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EDITORIAL

INTER-PROFESSIONAL TEAMWORK CHALLENGES IN THE EMERGENCY ROOM AND CRITICAL CARE UNIT

BRIEF REPORT

FAMILIAL HYPERCHOLESTEROLEMIA. PERSPECTIVES ON FH REGISTRY SYSTEMS

RESEARCH ARTICLES

ORGANIZATION AND MANAGEMENT OF INTENSIVE CARE UNIT, CORRELATION OF TEAM CLIMATE WITH JOB SATISFACTION OF THE NURSES IN THE ICU

COST-EFFECTIVE SURGICAL MANAGEMENT OF LIVER DISEASE IN AN UNIVERSITY HOSPITAL: A RETROSPECTIVE STUDY

NUTRITIONAL PREFERENCES OF PRESCHOOL CHILDREN FOR BREAKFAST

DETERMINATION OF FEVER MANAGEMENT AND RATIONAL DRUG USE OF MOTHERS WITH CHILDREN UNDER SIX YEARS OLD

RELIGIOSITY AND CORONARY HEART DISEASE IN GREEK ADULTS

SYSTEMIC REVIEW

MANAGEMENT OF ACUTE PANCREATITIS IN THE EMERGENCY DEPARTMENT

INVASIVE TECHNIQUES FOR THE REMOVAL OF NECROTIC TISSUE IN CHRONIC WOUNDS, A SYSTEMATIC REVIEW

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Management of acute pancreatitis in the Emergency Department

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SYSTEMATIC REVIEW

MANAGEMENT OF ACUTE PANCREATITIS IN THE EMERGENCY DEPARTMENT

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Abstract

Background: Heterogeneity in clinical manifestations and outcome of pancreatitis constitutes an obstacle for the creation of a common treatment algorithm by the scientific community.

Aim: The aim of the present study was to systematically review the management of cases of acute pancreatitis in Emergency Department (ED) and her correlation with outcome.

Methods: Search the database Pubmed and were included observational studies and randomized trials in adults in English.

Results: The search yielded 13 studies. Of these, 3 concerned the diagnostic approach of the disease in ED and concluded that lipase is the most reliable test in diagnosis, while computed tomography of the abdomen is not recommended as a routine examination. 5 out of 13 studies analyzed the usefulness of disease severity classification systems, with the BISAP and HASP score appearing as reliable as the APACHE II and RANSON score, but having an advantage in rapid patient evaluation. The last 5, studied the need for immediate therapeutic / invasive method, with the time of surgery from the arrival at the ED being decisive as it affects the outcome of the disease. It is generally seen that the early invasive method is gaining ground in the treatment of the disease.

Conclusion: The main goal is to predict the most severe forms of the disease in order to receive the right (invasive or not) treatment to improve survival and quality of life.

Keywords: Acute pancreatitis, management, emergency department.

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INTRODUCTION

Acute pancreatitis is a disease of the pancreas caused by inappropriate release and activation of pancreatic enzymes result in pancreatic inflammation and subsequent triggering of the inflammatory cascade. It is one of the most common gastrointestinal disorders requiring hospitalization worldwide, with a reported annual incidence of 13-45 new cases per 100,000 people.¹ From the studies so far, it seems that the frequency of patients with acute pancreatitis in the Emergency Departments (EDs) is increasing, while it was seen that 1% of the cases in the ED, pass away at their arrival.² The most common age of onset of the disease is the 5th-6th decade, with mortality increasing with age.³

The most common causes of the disease are gallstones (including microlithiasis) and alcohol, which together are responsible for the 70-80%.⁴ Most patients develop a mild and limited form of the disease, with a mortality rate of less than 1%. Nevertheless, 15-25% of patients with acute pancreatitis will develop the severe form of the disease and mortality reaches 30% in these cases. During the first 2 weeks of the disease, the main cause of death is the multiorgan deficiency syndrome, which is usually the result of a systemic inflammatory response to the most severe pancreatic inflammation.⁴ Over the next 2 weeks, death is usually due to septic complications.⁵ The recurrence rate of acute pancreatitis ranges between 0.6% to 5.6%, with the highest observed in the case of alcohol abuse.⁶

