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ORIGINAL PAPER

Validation of the ASALT Score for Predicting Biliary Etiology in Acute Pancreatitis: a Single-Center Study of 441 Patients

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ABSTRACT

Background: *Early identification of biliary etiology in acute pancreatitis (AP) is essential because it directly influences therapeutic decisions and secondary prevention. However, determining biliary origin in the early phase remains challenging, especially when initial ultrasonography is inconclusive. The ASALT score, based on age, sex and alanine aminotransferase (ALT), was previously proposed as a simple bedside tool for predicting biliary etiology.*

Aim: *To evaluate the performance of the ASALT score in a larger cohort of patients with acute pancreatitis and to externally validate its diagnostic accuracy for predicting biliary etiology.*

Methods: *We performed a retrospective study including 441 patients admitted with acute pancreatitis between January 2014 and December 2024. Biliary etiology was established by serial abdominal ultrasonography, endoscopic ultrasonography, or magnetic resonance imaging. Independent predictors*

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were evaluated by multivariable logistic regression. Discriminative ability of the ASALT score was assessed by receiver operating characteristic analysis.

Results: *A total of 436 patients (56.5% males) with a median age of 60 years (range 18–95) were included. Biliary etiology was most frequently found (60.1%) and it was associated with the highest median age (65 years), followed by alcohol (22.5%). Biliary pancreatitis predominated in females (60.7%), while non-biliary etiologies showed a marked male predominance. A history of acute pancreatitis significantly differentiated biliary from non-biliary causes (χ^2=39.7, p<0.001). Multivariable binary logistic regression identified age (p < 0.001), sex (p < 0.001) and ALT (p = 0.002) as variables independently associated with biliary etiology. The ASALT score demonstrated good discrimination [area under the curve (AUC)=0.820, 95% confidence interval (CI) 0.777–0.862, p<0.0001)], with an optimal cutoff of 1, yielding 77.6% accuracy and 69% negative predictive value. Each 1-point increase in ASALT score tripled the odds of biliary etiology (p<0.001).*

Conclusions: *The ASALT score is a simple and practical tool with good diagnostic performance for early prediction of biliary etiology in acute pancreatitis, which is particularly useful when access to advanced imaging is limited.*

Keywords: acute pancreatitis, gallstone, etiology, biliary pancreatitis, risk score, biochemical prediction, ASALT score.

ABBREVIATIONS

AP=acute pancreatitis
ALT=alanine aminotransferase
EUS=endoscopic ultrasound
MRCP=magnetic resonance cholangiopancreatography
MRI=magnetic resonance imaging
NPV=negative predictive value

INTRODUCTION

Acute pancreatitis (AP) is one of the most common gastrointestinal causes of hospitalization worldwide, with an increasing incidence and a substantial burden on healthcare systems. In the United States alone, AP is responsible for approximately 270,000 hospital admissions annually, a figure that highlights its clinical and economic impact (1). Gallstones and alcohol consumption account for nearly 70–80% of the etiologies, while hypertriglyceridemia and other causes, such as drugs, metabolic disorders, neoplasia, or genetic predisposition, are less common (2).

Acute pancreatitis of biliary etiology represents a distinct clinical entity, as its incidence continues to increase in parallel with the prevalence of cholelithiasis (3), being more frequently observed in women and the elderly, thus reflecting the known epidemiological patterns of cholelithiasis (4). Given its frequency and therapeutic implications, early identification of biliary etiology is essential for optimal patient management. However, determining the etiology of AP in the early phase remains a challenge. Although abdominal ultrasound is recommended as the initial imaging modality in acute pancreatitis, its sensitivity for establishing biliary etiology is imperfect, not only because intestinal distension and superimposed gas frequently impair visualization, but also because small calculi and distal common bile duct stones may escape detection, especially in the absence of ductal dilatation (5, 6). Advanced imaging techniques, such as magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS), offer superior diagnostic accuracy, especially for the detection of common bile duct stones, but their availability is often limited, especially in emergency settings (7, 8). It is important to note that acute pancreatitis may be the first clinical manifestation of gallstones in a significant proportion of patients (9) .

Accurate identification of the etiology in acute pancreatitis is essential, as it directly guides therapeutic decisions, with a resounding impact on outcome (10). Conversely, delayed identification of the biliary origin may lead to the postponement of targeted etiological interventions, such as cholecystectomy, which plays a key role in preventing recurrence and disease-related morbidity (11, 12). In this context, both overestimation and underestimation of the biliary origin pose clinically significant risks, either through unnecessary invasive

procedures or through failure to prevent recurrence.

