The role of the BISAP score in predicting acute pancreatitis severity according to the revised Atlanta classification: a single tertiary care unit experience from Turkey

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Abstract

Background/Aims: **In this study, we examine the utility of Bedside Index of Severity in Acute Pancreatitis (BISAP), which is an increasingly more commonly used simple and practical novel scoring system for predicting the prognosis and severity of the disease at presentation.**

Materials and methods: **Consecutive patients diagnosed with AP between January 2013 and December 2020 were evaluated retrospectively. The AP severity was assessed using the revised Atlanta classification (RAC). BISAP score, demographic characteristics, pancreatitis etiology, pancreatitis history, duration of hospital stay, and mortality rates of the patients were recorded.**

Results: **A total of 1000 adult patients were included, of whom 589 (58.9%) were female and 411 (41.1%) were male. The mean age in female and male patients was 62.15 ± 17.79 and 58.1 ± 16.33 years, respectively (p >0.05). The most common etiological factor was biliary AP (55.8%), followed by idiopathic AP (23%). Based on RAC, 389 (38.9%), 418 (41.8%), and 193 (19.3%) patients had mild, moderate, and severe AP. Of the 1000 patients, 42 (4.2%) died. Significant predictors of mortality included advanced age (>65 y) (p=0.003), hypertension (p=0.007), and ischemic heart disease (p=0.001). A BISAP score of ≥3 had a sensitivity, specificity, positive predictive value, and negative predictive value (NPV) of 79.79%, 91.57%, 69.37%, and 94.99%, respectively, for determining SAP patients according to RAC.**

Conclusion**: BISAP is an effective scoring system with a high NPV in predicting the severity of AP in the early course of the disease in a Turkish population.** (Acta gastroenterol. belg., **2021**, 84, **571-576**).

Keywords: Acute pancreatitis, BISAP scoring, RAC, mortality.

Introduction

Globally, acute pancreatitis (AP) is the most common gastrointestinal system (GIS) related disorder that requires hospital admission (1). Despite regional differences, biliary AP (BAP) is the most common etiological factor, comprising 40% to 70% of all cases (2). Although the incidence of AP is increasing, early diagnosis and new insights into the pathophysiology of the disease have led to reduced length of hospital stay, treatment costs, and mortality in the last couple of decades (3-7). Thus, the mortality associated with AP decreased from approximately 10% in 1980s to 5%, although the mortality remains in the range of 5% to 20% in severe disease. The rate of mortality is further elevated to 30% in the presence of multiorgan failure, and to 50% when this continues beyond 48 hours (4,8).

AP is divided into 3 groups as mild, moderate, and severe according to the revised Atlanta classification (RAC), which is used to determine the severity of the disease (9). RAC takes into consideration several factors such as localized and systemic complications, presence of organ failure, and the duration of the existing organ failure. RAC is useful in standardization of patients retrospectively, but it is not effective at the time of presentation, as the necessary information is based on results. Many scoring systems have been developed to assess the prognosis and disease severity in AP, including the Ranson Criteria, Modified Glasgow Scoring, and Acute Physiological and Chronic Health Evaluation (APACHE) II-IV etc. Studies utilizing these different scoring systems consistently indicated that the morbidity and mortality are closely related to disease severity and organ failure persisting more than 48 hours. On the other hand, simpler scoring systems such as BISAP (Bedside Index of Severity in Acute Pancreatitis) are being more commonly used, due to the complexity and difficulty of use associated with other scoring systems.

In this study, our aim was to examine the value of BISAP in predicting mortality and disease severity in a group of patients admitted to our center with a diagnosis of AP, with consideration of demographic data, distribution of pancreatitis etiologies, comorbid conditions that may be associated with mortality, and RAC.

Materials and methods

Patient groups and the study design

This single-center, retrospective, and cross-sectional study was carried out with the inclusion of patients over 18 years of age presenting to emergency room with complaints of abdominal pain who were diagnosed with AP and were admitted to our unit between January 2013 and December 2020. The diagnosis of AP was based

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on the presence of two of the following three criteria: (i) abdominal pain characteristic of AP; (ii) serum amylase and/or lipase levels at least three times the upper limit of normal; and (iii) characteristic findings of AP on abdominal ultrasonography and/or computerized tomography (CT) scan. Patients with a history of chronic pancreatitis, or those who were found to have signs of chronic pancreatitis such as pancreatic calcification, dilated pancreatic canal, or atrophy in imaging studies were excluded.

