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PERSPECTIVE

Ranson score to stratify severity in Acute Pancreatitis remains valid – Old is gold

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ABSTRACT

Introduction: Acute pancreatitis (AP) is a common gastrointestinal disease with a wide spectrum of severity and morbidity. Developed in 1974, the Ranson score was the first scoring system to prognosticate AP. Over the past decades, while the Ranson score remains widely used, it was identified to have certain limitations, such as having low predictive power. It has also been criticized for its 48-hour requirement for computation of the final score, which has been argued to potentially delay management. With advancements in our understanding of AP, is the Ranson score still relevant as an effective prognostication system for AP?

Areas covered: This review summarizes the available evidence comparing Ranson score with other conventional and novel scoring systems, in terms of prognostic accuracy, benefits, limitations and clinical applicability. It also evaluates the effectiveness of Ranson score with regard to the Revised Atlanta Classification.

Expert opinion: The Ranson score consistently exhibits comparable prognostic accuracy to other newer scoring systems, and the 48-hour timeframe for computing the full Ranson score is an inherent strength, not a weakness. These aspects, coupled with relative ease of use, practicality and universality of the score, advocate for the continued relevance of the Ranson score in modern clinical practice.

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Acute pancreatitis; mortality; predictor; Ranson score; scoring system; severity

1. Introduction

Acute pancreatitis (AP) is a common cause of hospital admission and has a mortality risk of up to 60 deaths per 100,000 patients [1]. Delay in seeking medical attention, delay in diagnosis, inadequate resuscitation, lack of access to critical care facilities, unpredictable clinical course, and absence of direct pharmacological intervention are factors which contribute to the risk of morbidity and mortality. While most patients have mild and self-limiting illnesses, about 10–20% of patients manifest severe illness, and this group of patients contributes to the burden of mortality [2–4]. Clinicians must remain vigilant in identifying patients at risk of developing severe AP (SAP) to ensure timely and appropriate interventions are delivered to improve outcomes. This understanding is not new. Almost five decades ago, JH Ranson first introduced the concept of a 'score,' which enabled clinicians to stratify the severity of AP and predict the risk of mortality associated with the condition [5–7]. The scoring system, widely popularized as the Ranson score, formed the basis upon which subsequent refinements were made to improve predictive ability. Over the past five decades, the diagnosis of AP has become homonymous with scoring systems. The Glasgow score, Acute Physiology and Chronic Health Evaluation II (APACHE II), Bedside Index of Severity in Acute Pancreatitis (BISAP), Systemic Inflammatory Response Syndrome (SIRS) and numerous other scoring systems were proposed over the years and continue to be validated until today [3]. AP and its associated scoring systems are widely incorporated in medical training curricula, care pathways, and management protocols globally. While the Ranson score is still widely used internationally for the evaluation of AP, there have been criticisms regarding its low predictive power [8] and its 48-hour requirement to compute the final score with a potential for delaying management and having a detrimental impact on clinical outcomes [9]. The third limitation is that it was developed for use in adults aged 30–75 years old and is not widely validated in pediatric and adolescent populations. Though the Ranson score has these limitations, it is also widely acknowledged that the mere existence of many scoring systems is a testament that there is no one perfect system, and the pursuit of an ideal system continues even at the time of this writing [10,11]. Is the Ranson score outdated and irrelevant in modern medicine, or is it still valid for clinical utility in the 21st century? This paper aims to critically appraise current evidence related to the Ranson score in comparison with other scoring systems, so that clinicians remain guided to make bedside decisions.

2. Overview of the Ranson score

The basis of a scoring system lies in its ability to predict a future event or outcome, such as disease severity, morbidity, and mortality. The variables and parameters included in the scoring system confer this ability. For a scoring system to be clinically relevant for bedside use, it should include simple variables which are recorded as part of routine clinical care

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Article highlights

- Comprehensive literature review of both conventional and novel scoring systems for predicting adverse outcomes in acute pancreatitis (AP), in comparison with the Ranson score
- Evaluation of the clinical relevance of the Ranson score with regard to the Revised Atlanta Classification 2012, the current international standard for the classification of severity in AP
- Addressing key criticisms of the Ranson score with current available evidence of its effectiveness
- Discussion of results from all available systematic reviews comparing the Ranson score with other scoring systems, to critically evaluate the prognostic accuracy of the Ranson score
- Exploring recent advancements in prognosticating AP, including novel biomarkers and technological tools, which pave the way for future improvements in the management of AP

and should be easy to compute. The ease of obtaining the variables and computing the score also influences the timeliness of care delivered to patients, and this is especially significant in the context of resource allocation and prioritization of care [12].