Now, according to international guidelines, the diagnosis of acute pancreatitis is based on the coexistence "2 in 3" of the following criteria: clinical criterion (upper abdominal pain), laboratory criterion (Serum amylase or lipase > 3 times the maximum) and/or imaging findings (computed tomography (CT), magnetic resonance imaging (MR), ultrasound criteria).³

Studies have shown that the use of disease severity classification systems is particularly helpful in the management of ED, and that it is associated with early recognition of local complications of the disease, affects the duration of hospitalization and is helpful in assessing the possibility of occurrence of complications and of mortality.⁷⁻⁹ An important parameter in the management of the disease at the level of ED are the various imaging and laboratory examinations, the findings of

which are often of particular importance in the diagnosis, severity and recognition of local complications of the disease and which may be associated with higher morbidity rates and mortality.^{10,11}

AIM

The aim of the present study was to correlate the management of acute pancreatitis in the Emergency Department with the outcome of the disease. Sub-purposes:

- Diagnostic approach of the disease in the Emergency Department
- Usefulness of disease severity classification systems
- Indications for hospitalization in an intensive care unit and/or need for an immediate invasive therapeutic method.

MATERIAL - METHOD

The methodology used to achieve the above purpose is the systematic review and has been carried out based on the guidelines "Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA)". The selection criteria were observational studies (prospective and retrospective) and randomized studies, which refer to the adult population with acute pancreatitis, studies in humans and publications in English. Animal studies, pediatric studies, individual case reports, conference excerpts, unpublished studies in English, full text not available and duplicated reports were excluded.

This search was performed on the Medline database (<http://www.ncbi.nlm.nih.gov/sites/entrez>) (pubmed) and included studies published in the last five years. The keywords used were: "acute pancreatitis", "acute pancreatitis in emergency department", "severe acute pancreatitis", and "management of acute pancreatitis in the emergency department".

All articles resulting from the online search were evaluated based on the title, summary and full text in order to find those that met the predefined criteria.

Data indexing was done in a Microsoft Excel spreadsheet (Microsoft Corp, Redmond, WA, USA). The following data were recorded for each study: name of first author, year of publication, study design, total number of participants, and study results.

The initial search yielded 228 results. Following the removal of duplicate publications, 223 articles were evaluated, 184 were excluded based on title and summary as they met exclusion criteria. Of the remaining 39 articles, 26 were also removed due to content. The articles remained were 13.

RESULTS

Diagnostic approach of the disease in the Emergency Department (ED)

Acute pancreatitis is a clinical syndrome with extremely great heterogeneity in clinical manifestation and severity. To this end, multiple studies have been performed to evaluate the appropriate biochemical markers that will diagnose acute pancreatitis on time and with relative accuracy. The role of amylase and lipase in the diagnosis is unquestionable. According to a review of 5,500 patients, the lipase test has become much more sensitive and specific for diagnosing the disease and offers a larger diagnostic window compared to amylase.¹² However, it is not available in every hospital and so the use of amylase has prevailed.

There is great controversy is in the use of imaging in acute pancreatitis, the type of imaging and the time at which it will prove most beneficial. In a retrospective study, it was examined whether the use of computed tomography (CT) of the abdomen in the ED is beneficial in patients with clinically mild acute pancreatitis. Specifically, out of 405 patients with acute uncomplicated pancreatitis, 210 (51.85%) underwent CT. Of these, only 1 (0.47%) had findings of pancreatic necrosis, 1 (0.47%) findings of pancreatic cyst, and the remaining 208 had no findings of complicated pancreatitis. This study concluded that abdominal CT is only necessary in cases of questionable diagnosis or suspected complicated disease, and not as a routine examination.¹³ The same conclusion was reached by the cohort study of Shinagare et al¹⁴, with 101 patients with acute pancreatitis, of which only 12 patients with a doubtful diagnosis had CT. In their study, 87.1% could be successfully diagnosed as cases of acute pancreatitis without performing CT.¹⁴

Usefulness of disease severity classification systems

Due to the exceptional diversity in the clinical appearance and the outcome of acute pancreatitis, for more than 100 years efforts have been made to create a staging-classification system capable of helping to assess the severity of the disease, but also in the clinical management of these patients.