Following detailed history taking, physical examination, and laboratory assessment, the BISAP scores (0 to 5) at presentation were recorded, in which presence of each parameter was scored with 1-point (BUN >25 mg/dl, presence of mental impairment, presence of Systemic Inflammatory Response Syndrome (SIRS), age >60, presence of pleural effusion) (10). SIRS was defined as the presence of at least two of the following: heart rate >90 bpm, respiratory rate >20/min, or arterial paCO2 <32 mmHg, body temperature <36°C or 38°C, leukocyte count >12000/ml or <4000/ml. AP severity was classified according to RAC, in which mild acute pancreatitis (MAP) was defined on the basis of the absence of organ failure and local/systemic complications; moderately severe acute pancreatitis (MSAP) was defined on the basis of the presence of temporary organ failure or local/systemic complications; and severe acute pancreatitis (SAP) was defined on the bases of persistent (>48 h) presence of organ failure (9). Organ failure, SIRS and death comprised the systemic complications. Organ failure was classified using the modified Marshall scoring systems, where a score of ≥2 was obtained for complications developing in three different organ systems (respiratory, cardiovascular, and renal). Age, gender, comorbid conditions, history of pancreatitis, etiology, BISAP scores, disease severity based on RAC, duration of hospital stay, and rate of mortality were recorded. The comorbid conditions as per the study protocol included hypertension (HT), diabetes mellitus (DM), ischemic heart disease (IHD), cerebrovascular disease (CVD), chronic renal failure (CRF), chronic obstructive pulmonary disease/asthma (COPD/asthma), and non-GIS malignancy.

Patients were divided into 5 groups according to the AP etiology; biliary, hyperlipidemia, alcohol, miscellaneous, and idiopathic. The diagnosis of BAP was based on the presence of sludge/stones in the gall bladder and/or dilatation of the common bile duct or presence of sludge/biliary stones without dilation in the imaging studies. Alcohol related AP (AAP) was diagnosed by the presence of a history of daily alcohol intake of ≥50 g for >5 years, or by ruling out other causes and presence of history of alcohol intake shortly before the development of AP. In patients with absence of gallbladder stones and/or significant alcohol intake, the disease was classified as hyperlipidemia related AP (HAP) if serum triglyceride levels were >1000 mg/dL or when triglycerides were >500 mg/dL together with the presence of lipemic serum. Other rare causes that were classified as miscellaneous AP included pancreas or papilla tumor, abdominal trauma, dysfunction of the sphincter of Oddi, drug use, infectious etiology, autoimmune pancreatitis. On the other hand, idiopathic AP (IAP) included those cases who met the diagnostic criteria for AP without having an etiological clue in laboratory or imaging studies. Post-ERCP AP (PEP) patients were excluded from the study in order to obtain epidemiological data for newly diagnosed AP patients.

The study protocol was approved by the Local Ethics Committee of Tepecik Education and Research Hospital (No: 2020/8-23).

Statistical analysis

Descriptive analyses were given using mean (standard deviation –SD) or median (interquartile range –IQR) values for continuous variables and numbers (percentages) for categorical variables. Chi-square test or Fisher exact test was used to analyze differences between categorical data, while Mann-Whitney U tests for independent or Wilcoxon signed test were applied to test statistical differences between continuous data, as appropriate. Mortality rate was evaluated by Kaplan-Meier method and predictive factors of mortality were evaluated by the Cox proportional hazard model.

Statistical analyses for the study were performed with SPSS 22.0 (IBM Statistical Package for Social Sciences software version 22) package program. P-value <0.05 was accepted as statistically significant.

RESULTS

Demographic data and comorbid conditions

A total of 1000 adult patients were included, of whom 589 (58.9%) were female and 411 (41.1%) were male. The mean age in female and male patients was 62.15 ± 17.79 and 58.1 ± 16.33 years, respectively. There were no comorbid conditions in 364 patients (36.4%), while 335 (33.5%), 190 (19%), and 110 (11%) patients had one, two, and three or more comorbid conditions. Table 1 summarizes the number of comorbid conditions and their distribution.