The Ranson score was initially developed from 43 clinical and laboratory parameters in 100 AP patients within 48 hours of admission [5–7]. The final score (comprising 11 clinical and laboratory parameters) (Table 1) includes five parameters obtained at admission (age, white cell count, blood glucose, aspartate transaminase (AST), and lactate dehydrogenase (LDH)) and six parameters captured at 48 hours after admission (reduction in hematocrit, increase in blood urea nitrogen (BUN), serum calcium, arterial PO_2, base deficit, and fluid sequestration) with different cutoffs depending on the cause of AP – biliary AP or non-biliary AP [5,13].

The score calculated on admission allows for triaging patients for admission into critical care units. It also guides initial management, resuscitation efforts, and patient counseling. The variables calculated at the 48-hour timepoint, on the other hand, provide a cumulative assessment of predicted severity and mortality to guide subsequent management of the patient.

Some of these parameters were studied later on and their associations with SAP and mortality were better defined, further supporting their clinical value when tabulated as part of the Ranson score. Elevations in BUN at 48 hours post-admission was found to have a 90% predictive accuracy for mortality in AP [14]. Increased fluid sequestration within 48 hours of admission was significantly associated with persistent organ failure which is characteristic of SAP [15–17].

In recent years, the recommendation for fluid replacement therapy in AP has shifted from aggressive resuscitation to goal-directed fluid therapy [18,19]. This change may improve the predictive value of the fluid sequestration parameter in the Ranson score, because there will potentially be less patients who develop fluid sequestration due to excessive fluid replacement mistakenly identified as patients who develop fluid sequestration due to the inflammatory process of SAP. Future studies should evaluate how these changes in management guidelines can influence the prognostic accuracy of scoring systems such as the Ranson score.

Patients who develop local and systemic complications of AP often have higher levels of fluid sequestration and require more fluid replacement to maintain intravascular volume [15,20,21]. Changes in hematocrit and BUN are used routinely to assess responsiveness to fluid replacement in AP [18,19,22,23]. Although the Ranson score was originally created to prognosticate AP, these findings suggest that it may also be useful in guiding management because it assesses parameters which are used to guide fluid therapy. It must be noted that the parameter fluid sequestration is unique to the Ranson score; thus, other scoring systems may not have such an advantage.

Table 1. Ranson score for prognostication of severe Acute Pancreatitis.

Non-Biliary Etiology of AP	Biliary Etiology of AP
At admission	**At admission**
Age > 55 years	Age > 70 years
White cell count >16 000/mm^3	White cell count > 18 000/mm^3
Blood glucose > 200 mg/dl	Blood glucose > 220 mg/dl
Serum LDH > 350 U/l	Serum LDH > 250 U/l
Serum AST > 250 U/l	Serum AST > 250 U/l
At 48 hours after admission	**At 48 hours after admission**
Reduction in hematocrit > 10%	Reduction in hematocrit > 10%
Increase in BUN > 5 mg/dl	Increase in BUN > 2 mg/dl
Serum calcium < 8 mg/dl	Serum calcium < 8 mg/dl
Arterial PO_2 < 60 mm Hg	Arterial PO_2 < 60 mm Hg
Base deficit > 4 mmol/l	Base deficit > 5 mmol/l
Estimated fluid sequestration > 6 L	Estimated fluid sequestration > 4 L

AP: Acute Pancreatitis, LDH: Lactate dehydrogenase, AST: Aspartate transaminase, BUN: Blood urea nitrogen

Each parameter contributes one point. 3 or more points indicate severe AP.