Several clinical and biochemical predictors have been investigated, among which elevated alanine aminotransferase (ALT) has consistently been identified as one of the most reliable markers of biliary origin, especially when values exceed three times the upper limit of normal (13, 14). More recently, advanced predictive approaches based on artificial intelligence have demonstrated promising diagnostic performance, although their complexity limits routine clinical applicability (15, 16).

Despite these advances, there is still a lack of simple, validated tools that can be easily applied at the patient's bedside. In a previous study, we proposed the ASALT score (age, sex, ALT), a clinical-biochemical model based on readily available parameters, which was designed to predict the biliary origin of acute pancreatitis (17). However, the initial study was conducted on a relatively small cohort and lacked external validation. The aim of the present study is to evaluate the performance of the ASALT score in a larger patient population and to externally validate its diagnostic accuracy, with particular emphasis on its discriminative capacity and potential utility in daily practice. ❑

MATERIALS AND METHODS

Study design and patient population

We conducted a retrospective study of patients admitted to the surgical and medical departments of the University Emergency Hospital Bucharest, Romania, with a diagnosis of acute pancreatitis (AP) between January 2014 and December 2024. Data were abstracted retrospectively from de-identified electronic medical records and partially collected prospectively as part of the APPRENTICE consortium, with the study protocol previously published (17, 18). The study was approved by the Institutional Review Board of the University Emergency Hospital Bucharest, Romania (No. 25640/28.05.2015, 12140/17.02.2025).

Diagnostic criteria

Acute pancreatitis was diagnosed according to the revised Atlanta classification, requiring at least two of the following three criteria: (18) characteristic upper abdominal pain, (19) serum amylase or lipase level greater than three times the upper limit of normal and (17) characteristic findings on abdominal imaging. Biliary etiology was confirmed by serial abdominal ultrasonography, endoscopic ultrasonography, or magnetic resonance imaging (MRI). Abdominal ultrasound was performed in the emergency department or after ward admission. Hypertriglyceridemia was defined as serum triglycerides above 1000 mg/dL, while a relevant history of alcohol consumption indicated alcoholic etiology. Exclusion criteria were: history of organ transplantation, trauma induced AP, chronic pancreatitis and pancreatic cancer.

Data collection and variables

Variables analyzed included demographics (age, sex, obesity), clinical features (fever, onset-to-admission interval, prior acute pancreatitis episodes, blood pressure) and laboratory parameters (white blood cell count, hemoglobin, hematocrit, amylase, lipase, glucose, blood urea nitrogen, creatinine, aspartate aminotransferase [AST], alanine aminotransferase [ALT], total and direct bilirubin, triglycerides).

The ASALT (Age, Sex, ALT) score (Table 1), a previously published composite predictor of biliary etiology in AP, was calculated using age, sex and ALT levels (17).

Statistical analysis

Continuous variables are expressed as medians with interquartile ranges (IQRs) or proportions, as appropriate. Normality was assessed using the Shapiro-Wilk test. Between-group comparisons were performed using the independent t-test or Mann-Whitney U test for continuous variables, depending on data distribution, and the chi-square or Fisher's exact test for categorical variables. Multivariable logistic regression was used to identify factors independently associated with biliary etiology of AP. Candidate predictors were selected

Variables	Points
Gender	
Male	0
Female	1
Age	
< 60 years	0
> 60 years	1
ALT	
< 50	0
50 – 150	1
> 150	2

TABLE 1. The ASALT score descriptive variables

based on significant bivariate associations ($P < 0.10$). The previously published clinico-biochemical score was evaluated using receiver operating characteristic (ROC) curves, with model discrimination quantified by the area under the curve (AUC) and goodness-of-fit assessed by the Hosmer-Lemeshow test. Optimal score cutoffs were determined using the Youden index. The Cochran-Armitage trend test evaluated the correlation between score categories and outcome prevalence. A two-sided P value < 0.05 was considered statistically significant. All analyses were conducted using SPSS version 22 (IBM Corp., Armonk, NY). ❑

RESULTS

The present study included 436 patients with a median age of 60 within a range of 18 to 95 years (after exclusion of five individuals), of whom 56.5% were males. Biliary etiology accounted for 60% of cases and the highest median age (65 years), while alcohol one was the second most frequently found etiology, with 22.5% of cases (Table 2).

In our cohort, isolated biliary pancreatitis was more common in females (60.7%), whereas male predominance was observed in the following etiologies: alcohol (94.9%), hypertriglyceridemia (77.8%), mixed alcohol & biliary (70.8%), alcohol & hypertriglyceridemia (75%) and idiopathic (66.7%).