Table 1. — **Distribution of comorbid conditions**

Comorbid condition	n (%)
Hypertension	425 (42.5%)
Diabetes	266 (26.6%)
IHD	135 (13.5%)
COPD/asthma	51 (5.1%)
CVD	41 (4.1%)
CRF	36 (3.6%)
Non-GIS malignancy	21 (2.1%)

IHD=ischemic heart disease, COPD=chronic obstructive pulmonary disease, CVD=cerebrovascular disease, CRF=chronic renal failure, GIS=gastrointestinal system.

Etiology

When the etiology of AP was examined, 558 (55.8%), 230 (23%), 78 (7.8%), 45 (4.5%), and 89 (8.9%) patients were found to have BAP, IAP, HAP, AAP, and miscellaneous AP, respectively. Table 2 shows the gender distribution of the etiology. Although BAP was the most common type in both gender, it was significantly more common among females (63.6% vs. 44%, p <0.001). Among female patients, BAP was the most common type of AP in all age groups, HAP and AAP were significantly more common among males (11.6% vs. 5%, p <0.001, and 9% vs. 1.3%, p <0.001, respectively). In males, HAP was the most common etiology in those under 50 years of age, while like female patients, BAP was the most common type of AP in those over 50 years of age.

Overall, 141 patients (14.1%) had recurrent AP (RAP) episodes. Subgroup analyses showed that 58 of the BAP patients (10.3%), 27 of HAP patients (34.6%), 15 of AAP patients (33.3%), and 22 of IAP patients (11.7%) had RAP, respectively.

Table 2. — **Gender distribution of the etiology of AP**

Etiology	Male, n (%)	Female, n (%)	*p*
Biliary	183 (32.8%)	375 (67.2%)	**<0.001**
Hyperlipidemia	48 (61.5%)	30 (38.5%)	**<0.001**
Alcohol	37 (82.2%)	8 (17.8%)	**<0.001**
Miscellaneous	39 (43.8%)	50 (56.2%)	>0.05
Idiopathic	104 (45.2%)	126 (54.8%)	>0.05
Total	411	589	

Disease severity and mortality rate

Regarding RAC of our population, 389 (38.9), 418 (41.8%), and 193 (19.3%) patients had MAP, MSAP, and SAP, respectively. BISAP score at admission was 0, 1, 2, 3, 4, and 5 in 191 (19.1%), 202 (20.2%), 385 (38.5%), 80 (8%), 80 (8%), and 62 (6.2%) patients, respectively. The mean length of hospital stay was 6.16 ± 3.2 days in MAP group, 7.66 ± 4.42 days in MSAP group, 13.80 ± 12.04 days in SAP group. Forty-two of the 1000 patients (4.2%) died. Table 3 and 4 summarizes the distribution of the patients according to RAC and BISAP scores, and mortality rates according to disease severity. The mean age of the patients who died was 71.43 ± 16.23 years vs. 57.88 ± 14.01 years in the remaining subjects (p=0.001). Of the 42 patients who died, 27 (4.5%) were male and 15 (3.6%) were female. Mortality rates in BAP, HAP, AAP, IAP, and other patients were 4.4%, 2.5%, 6.6%, 4.3%, and 2.2%, respectively. There was no statistically significant difference between the groups in terms of mortality rates (p <0.05).

A univariate Cox regression analysis showed that age >65 y (p=0.003), HT (p=0.07), and IHD (p=0.001) were significantly associated with mortality, while no such significant relationships with mortality were detected for DM (p=0.336), hyperlipidemia (p=0.593), SVH (p=0.95), COPD/asthma (p=0.209), CRF (p=0.209), malignancy (p=0.101), gender (p=0.171), and mechanical/non-mechanical causes (p=0.261) (Table 5). In multivariate regression analysis, IHD was found to be associated with a 3.2-fold increase in mortality (%95 CI; 1.5-6.5; p=0.001).