3. The Ranson score in comparison with other scoring systems

Many scoring systems are available to guide the management of AP, ranging from radiologic systems, single parameter scores, and multiple parameter scoring systems [24–26]. This section will summarize the strengths and limitations of commonly used scoring systems in comparison with the Ranson score.

3.1. Radiologic scoring systems

The most widely known radiologic scoring system for AP is the Computed Tomography Severity Index (CTSI). It was developed by Balthazar to stratify the severity of AP based on findings of pancreatic inflammation and necrosis in contrast-enhanced CT scans [27] and was an improvement of the Balthazar score [28]. While the CTSI has acceptable sensitivity and specificity in predicting SAP, it did not significantly correlate with organ failure and extra-pancreatic complications which define SAP [27,29]. In view of these disadvantages, the modified CTSI (mCTSI) was developed to better evaluate pancreatic necrosis and extra-pancreatic complications [30], and it had a higher sensitivity but lower specificity than CTSI in stratifying severity [31]. Later in 2004, the Magnetic Resonance Severity Index (MRSI) was derived from CTSI [32]. However, like CTSI, it also has a limited role in determining systemic complications and predicts mortality less accurately than APACHE II [33].

The Extra-Pancreatic Inflammation on CT (EPIC) score was later introduced in 2007 and it assessed the presence of fluid

collections on unenhanced CT scans [34]. The initial study showed that the EPIC score can give an accurate estimation of severity and mortality within 24 hours of admission; however, it cannot differentiate transient and persistent organ failure, which is key in the definition of SAP [35]. Zhou et al. later adapted this score for use in MRI scans, naming it the Extra-Pancreatic Inflammation on MRI (EPIM) score, and found that not only was it comparable to APACHE II and BISAP in predicting SAP and organ failure, it was also better than MRSI [36].

Other imaging-based morphological indicators for prognosticating AP have been proposed in recent years. The Visceral Adipose Tissue (VAT) and ratio of VAT to skeletal muscle tissue (VAT/SMT) was found to predict SAP more accurately than the Ranson score, APACHE II, BISAP and SIRS [37]. Increased pancreatic stiffness predicted SAP as accurately as CTSI, APACHE II and BISAP [38]. More data is needed before meaningful conclusions can be derived.

Despite these advancements in radiologic scoring systems for AP, several limitations persist for imaging-based scoring systems. Firstly, the presence of interobserver variability can affect the accuracy of score calculation [39]. Secondly, it is difficult to incorporate them into routine clinical protocols due to practical concerns of cost and logistical limitations in resource-limited healthcare facilities [40]. Thirdly, due to the dynamic nature of AP – a CT or MRI scan showing interstitial edematous pancreatitis on admission may evolve with time to develop necrotizing pancreatitis and extra-pancreatic complications, repeated imaging may often be required to detect these changes [27,41–43]. Lastly, as imaging is not mandatory to diagnose AP, many patients would not have imaging scans done in the acute stages of illness, hence making it difficult for risk stratification to be conducted solely based on imaging findings [44].

Therefore, in most practical clinical settings, scoring systems that make use of primarily laboratory and clinical data such as the Ranson score are often preferred for risk stratification in the early phases of AP. In our opinion, the primary utility of advanced imaging is to exclude differential diagnoses for acute pancreatitis, such as perforated peptic ulcer and mesenteric ischemia, and cannot be reasonably expected to be conducted for every patient for prognostic reasons. Advanced imaging can be useful in monitoring evolving morphological changes and guiding any subsequently necessary interventional radiology procedures. However, due to their inherent limitations, these radiologic systems should remain adjuncts instead of primary modes of risk stratification.

3.2. Single parameter scores

C-reactive protein (CRP) is an acute-phase reactant synthesized in liver in response to inflammatory stimulus. CRP is widely recognized as an accurate biomarker for predicting SAP [45,46] amongst other acute-phase proteins which lack significant clinical value in stratifying the severity of AP [47]. However, a key challenge in using CRP is the lack of a consensus regarding the optimal cutoff value and timing of measurement – the sensitivity and specificity of CRP reportedly ranges from 38% to 100% and 89% to 90%, depending on the cutoff value used and the time it was measured, ranging from admission, 24, 48 and 72 hours [48,49]. Furthermore, CRP often requires 72–96 hours to reach its peak after onset of symptoms [50], and thus it has limited clinical value in the early phases of AP, as compared to the Ranson score which is fully computed by 48 hours.