A history of acute pancreatitis was statistically significant in discriminating between biliary and non-biliary etiologies (Chi-Square 39.7, $p<0.001$). Multivariable binary logistic regression identified age, sex and ALT as independent variables associated with the etiology of acute pancreatitis. In the logistic regression model, non-biliary pancreatitis was defined as the outcome event. Therefore, odds ratios (ORs) greater than 1 indicate an association with non-biliary etiology, whereas ORs below 1 show an association with biliary etiology. Accordingly, ORs <1 observed for age (OR 0.954, 95% CI 0.939–0.969, $p < 0.001$) and ALT (OR 0.998, 95% CI 0.996–0.999, $p = 0.002$) indicate an association with biliary etiology. Likewise, the association noted for male sex (OR 5.323, 95% CI 3.001–9.442, $p < 0.001$) reflects the higher likelihood of non-biliary etiology among male patients, which is consistent with the female predominance of biliary pancreatitis observed in the descriptive analysis. Aspartate aminotransferase, white blood cell count, amylase and lipase were not significantly associated with biliary etiology in the multivariable model (Table 3).

The clinical utility of ASALT score was estimated using the ROC curve analysis and the plotted graph is presented in Figure 1. An AUC (area under the curve) of 0.820 was obtained, with a standard error of the AUC estimate of 0.022. The probability level p-value was <0.0001 and the 95% confidence lower and upper limits were

Etiology		Frequency	Percentage	Median age
Biliary		262	60.1%	65
Alcohol		98	22.5%	49
Hypertriglyceridemia		18	4.1%	43
Mixed	Biliary & alcohol	24	5.5%	63
	Alcohol & hypertriglyceridemia	12	2.8%	41
Other		13	3%	52
Idiopathic		9	2.1%	45

TABLE 2. Etiology of patients included in the study and their median age

Variable	P-value	OR	95% CI
Age	<0.001	0.954	0.939-0.969
Sex (male)	<0.001	5.323	3.001-9.442
ALT	0.002	0.998	0.996-0.999
AST	0.446	1.000	1.000-1.001
White blood cell count	0.538	1.000	1.000-1.000
Amylase	0.682	1.000	0.999-1.000
Lipase	0.094	1.000	1.000-1.000

OR=odds ratio; CI=confidence interval;
ALT=alanine aminotransferase;
AST=aspartate aminotransferase

TABLE 3. Multivariable binary logistic regression analysis of variables associated with biliary acute pancreatitis

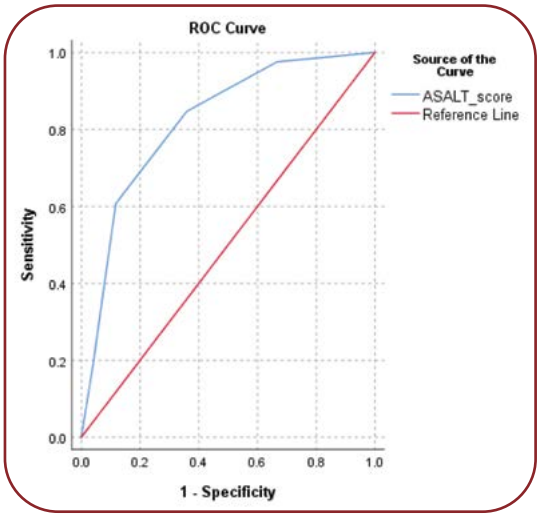

FIGURE 1. ASALT score estimation using the receiver operating characteristic (ROC) curve graph

TABLE 4. Operating points of the receiver operating characteristic (ROC) curve

Cutoff	Sensitivity	Specificity	Youden index
0.5	0.976	0.667	0.643
1.5	0.847	0.359	0.206
2.5	0.608	0.118	-0.274
3.5	0.184	0.039	-0.777

0.777 and 0.862, with an overall model quality of 0.78.

Evaluating the best cutoff value of the ASALT score using the Youden index identified a threshold of 1 as optimal (Table 4). Because the ASALT score is based on integer values, ROC cutoff points are displayed as intermediate values (0.5, 1.5, 2.5), clinically corresponding to ASALT scores ≥1, ≥2 and ≥3. Testing our confusion matrix with a cutoff value of 1 produced an accuracy of 77.6% with a negative predictive value (NPV) of 69%, increasing the threshold by 1 point reduced the accuracy to 70.5% and NPV to 54.7%, and increasing the threshold to a value of 3 further reduced accuracy to 45% and NPV to 38.5%.