Table 3. — **Number of patients and mortality according to RAC**

RAC	Patients n (%)	Mortality n (%)
Mild	389 (38.9%)	0
Moderate	418 (41.8%)	7 (1.7%)
Severe	193 (19.3%)	35 (18.1%)

RAC= Revised Atlanta Classification

Table 4. — **Number of patients and mortality according to BISAP scoring**

BISAP	Patients n (%)	Mortality n (%)
0	191 (19.1)	0
1	202 (20.2)	0
2	385 (38.5)	7 (1.4%)
3	80 (8)	8 (10%)
4	80 (8)	13 (16.2%)
5	62 (6.2)	14 (22.5%)

BISAP= Bedside Index for Severity in Acute Pancreatitis

Table 5. — **Association between comorbidities and mortality***

Variable	Hazard ratio (CI; %95)	*p*
IHD (present/absent)	4.2 (2.1-8.4)	**<0.001**
DM (present/absent)	1.3 (0.7-2.5)	0.336
HT (present/absent)	2.8 (1.3-6)	**0.007**
COPD (present/absent)	1.2 (0.3-4)	0.72
SVH (present/absent)	0.95 (0.22-4.05)	0.95
CRF (present/absent)	2.14 (0.65-7.01)	0.209
Malignancy (present/absent)	2.7 (0.8-9.3)	0.1
Gender (E/K)	1.5 (0.81-3.1)	0.171
Age >65 y	3.11 (1.4-6.5)	**0.003**
Mechanical/non-mechanical causes	1.4 (0.7-3)	0.261

**Cox regression test was used for this univariate variables assessment. IHD=ischemic heart disease, DM=diabetes mellitus, HT=hypertension, COPD=chronic obstructive pulmonary disease, CVD=cerebrovascular disease, CRF=chronic renal failure*

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of a BISAP score of ≥3 to determine SAP patients according to RAC were 79.79%, 91.57%, 69.37%, and 94.99%, respectively (kappa=0.85).

Discussion

Although AP incidence and etiology differs between countries and geographical regions, BAP and AAP frequently comprise the two most common etiological factors (in 60% to 80%) in most reports (2). While more than 60% of the patients had BAP in studies performed

a decade ago in our country, now this figure seems to have declined to 55%, with an increase in the proportion of HAP and miscellaneous AP (11-13). This seems to be due to causes such as increased sedentary life, medical drug use, hyperlipidemia, and malignancy. Consistent with published data, AAP was more common among males, and BAP was more common among females in our study (2,6). Although BAP is the most common etiology in both genders, it has been observed to be more common in female patients. BAP was the most common type of AP in all age groups among females, HAP and AAP were significantly more common among males. Among male patients under 50 years of age, HAP was the most common, while as in female patients, BAP was more common among male patients over 50 years of age. When compared with the data in the literature, it was seen that the rate of AAP in our country was lower when compared to European countries such as Iceland, Germany, Norway, Sweden, and the USA (14-18). Despite the advances in imaging and laboratory methods, IAP remains a major etiological factor in more than 20% of the patients. It should also be noted that RAP was not uncommon. The reported incidence of RAP varies between 10% and 30%, and etiologically BAP and AAP represent most of the cases (19-22). On the other hand, RAP was present in 14.1% of the overall population in our study. RAP in our BAP patients occurred at a lower frequency as compared to the published data, which may be explained on the basis of early referral of patients to cholecystectomy following the first AP episode as well as on the basis of lower frequency of AAP, which is one of the most common causes of RAP.

While some studies suggested that BAP was associated with lower mortality compared to idiopathic AP or those due to hyperlipidemia and alcohol, others found no effect of etiological factors on mortality (23-27). In the current study, although mortality was slightly higher among AAP and BAP cases, the differences did not reach statistical significance.

In the studies of Lankisch et al. and Uomo et al., no statistically significant difference was found between gender and AP severity (28,29). In contrast with these findings, Pezzilli et al. reported an increased likelihood of severe disease among male patients, although direct comparison of these results is not possible due to imbalanced distribution of female patients in study groups, absence of female patients in the alcoholic and other groups, and as well as due to the presence of only two female patients in the idiopathic group (30). In our study, in accordance with many studies in the literature, no statistical difference was observed between genders in terms of mortality.