It has recently been reported that serum procalcitonin, another acute-phase reactant, was better than CRP and other scoring systems such as Ranson score and APACHE II in predicting severity in AP [51,52]. An increased serum procalcitonin level was found to be an early predictor of severity, organ failure and pancreatic necrosis [53–55]. The changes in serum procalcitonin with time was found to be more useful in predicting mortality than the changes in APACHE II score [56]. However, serum procalcitonin lacks the ability to discriminate moderately severe AP from SAP and is inferior to Ranson score for predicting mortality [57].

Interleukin-6 (IL-6) is the principal cytokine which induces the production of CRP and other acute-phase proteins. IL-6 levels peak 24–36 hours earlier than CRP and remain elevated for a longer duration [50]. IL-6 is reported to have a higher sensitivity and specificity than CRP, Ranson score and APACHE II in predicting SAP [58,59]. However, IL-6 serum concentrations decrease drastically after peaking, and the high cost and complexity of the assay make it less feasible for routine clinical practice [60]. Additionally, there are also various cutoff values proposed for IL-6 [58,59,61].

Obesity is an independent risk factor associated with the risk of mortality and local and systemic complications in AP [62,63]. However, there is a lack of consensus in the method of measuring obesity – some studies measured Body Mass Index (BMI), while others measured waist circumference; and various cutoff values for BMI were proposed [62–65]. Furthermore, the BMI cutoff for obesity varies across populations such as Asian-Pacific and Western populations [66]. When BMI is combined with the APACHE II, the combined APACHE-Obesity (APACHE-O) score has a slightly better prognostic accuracy than the APACHE II alone [67,68]. There is still a lack of scientific evidence comparing obesity with the Ranson score and other scoring systems.

Despite their relatively high prognostic accuracy levels, there are some disadvantages to using single parameter scores. Most of these biomarkers are products of inflammation, and hence they are not specific for AP and can be affected by concomitant infection and autoimmune disease. For example, CRP and IL-6 are affected by existing hepatic dysfunction [69] and hematological malignancy [70] respectively. Thus, while it is convenient to risk stratify AP with a single prognostic marker, there may be issues of reliability and the need to individualize specific cutoff thresholds for groups of patients with specific co-morbidities. This is also the reason why multiple parameter scoring systems such as the Ranson score are more widely used, because the consideration of multiple parameters provides a more holistic consideration of the patient which increases their reliability of prediction. Another disadvantage is the lack of homogeneity in the cutoff thresholds for these single parameter scores where different cutoffs proposed by various groups make it difficult for a standard threshold to be recommended for routine practice.

Several novel biomarkers have been explored in recent years to predict severity and mortality in AP. Serum bilirubin and albumin were found to exhibit good discriminative abilities in predicting SAP and mortality [71]. CRP/Albumin ratio, Albumin-Bilirubin score (ALBI) and Plasma D-Dimer level was found to predict mortality and SAP with accuracy rates comparable to other scoring systems such as Ranson score, APACHE II, CRP and Glasgow score [11,72,73]. These initial studies are promising, and more large-scale prospective studies should be done to further evaluate the predictive accuracy of these biomarkers in comparison to conventional predictors.

3.3. Multiple parameter scoring systems

Perceived limitations of the Ranson score and the ongoing quest to improve the predictive accuracy for adverse outcomes in AP fueled efforts to develop other multiple parameter scoring systems. These efforts led to the growth of many scoring systems over the past few decades.