In a large retrospective study of 3,212 patients with acute pancreatitis, the ability of the revised Atlanta criteria to predict disease severity and mortality was analyzed and compared with that of the standard Atlanta criteria.¹⁵ The revised classification had a higher prognostic value for severity and poor outcome. However, the fact that fewer cases of severe acute pancreatitis were diagnosed, especially in the early stages, resulted in fewer admissions to Intensive Care Units (ICU) and higher mortality. In conclusion, it appeared that the revised criteria were superior in assessing the severity of the disease to the classical Atlanta classification.¹⁵

In a prospective study,¹⁶ the ability of the BISAP score to predict cases of severe acute pancreatitis was evaluated compared to the Ranson score. Specifically, in 206 patients with acute pancreatitis whose severity of the disease was assessed as mild, moderate to severe and severe based on the revised Atlanta criteria, the Ranson and BISAP systems were applied, with BISAP applied within the first 24 hours of patient arrival. The BISAP score showed a sensitivity of 69.2% to distinguish severe acute pancreatitis (for BISAP score > 2) while the Ranson score 97.4% (for Ranson score > 2). The accuracy of the two systems was 76.2% and 82% correspondingly.¹⁶

Furthermore, in another prospective observational study, the ability of the BISAP score in the first 24 hours to predict severe disease and mortality was studied and compared with other classification systems, such as the APACHE II and the Ranson score. And in this study, 60 patients with acute pancreatitis initially were categorized based on the revised Atlanta criteria. In these patients the above classification systems were applied with the main purpose of assessing the ability of the BISAP score to predict the severity and mortality of the disease with the data resulting from the assessment of the patient in the ED. The sensitivity of BISAP for prediction of severe acute pancreatitis was 87.5% while Ranson score 81% and APACHE II 87.2%. The BISAP score was equal to APACHE II in identifying cases

that developed severe acute pancreatitis and slightly above Ranson criteria, with no statistically significant result for the latter.¹⁷

In a study by Al-Qahtani HH et al¹⁸, HAPS (Harmless Acute Pancreatitis Score), which can be performed 30 minutes after the patient arrives at the ED, was applied to 116 patients with acute pancreatitis and its ability to predict cases with non-severe form of the disease was studied, compared to the full Ranson score. The results were encouraging, as out of 116 patients, 104 (89.6%) were HAPS positive and 'candidates' for mild disease. Of these, according to Ranson criteria, mild pancreatitis was diagnosed in 101 patients (87%) and severe in 3 patients (2.6%) with Ranson score ≥ 3 . Of the remaining 12 patients who were predicted by HAPS to develop severe acute pancreatitis, 10 had Ranson score ≥ 3 and 2 (1.7%) with 2 positive Ranson criteria developed mild pancreatitis. HAPS therefore correctly predicted the severity in 87% of cases, with 98% sensitivity, 77% specificity and 96% accuracy for predicting the non-serious form of the disease.¹⁸

In a prospective observational study with 50 patients with acute pancreatitis, the severity classification systems (acute physiology and chronic health evaluation (APACHE) II score, bedside index for severity in AP (BISAP), modified Computed Tomography Severity Index (CTSI) and Ranson score at 24 and 48 hours), were compared, based on the modified Atlanta criteria. It therefore appeared that the modified CTSI was superior to identify the cases of severe acute pancreatitis as recorded by the modified Atlanta criteria (Area Under the Curve (AUC) for Modified CTSI=0.919). In the present study, based on AUC comparisons, only APACHE II was found to be comparable to the modified CTSI in terms of the severity of acute pancreatitis, statistically insignificant finding ($p=0.13$). On the other hand, the AUC of the modified CTSI was significantly higher than the Ranson score ($p=0.02$) and the BISAP ($p=0.002$) in predicting the severity of acute pancreatitis. The AUC of APACHE II was also found to be significantly higher than the BISAP score in predicting the severity of acute pancreatitis ($p=0.02$). APACHE II was also found to have high sensitivity and a negative prognostic value for the prediction of pancreatic necrosis (93.33% and 96.15%), organ failure (92.86% and 96.15%) and ICU ad-

mission (92.31% and 95.8%), which makes it an ideal scoring system for decision making. Although the study is limited by its small sample size, it concluded that APACHE II is a useful tool for predicting patients who are likely to develop a severe form of the disease.¹⁹

Need for immediate therapeutic and/or invasive method

The need for immediate resuscitation with fluids and restoration of intravascular volume and the need for immediate and effective analgesia are basic principles of the initial treatment of the disease. Aggressive fluid administration, which translates to at least 33% of total fluid volume within the first 24 hours, has been found to be associated with significantly lower rates of organ insufficiency. Nevertheless, the type of intravenous fluids, the type of analgesia, early feeding and the need for immediate intervention are still hotly debated.

