using technology Big Data as the union of a large array of multicenter studies data (APPRENTICE) [6, 13, 31] studied PROM technology s (Patient Reported Outcome Measures) - evaluation of gravity disease on the basis of patient complaints (PROMISE Study) [22, 28], the data and traditions of individual regions are used to find the most informative criteria for severity of AP (EASY Study - a multicenter study in the countries of Central and Eastern Europe under the leadership of the Hungarian Pancreatology Club) [20].

Conclusion

Currently, the medical literature presents a large number of both traditional and new scales for assessing the severity of acute pancreatitis. The ongoing search for new models of differential diagnosis of various forms of this disease testifies to the lack of a simple and universal evaluation methodology that fully meets the requirements of practical medicine. At the same time, multicenter clinical studies on development of modern prognostic and diagnostic systems, including EASY and PROMISE, in which we participate, allow us to positively assess prospects for identifying effective 's put it stratification of acute pancreatitis.

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References:
1. Диагностика и лечение острого панкреатита / А. С. Ермолов, П. А. Иванов, Д. А. Благовестнов, А. А. Гришин. — М. : «ВИДАР», 2013.
2. Литвин А. А. Система поддержки принятия решений в прогнозировании и диагностике инфицированного панкреонекроза / А. А. Литвин, О. Г. Жариков, В. А. Ковалев // Врач и информационные технологии. — 2012. — №2. — С. 54–63.
3. Литвин А. А. Системы поддержки принятия решений в хирургии / А. А. Литвин, В. А. Литвин // Новости хирургии. — 2014. — №1. — С. 96–100.
4. Лутфарахманов И. И. Современные пути прогнозирования развития сепсиса у больных тяжелым острым панкреатитом / И. И. Лутфарахманов, П. И. Миронов // Практическая медицина. — 2016. — №5 (97). — С. 21–24.
5. Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis—2012 : revision of the Atlanta classification and definitions by international consensus / P. A. Banks, T. L. Bollen, C. Dervenis [et al.] // Gut. — 2013. — Vol. 62, No 1. — P. 102–111.
6. Acute pancreatitis patient registry to examine novel therapies in clinical experience (APPRENTICE) : an international, multicenter consortium for the study of acute pancreatitis / G. I. Papachristou, J. D. Machicado, T. Stevens [et al.] // Ann. Gastroenterol. — 2017. — Vol. 30, No 1. — P. 106–113.
7. Acute Pancreatitis: What's the Score? / D. C. Kuo, A. C. Rider, P. Estrada [et al.] // J. Emerg. Med. — 2015. — Vol. 48, No 6. — P. 762–770.
8. APACHE II: a severity of disease classification system / W. A. Knaus, E. A. Draper, D. P. Wagner, J. E. Zimmerman // Crit. Care Med. — 1985. — Vol. 13, No 10. — P. 818–829.
9. Artificial neural networks predict the incidence of por-tosplenomesenteric venous thrombosis in patients with acute pancreatitis / Y. Fei, J. Hu, W. Q. Li [et al.] // J. Thromb. Haemost. — 2017. — Vol. 15, No 3. — P. 439–445.
10. Bedside index for severity in acute pancreatitis: comparison with other scoring systems in predicting severity and organ failure / J. Y. Park, T. J. Jeon, T. H. Ha [et al.] // Hepatobiliary Pancreat. Dis. Int. — 2013. — Vol. 12, No 6. — P. 645–650.
11. Beger H. G. Acute Pancreatitis: Research and Clinical Management / H. G. Beger, M. Buchler. — Springer Science & Business Media, 2012.

12. Chauhan S. The difficulty in predicting outcome in acute pancreatitis / S. Chauhan, C. E. Forsmark // Am. J. Gastroenterol. — 2010. — Vol. 105, No 2. — P. 443–445.

13. Clinical decision support systems for improving diagnostic accuracy and achieving precision medicine / C. Castaneda, K. Nalley, C. Mannion [et al.] // J. Clin. Bioinforma. — 2015. — Vol. 5. — P. 4.

14. Comparison of BISAP, Ranson's, APACHE-II, and CTSI scores in predicting organ failure, complications, and mortality in acute pancreatitis / G. I. Papachristou, V. Muddana, D. Yadav [et al.] // Am. J. Gastroenterol. — 2010. — Vol. 105, No 2. — P. 435–441; quiz 442.

15. Comparison of existing clinical scoring systems to predict persistent organ failure in patients with acute pancreatitis / R. Mounzer, C. J. Langmead, B. U. Wu [et al.] // Gastroenterology. — 2012. — Vol. 142, No 7. — P. 1476–1482; quiz e15–16.