Binary logistic regression on the ASALT score ability to predict the biliary etiology of AP revealed a significant model (Chi-square 147, Omnibus test with $p<0.001$), inadequate calibration (Hosmer – Lemeshow $p = 0.035$), good explanatory power (Nagelkerke $R2 = 0.391$), 77.8% accuracy. We identified that each one point in the ASALT score increases the odds of acute pancreatitis with biliary etiology by 3, corresponding to predicted probabilities rising from 17% at ASALT 0, 40% at ASALT 1, 68% at ASALT 2, 87% at ASALT 3 and 96% ASALT 4 ($p<0.001$). ❑

DISCUSSIONS

Early identification of biliary etiology in acute pancreatitis remains a clinically relevant challenge, especially when initial imaging findings are inconclusive. In this context, simple and reliable tools that can support early etiological stratification are of considerable interest. Accordingly, the present study aimed to evaluate the performance of the ASALT score in a larger and more heterogeneous cohort. In our study, the ASALT score demonstrated a good discriminative ability (AUC 0.820), supporting its reliability as a clinical prediction tool. Our findings demonstrate that the score maintains good discriminative capacity, supporting the reproducibility of the association between age, sex and ALT as markers of biliary etiology in AP.

These findings are consistent with previous studies, including the original ASALT study, which identified age, female sex and ALT as independent predictors of biliary etiology (17, 20). Thus, while female sex and older age reflect the underlying epidemiology of cholelithiasis, elevated ALT is most likely a biochemical consequence of transient biliary obstruction (21). Individual clinical and biochemical parameters often lack sufficient discriminatory power when considered in isolation, particularly in the early phase of AP (22-24). In our cohort, individual variables showed limited discriminatory power when analyzed independently, while their integration into the ASALT score significantly improved predictive performance. The identification of an optimal cutoff value of 1 point through the Youden index has direct clinical implications. At this threshold (score ≥1), the ASALT score provides a high sensitivity (97.6%), allowing the identification of most patients with biliary etiology. However, the NPV of 69% indicates that a score below 1 does not reliably exclude a biliary etiology, emphasizing the need to correlate the result with the available clinical and imaging data in this subgroup. The estimated probabilities further reflect the clinical utility of the score. Thus, a patient with a score of 0 has only a 17% probability of biliary etiology, a context in which advanced imaging investigations could potentially be postponed without major

risk. In contrast, a patient with a score of 3 or 4 has an 87–96% probability of biliary etiology.

At the same time, our findings should be interpreted in the context of emerging predictive approaches. In recent years, machine learning models have shown promising performance in predicting biliary etiology and choledocholithiasis, but with important limitations, such as heterogeneity in model design, limited external validation and challenges in clinical implementation (25). In contrast, the ASALT score offers a transparent and immediately applicable alternative that can be easily used at the patient's bedside without requiring additional resources.

Beyond its diagnostic role, early identification of biliary etiology has important implications for secondary prevention. Timely cholecystectomy significantly reduces the risk of recurrent biliary events, including recurrent pancreatitis (26, 27). In this context, early etiological stratification may contribute to more appropriate patient selection and facilitate timely targeted treatment.

Several limitations should be considered when interpreting these results. First, the present study was conducted in a single center, which may limit the generalizability of the results. Also, the reference standard for biliary etiology was not uniform across patients, as not all cases underwent systematic evaluation with advanced imaging modalities such as endoscopic ultrasound, which may represent a potential source of diagnostic uncertainty, especially in patients with small stones or biliary sludge. One aspect that warrants an in-depth discussion is the inadequate calibration of the model, as highlighted by Hosmer–Lemeshow test ($p = 0.035$). Calibration evaluates the agreement between the probabilities estimated by the model and the observed frequencies of the event across different subgroups of the sample. Inadequate calibration indicates that, although the model discriminates well between patients with and without biliary etiology (AUC = 0.820), the estimated absolute probabilities may be inaccurate in certain specific subgroups. This limitation is commonly encountered in external validation studies, as the characteristics of the validation population inevitably differ from those of the original study population. In the case of the ASALT score, the inadequate calibration may reflect differences in the distribution of ALT values or in the prevalence of biliary etiology between the original study cohort and the validation cohort. From a clinical perspective, the practical implication is that the absolute probabilities provided by the model should be interpreted with caution and that the score is more appropriately used as a risk stratification and clinical decision-support tool rather than as a provider of exact probabilities for each individual patient.

Despite these limitations, the main objective of the study, to provide a simple and easy to apply tool for early prediction of biliary etiology in AP, remains valid. The performance of the ASALT score in a larger cohort supports its reproducibility and highlights its potential to help in early identification of biliary etiology in clinical practice. Future research should focus on prospective validation in diverse populations. It is important to note that any further refinement of the ASALT score should preserve its simplicity and ease of use, which are its main strengths. ❑

CONCLUSION

The ASALT score represents a simple and clinically applicable approach to early identification of biliary etiology in acute pancreatitis, with potential utility in routine practice, particularly where access to advanced imaging is limited. Prospective multicenter studies are needed to further validate its clinical applicability. ❑

Ethical statement: The present study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee (No. 25640/28.05.2015, 12140/17.02.2025). All patients provided an informed consent for data collection and research participation.

Conflicts of interest: none declared.

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