In a randomized clinical trial, efficacy in reducing the abdominal pain in patients with acute pancreatitis was evaluated with 3 different drugs, 1 g paracetamol, 50 mg dexketoprofen and 1 mg / kg tramadol in 100 ml normal saline (N/S) in 4-5 minutes of infusion. 90 patients were included in the study, in which they were divided into 3 groups of 30 patients each. Pain was assessed based on a pain assessment scale completed by each patient before and 30 minutes after administration. Allergic reactions, side effects and the need for additional medication after 30 minutes were also assessed. So it seemed that all 3 drugs reduced the pain equally. The incidence of nausea and vomiting after analgesic administration was the same in the 2 groups (2 for dexketoprofen and 2 for tramadol and 1 case in the paracetamol group). Therefore, it appeared that dexketoprofen and tramadol were not superior to paracetamol.²⁰

Another major issue regarding the immediate treatment of acute lithiasic pancreatitis is the efficacy of early ERCP - within the first 24 to 72 hours of the onset of symptoms. In a randomized multicenter study, the efficacy of ERCP was evaluated in patients with predicted severe (APACHE II ≥ 8 , Imrie grade ≥ 3 or C-reactive protein > 150 mg/L) cholelithiasic pancreatitis without cholangitis. Specifically, 232 patients were divided into 2 groups [1]ERCP with sphincterotomy in the first 24 hours after the onset of symptoms ($n = 118$) and 2) conservative

treatment (n = 114)]. The final assessment was made by calculating mortality and rates of major complications (new onset organ failure, cholangitis, bacteremia, pneumonia, pancreatic necrosis or insufficiency) within the first 6 months. 38% in the ERCP emergency group and 44% in the conservative treatment group died or suffered a major complication of pancreatitis (RR 0.87, 95% CI 0.64–1.18, p = 0.37). The authors concluded that in patients with predicted severe gallstone pancreatitis but without cholangitis, emergency ERCP with sphincterotomy did not reduce the rate of serious complications or mortality compared with conservative treatment.²¹

Early ERCP does not appear to have positive effects in cases of necrotic pancreatitis. In a randomized prospective study of 25 patients with necrotic acute pancreatitis, the use of early ERCP and prophylactic stent placement in the pancreatic duct was evaluated. The 25 patients were divided into 2 groups, one group undergoing ERCP in the first 24 hours after the onset of symptoms (n=12) and one group treated conservatively (n=13). 5 of the 7 patients undergoing ERCP developed infected necrosis after the intervention. They therefore concluded that prophylactic placement of a stent in the pancreatic duct endoscopically in patients with acute necrotic pancreatitis is associated with high rates of infection.²²

The treatment of infected necrotic pancreatitis is also a major and controversial issue. In a randomized study, 98 patients with acute infected pancreatic necrosis were studied, of whom 51 underwent endoscopic treatment and 47 underwent surgery. The endoscopic approach consists of endoscopic ultrasound-assisted drainage and surgical treatment consists of percutaneous peritoneal or extraperitoneal lavage. The comparison of the 2 methods was based on mortality and the occurrence of major complications in the first 6 months of the intervention. Mortality did not differ between the 2 groups [9 (18%) patients in the endoscopy group versus 6 (13%) patients in the surgery group - finding not statistically significant (p = 0.5, CI (95%): 0.53 –3.59)]. Therefore, in patients with infected necrotic pancreatitis, the endoscopic approach did not prove superior to the surgical approach in reducing serious complications or death.²³