Another parameter that has been shown to be closely associated with mortality and morbidity of AP is the age. Factors that were associated with increased mortality in Carvalho et al. study included advanced age as well as temporary or persistent organ failure, prolonged intensive care unit stay, and the need for interventional procedures (31). Koziel et al. defined 3 age subgroups in their study, i.e. those <65 years, between 65-79 years, and >80 years, and found an increased risk of mortality in those over 65 years of age, and particularly in patients >80 years of age (32). Contrary to these data, in the study of Satiş et al., no significant difference was observed between patients >65 years and <65 years of age in terms of disease severity and complications (33). Similarly, age ≥65 years was an independent predictor of mortality in our study. Another factor that was found to be closely related to morbidity and mortality was the presence of comorbid conditions. Many studies reported a link between morbidity and mortality of AP and presence of DM, IHD, malignancy, and CRF (34-40). In our study, HT and IHD were significantly linked with increased mortality, while no such associations could be observed for DM, HL, CVD, COPD/asthma, CRF, and malignancy. In the multivariate regression analysis, IHD was found to be associated with a 3.2-fold increased risk of mortality. This is supported by Kiat et al. study, where only IHD and HT were closely related to SAP (41). In our study, although the length of hospital stay was lower in the MAP group compared to the MSAP and SAP groups, it was observed to be moderately higher than the data in the literature. This suggests that the pain and clinical response in the MAP group in the foreground have similar characteristics with the MSAP group.

Determination of disease severity of AP at the time of presentation is a significant factor to consider when evaluating the need for intensive care. Previous studies established that presence of findings of organ failure at presentation is closely linked with mortality and morbidity (32-41). In this regard, BISAP scoring system is gaining popularity among clinicians as a practical and rapid assessment tool that provides quick information on organ failure. In a meta-analysis of Chandra et al. involving 12 prospective cohort studies, BISAP was found to perform well in predicting SAP across different patient populations and severity levels (42). In a large cohort study by Wu et al., BISAP's accuracy in predicting mortality was found to be close to that of APACHE II (10). Again, in a study by Cho et al. involving 299 patients, there was a statistically significant association between increasing BISAP scores and mortality. A BISAP score of 3 was found to provide an optimal sensitivity and specificity cut-off for SAP and mortality. Again, in that study, among patients with a BISAP score of ≥ 3, the risk of SAP was 76.1-fold higher and the risk of death was 121.7-fold higher (43). In the large population-based study of Wu et al. showing a close link between BISAP score at presentation and mortality, the mortality rate was <1% with a BISAP score of <2 and was %5 to 20% with a score of ≥3 (10). In addition, in the study of Zheng et al., BISAP scoring was found to have a higher accuracy rate in predicting AP disease severity than the change in amylase and body mass index scoring (44). In the light of all these data, in 2018, European Society of Gastrointestinal Endoscopy suggests using the BISAP score within the first 24 hours of presentation as

an early predictor of severity and mortality in AP with weak recommendation and moderate quality evidence (45). Similarly, we found that BISAP scoring provided an effective means for predicting mortality. Accordingly, the mortality increased from 1.8% in those with a BISAP score of 2 to 22.5% in those with a BISAP score of 5. Furthermore, the sensitivity, specificity, PPV, and NPV of a BISAP score of ≥3 in determining SAP patients according to RAC classification were 79.79%, 91.57%, 69.37%, and 94.99%, respectively.

Our study had some limitations, such as its retrospective design and inclusion of patients presenting to an emergency room only. Also, data for patients presenting to the emergency room with a possible diagnosis of SAP who required intensive care unit but referred to other centers due to lack of patient beds is missing. Additionally, lack of iatrogenic AP cases such as those with PEP is another limitation.

In conclusion, we may suggest that RAC assists in planning the proper management strategy for AP patients by providing a standard terminology. In addition to high NPV, the BISAP scoring system is an effective, fast, and practical scoring tool that can be used to determine disease severity and prognosis in Turkish AP patients. Although an increase in HAP and other types of AP has been occurring probably owing to factors such as increased lifespan, medication use, or fatty diet, we may conclude that BAP remains the most common etiology of AP in Turkey. In addition to the diagnostic role of laboratory and vital findings at presentation, further prospective studies are warranted to evaluate advanced scoring systems that also consider comorbid conditions with a potential effect on morbidity and mortality in these patients.

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