16. Comparison of Predictive Systems in Severe Acute Pancreatitis According to the Revised Atlanta Classification / K. J. Lee, H. M. Kim, J. S. Choi [et al.] // Pancreas. — 2016. — Vol. 45, No 1. — P. 46–50.

17. Comparison of scoring systems in predicting the severity of acute pancreatitis / J. H. Cho, T. N. Kim, H. H. Chung, K. H. Kim // World J. Gastroenterol. — 2015. — Vol. 21, No 8. — P. 2387–2394.

18. The early prediction of mortality in acute pancreatitis : a large population-based study / B. U. Wu, R. S. Johannes, X. Sun [et al.] // Gut. — 2008. — Vol. 57, No 12. — P. 1698–1703.

19. Early systemic inflammatory response syndrome is associated with severe acute pancreatitis / V. K. Singh, B. U. Wu, T. L. Bollen [et al.] // Clin. Gastroenterol. Hepatol. — 2009. — Vol. 7, No 11. — P. 1247–1251.

20. Hritz I. Early Achievable Severity (EASY) index for simple and accurate expedite risk stratification in acute pancreatitis / I. Hritz, P. Hegyi // J. Gastrointestin. Liver Dis. — 2015. — Vol. 24, No 2. — P. 177–182.

21. IAP/APA evidence-based guidelines for the management of acute pancreatitis / Working Group IAP/APA Acute Pancreatitis Guidelines // Pancreatology. — 2013. — Vol. 13, No 4, Suppl. 2. — P. e1–15.

22. International Alliance of Patients' Organizations. What is Patient-centred Health Care? A Review of Definitions and Principles. — 2nd ed. — London : IAPO, 2007. — P. 1–34.

23. The panc 3 score: a rapid and accurate test for predicting severity on presentation in acute pancreatitis / A. Brown, T. James-Stevenson, T. Dyson, D. Grunkenmeier // J. Clin. Gastroenterol. — 2007. — Vol. 41, No 9. — P. 855–888.

24. The Pancreas: An Integrated Textbook of Basic Science, Medicine, and Surgery / H. G. Beger, A. L. Warshaw, M. W. Büchler [et al.]. — John Wiley and Sons Ltd., 2009.

25. Prediction of severe acute pancreatitis at admission to hospital using artificial neural networks / B. Andersson, R. Andersson, M. Ohlsson, J. Nilsson // Pancreatology. — 2011. — Vol. 11, No 3. — P. 328–335.

26. Prognostic factors in acute pancreatitis / S. L. Blamey, C. W. Imrie, J. O'Neill [et al.] // Gut. — 1984. — Vol. 25, No 12. — P. 1340–1346.

27. Prognostic signs and the role of operative management in acute pancreatitis / J. H. Ranson, K. M. Rifkind, D. F. Roses [et al.] // Surg. Gynecol. Obstet. — 1974. — Vol. 139, No 1. — P. 69–81.

28. The PROMISE Study. Точка доступа: https://promisepancreatitis.com / Дата доступа: 20.02.18.

29. A prospective evaluation of the bedside index for severity in acute pancreatitis score in assessing mortality and intermediate markers of severity in acute pancreatitis / V. K. Singh, B. U. Wu, T. L. Bollen [et al.] // Am. J. Gastroenterol. — 2009. — Vol. 104, No 4. — P. 966–971.

30. Use of an artificial neural net-work to predict persistent organ failure in patients with acute pancreatitis / W. D. Hong, X. R. Chen, S. Q. Jin [et al.] // Clinics (Sao Paulo). — 2013. — Vol. 68, No 1. — P. 27–31.
31. The use of intelligent database systems in acute pancreatitis — a systematic review / M. van den Heever, A. Mittal, M. Haydock, J. Windsor // Pancreatology. — 2014. — Vol. 14, No 1. — P. 9–16.
32. Validation of the harmless acute pancreatitis score in predicting nonsevere course of acute pancreatitis / V. Oskarsson, M. Mehrabi, N. Orsini [et al.] // Pancreatology. — 2011. — Vol. 11, No 5. — P. 464–468.

New systems for assessing severity and predicting outcomes of acute pancreatitis

A. A. Litvin[1], A. A. Filatov[2], S. I. Sychev[1], A. S. Prokoptsov[1]
[1]Immanuel Kant Baltic Federal University, Kaliningrad, Russia
[2]Gomel Regional Clinical Hospital, Gomel, Belarus

Key words: acute pancreatitis, severity scales, EASY and PROMISE systems, stratification, prognosis

The article is a review of the literature on new systems for assessing the severity and predicting the outcomes of acute pancreatitis. The authors cite current literature data on the effectiveness of various new scales, as well as information on developed systems that undergo a clinical information test in determining the severity of acute pancreatitis.