A major ambiguous issue is the early cholecystectomy in cases of lithiasic pancreatitis. In a long-term randomized study of 66 patients with acute pancreatitis, early cholecystectomy (within 48 hours of the onset of symptoms) was evaluated in relation to second-time cholecystectomy (at another regular hospitalization). Patients were divided into 2 groups, 32 of whom underwent early cholecystectomy and 34 on a regular basis. The results showed that 1/32 patients of the first group in contrast to 9/34 patients of the second group had a complication of gallstones (specifically 1 patient had a recurrence of the disease). This difference was statistically significant (P = 0.013). Finally, the quality of life of patients who underwent early cholecystectomy improved compared to the other group, based on questionnaires on pain and psychological well-being of patients, a finding of statistical significance (P <0.001 and p=0.03 respectively). The authors therefore concluded that early cholecystectomy within 48 hours of the onset of symptoms in cases of acute mild lithic pancreatitis is beneficial for patients.²⁴

DISCUSSION

It is a fact that acute pancreatitis is still challenging for the clinician. Based on epidemiological data, it is ranked high in terms of incidence, mortality and hospital costs.

Many issues initially arise in the diagnosis of acute pancreatitis. Although acute abdominal pain located mainly in the epigastrium with reflection in the back and the consequent increase in laboratory values of serum amylase and / or lipase are now in the international guidelines for diagnosis, nevertheless, many questions arise about the imaging in the diagnosis attendance of the patient at the ED. The diagnosis of acute pancreatitis is determined by the clinician's index of suspicion, which is largely based on the patient's history and the findings of the clinical examination. From the literature search, it seems that most authors recommend performing CT only in cases of doubtful diagnosis or in cases where the severe form of the disease is the most likely diagnosis.⁶ Abdominal ultrasound is excluded and should be performed at the ED to confirm or rule out gallstone etiology of pancreatitis. While the measurement of pancreatic enzymes in serum, such as amylase, is the "golden rule" for the diagnosis of acute pancreatitis, the measured

value for pancreatic enzymes in serum should be interpreted taking into account the duration of the patient's symptoms.⁹ Lipase has higher diagnostic accuracy compared to amylase as serum lipase levels increase over time, but unfortunately this laboratory test is not always available.

There is a great controversy among the scientific community about the use of systems of classification and assessing of the severity of acute pancreatitis. The revised Atlanta 2012 Criteria for Classifying the Severity of the Disease are widely accepted.²⁵ This revised classification defines transient organ failure as organ failure that resolves completely within 48 hours, while failure to resolve organ failure is defined as persistent. The presence of persistent organ failure, usually with one or more local complications, indicates a serious disease. On the other hand, the absence of organ failure without local or systemic complications indicates mild acute pancreatitis. "Moderately severe acute pancreatitis", indicated by transient organ failure and / or local or systemic complications in the absence of permanent organ failure, is the new degree of severity between mild and severe introduced in the revised Atlanta classification. Nevertheless, as we have seen above, efforts are being made to find the ideal classification system that will diagnose severe acute pancreatitis in a timely and accurate manner. The BISAP and HASP score are constantly gaining ground and are considered, as we saw earlier, just as reliable as traditional systems such as APACHE II and RANSON score. The above is reinforced by the results of the meta-analysis of Yang et al.²⁶

Single biochemical markers have also been tested. These include CRP, procacitonin (PCT) and interleukin 6 (IL-6). Most other markers, include acute phase proteins (LBP, SAA, PTX3). They seem to be very promising, but they need further studies to evaluate them, as such a parameter would greatly improve the outcome of the disease with early diagnosis of the severe form.

The main discussion on severity classification systems has as its sub-purpose the finding of those patients who need more immediate treatment or those patients who need hospitalization in Intensive Care Units (ICU). Current guidelines for ICU admission are the diagnosis of severe acute pancreatitis upon admission in ED or persistent SIRS criteria within 48 hours of the on-

set of symptoms¹. In any other case, early admission to ICU not recommended, however, many studies will need to be performed to clarify the role of ICU in patient outcome.

The need for immediate treatment in acute pancreatitis is imperative. The principles of immediate resuscitation and immediate treatment of pain are now a fact. Isotonic crystalline solutions seem to be the best for the initial treatment of the patient¹ while only very few studies have investigated the effect of different types of fluids on the outcome of the disease.²⁷ The local and systemic inflammatory response to acute pancreatitis results in depletion of intravascular fluid by vomiting, decreased oral fluid intake, loss of third fluid and increased losses in sweat and respiration²⁸. Fluid replacement in acute pancreatitis can be performed using crystalloid, colloidal, or a combination of both. Lactated Ringer's (R/L) is the preferred crystalline fluid²⁹ but caution should be exercised in patients with hyperkalemia. R/L appears to be superior to N/S in the recovery of patients with acute pancreatitis. Finally, it has been shown that patients receiving R/L may be less likely to meet SIRS criteria within 24 hours, indicating the anti-inflammatory effects of R/L in patients with acute pancreatitis.²⁹

An additional major issue in the treatment of the disease is the need for invasive / surgical treatment and the correct time of its performance from the arrival in the ED. Surgical/invasive treatment of acute pancreatitis can be divided into surgical treatment of acute gallstone pancreatitis and surgical treatment of complications of acute pancreatitis. Cholecystectomy early, 24 to 72 hours after the arrival of the patient with mild cholelithiasic pancreatitis in the ED seems to be gaining ground in relation to the delayed operation (regular new admission for surgery). Early laparoscopic cholecystectomy in this group of patients can reduce the total hospital stay thus improving the patient's prognosis.^{24,30,31}

All patients with acute gallstone pancreatitis should have an imaging of the common bile duct to be assessed the coexistence or not of gallstones. The management of choledocholithiasis depends on the availability of local expertise and can generally be classified into 1)a one-stage approach-laparoscopic or open cholecystectomy with intraoperative cholangiography and a common bile duct examination or 2)a 2 stages ap-

proach- preoperative ERCP followed by laparoscopic or open cholecystectomy. There is no significant difference in morbidity and mortality between the 2 methods.⁹

The indications for immediate ERCP in cases of cholelithiasic pancreatitis without cholangitis are questionable. The study by Schepers NJ et al.²¹ showed no difference in mortality in patients after ERCP and in patients treated conservatively. Also, in a meta-analysis of 1091 patients with acute lithiasic pancreatitis without cholangitis, an attempt was made to compare the outcome of the disease in patients undergoing ERCP and patients treated conservatively. In conclusion, ERCP was associated with a lower rate of local complications ($p < 0.05$), with less pain during patient's hospitalization, with a shorter hospital stay, but without affecting mortality.³²

Local complications of acute pancreatitis include pancreatic necrosis with or without infection, pancreatic pseudocyst formation, pancreatic duct disruption, and walled-off necrosis. These local complications can be treated using a combination of endoscopic, radiological and surgical techniques.³³ Karjula H et al.²², in their study, concluded that a prophylactically placed stent in the pancreatic duct in cases of acute necrotic pancreatitis may increase the possibility of infection. In contrast, a study by Wroński M et al.³⁴ showed that the minimally invasive method for draining necrotic necrosis should be the primary step in treatment, as laparotomy is associated with increased morbidity and mortality. Gastroscopic or transdermal drainage of infected pancreatic necrosis or pancreatic pseudocysts is a technique associated with lower morbidity than laparotomy. These procedures should ideally be performed in centers where there is immediately available expertise for the management of any complications, always guided by the optimal outcome of the disease.

In conclusion, acute pancreatitis is a potentially life-threatening condition often seen in ED. Once diagnosed, clinical efforts should simultaneously focus on investigating the underlying etiology and treat the disease, while the use of the described severity classification systems could predict its complications. The treatment of acute pancreatitis is largely supportive. It is necessary to find low-cost methodologies, easily applicable in clinical practice, that can classify patients according to severity

in a timely manner, even by attending the ED. There is also an urgent need to determine the exact time in which patients must undergo invasive treatment, which seems to improve the outcome of the disease. Finally, regarding the possibility of non-hospitalization and discharge from the ED for patients with mild acute pancreatitis, there is a lack of data and more studies need to be conducted to draw detailed conclusions.

This systematic review has limitations. Initially, the search was done only in the MEDLINE (Pubmed) database and not in other databases. In addition, the search was conducted in English only, which may exclude valid and reliable studies published in another language. Also, the fact that its etiology is not always documented by the ED is also crucial, as it may need to be treated differently depending on the underlying cause. In addition, as a general rule, the samples of the studies selected were small, which limits the dynamics of the study for drawing conclusions. Finally, many of the studies reported were conducted in non - specialized centers. This limits the accuracy of the studies to draw valid conclusions to create a common management algorithm as not all diagnostic and therapeutic methods are available in all hospitals.

CONCLUSIONS

- Acute pancreatitis is a heterogeneous pathological entity, the main pathological lesion of which is inflammation and autolysis of the pancreatic wall. The range of clinical manifestations of the disease is particularly large and, consequently, the treatment must be individualized.
- In the diagnostic approach, lipase has been shown to be more reliable than biochemical markers, although its measurement has not become widespread. From the imaging test, CT is the most valid method in the diagnosis, but its use is not recommended as a routine examination in the ED.
- Early diagnosis and assessment of the severity of the disease is critical. The latest classification systems, especially the HASP and the BISAP score, are gaining ground in this direction, predicting with great accuracy from the first 24 hours the severe forms of the disease.
- Early treatment of the disease, starting with ED, is crucial, having a major impact on survival and quality of life, with fluid

intake and adequate analgesia being the cornerstone. Cases, that at the time of diagnosis show signs of SIRS or signs of failure of 2 or more organs require hospitalization in ICU.

- Many studies support early laparoscopic cholecystectomy in cases of mild cholelithiasic pancreatitis (in the same hospitalization), but it is not widely accepted.
- Performing ERCP in cases of lithiasic pancreatitis without cholangitis has not shown a significant improvement in survival, which needs further investigation.
- The aim is therefore to search for the most effective evaluation methods for the most valid prediction of severe forms and their correct treatment to improve survival and quality of life.

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ANNEX

Figure 1. PRISMA flow chart



PRISMA 2009 Flow Diagram

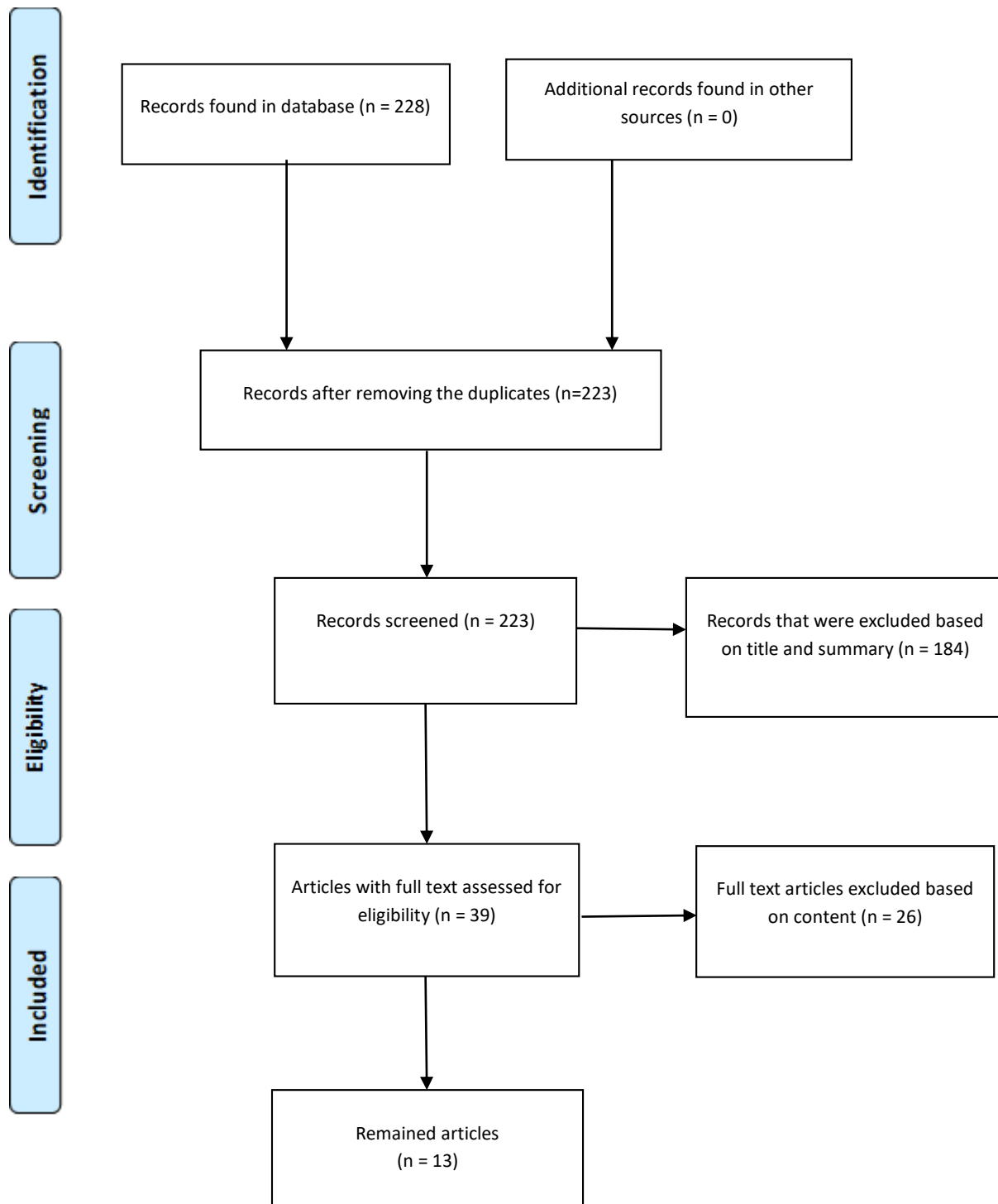


TABLE 1. Comparison of classification systems of the severity.

A/A	AUTHOR	TITLE	STUDY TYPE	SUMPLE	RESULTS
1	Gülen et al. (2016)	Pain treatment in patients with acute pancreatitis: A randomized controlled trial	Randomized	90	The analgesic effect of paracetamol is comparable to that of tramadol and dextetoprofen
2	Schepers et al. (2016)	Early biliary decompression versus conservative treatment in acute biliary pancreatitis (APEC trial): study protocol for a randomized controlled trial	Randomized	232	Emergency ERCP with sphincterotomy did not reduce the rate of serious complications or mortality, compared with conservative treatment in severe acute pancreatitis
3	Karjula et al. (2019)	Prophylactic pancreatic duct stenting in severe acute necrotizing pancreatitis: a prospective randomized study	Perspective - Randomized	25	Prophylactic placement of a stent in the pancreatic duct endoscopically in patients with acute necrotic pancreatitis is associated with high rates of infection.
4	van Brunschot et al. (2018)	Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial	Double blind randomized	98	In patients with infected necrotic pancreatitis, the endoscopic approach did not prove superior to the surgical approach in reducing complications
5	Noel et al. (2018)	Index versus delayed cholecystectomy in mild gallstone pancreatitis: results of a randomized controlled trial	Perspective - Randomized	66	Early cholecystectomy in cases of acute mild lithiasic pancreatitis is beneficial.

TABLE 2. Need for immediate therapeutic and/or invasive method.

A/A	AUTHOR	TITLE	STUDY TYPE	SAMPLE	RESULTS
1	Huang et al (2016)	The revised Atlanta criteria 2012 altered the classification, severity assessment and management of acute pancreatitis	Retrospective	3212	Atlanta Revised Criteria are superior to the Classical in demonstrating complicated cases of the disease
2	Arif et al (2019)	Accuracy of BISAP score in prediction of severe acute pancreatitis	Perspective	206	The BISAP score > 3 has comparable accuracy to the Ranson score in the identification of severe acute pancreatitis in the first 24 hours
3	Hagjer et al (2018)	Evaluation of the BISAP scoring system in prognostication of acute pancreatitis	Perspective	60	Comparable sensitivity of BISAP score > 3 in 24 hours with APACHE II score > 8 at 48 hours in diagnosis of severe acute pancreatitis.
4	Al-Qahtani HH et al (2017)	Comparison of Harmless Acute Pancreatitis Score with Ranson's Score in Predicting the Severity of Acute Pancreatitis	Perspective	116	The HAPS score can show cases of mild pancreatitis in time compared to the Ranson score
5	Kumar et al (2018)	A comparison of APACHE II, BISAP, Ranson's score and modified CTSI in predicting the severity of acute pancreatitis based on the 2012 revised Atlanta Classification	Perspective	50	The APACHE II system has exceptional sensitivity and negative prognostic value in the prediction of severe cases of the disease, with several limitations