The Glasgow score was developed in 1978 based on cases of AP secondary to alcohol and gallstone disease [74]. It was modified in two later studies to improve its prognostic accuracy [75,76]. However, the Glasgow score is considered one of the less widely used multiple parameter scoring system as it has several drawbacks. Firstly, it has been shown in multiple studies to have limited prognostic accuracy. Both the original score and modified score by Blamey et al. exhibit moderate prognostic accuracy (below 70%) and positive predictive values (less than 70%) [25,77–80]. In studies comparing the Glasgow score with Ranson score, the Ranson score has higher prognostic accuracy (80–90%) for predicting mortality and higher specificity for predicting SAP [81,82]. Secondly, as all the variables in the Glasgow score are calculated at 48 hours of admission, it does not afford the same level of timeliness as compared to the Ranson score which has variables calculated at admission and other scoring systems such as APACHE II which can be calculated at any timepoint.

The APACHE was first described by Knaus et al. to consist of 35 parameters and was created to stratify the severity of any disease in critically ill patients in the ICU [83]. The sheer number of parameters made it impractical for clinical application and it later had to be simplified into the APACHE II [84], which consists of 15 parameters calculated within 24 hours of admission. While this diversity of variables increased the sensitivity and specificity of the APACHE II [59,85], it made it cumbersome to use. In 1991, the APACHE II was further refined by its original authors again and the APACHE III was formed, consisting a system of 20 parameters computed on a point scale [86]. Although APACHE III was found to be equivalent to the Ranson score in predicting mortality and organ dysfunction [87], the APACHE II remains the most used version as it involves the least variables while preserving a reasonably high prognostic accuracy. The APACHE II was found in several studies to be comparable to the Ranson score in predicting severity and mortality in AP [82,88,89].

Many clinicians often claim that the APACHE II is better than the Ranson score as it can be used at any timepoint in the patient's course of disease; however, there are limitations of APACHE II. Firstly, multiple systematic reviews have reported low specificity of the APACHE II as compared to the Ranson score in predicting SAP [81,90]. Even if the APACHE II can be repeated at later points, it still has lower specificity than the Ranson score (0.62 versus 0.93) at 48 hours of admission [81]. By 48 hours of admission, most clinicians would have to make concrete decisions regarding a patient's disposition. The higher specificity of the Ranson score fully computed at 48 hours would be more useful than the APACHE II to help clinicians safely exclude SAP and decide which patients can be discharged or transferred to facilities with lower intensity of care. Secondly, the variables in the Ranson score can be calculated easily; thus, it is less labor intensive while achieving a similarly high level of prognostic accuracy. Thirdly, the APACHE II consists of dynamically changing variables (vitals, mental status) and one of its variables 'presence of acute renal failure' was not defined in the original study – these can cause variations in the data collected at different time points, resulting in systematic bias and inter-observer variability [91–94]. Polderman et al. found that 51% of APACHE II scores were over-estimated and a significant number of patients were under-scored as missing values were mistakenly interpreted as normal [94]. In comparison, the Ranson score minimizes these problems by using clear cutoff values for its variables. A recent study also found that the APACHE II predicted mortality, organ failure and local pancreatic complications less accurately than radiologic scoring systems CTSI and mCTSI [95]. In contrast, the Ranson score is more accurate than CTSI in predicting SAP and mortality [88]. For these reasons, the use of the Ranson score is arguably more beneficial.

The Simplified Acute Physiology Score (SAPS) was modeled after the original APACHE [96] and uses 14 variables within 24 hours of admission (later modified as the SAPS II, which uses 17 variables) [97]. The original study found SAPS to have comparable prognostic accuracy as APACHE, but it remained less popular than the APACHE II as it contained more variables and was thus more difficult to use. Furthermore, the SAPS has a much lower specificity as compared to the Ranson score and APACHE II for predicting mortality [82]. Additionally, the SAPS is measured at a 24-hour timepoint which is often too early to account for the dynamic evolving nature of AP and this can affect its reliability for prognostication.

The BISAP requires five parameters at the time of admission, including parameters such as impaired mental status, presence of SIRS, and the presence of pleural effusion [98]. Compared with the Ranson score, the small number of variables required in BISAP can improve the ease of score computation; however, a combination of clinical parameters, laboratory data and need for imaging can impose logistical burden. The assessment of mental status is also often subjective and may require comparison with the patient's baseline mental status, which may not always be known. Furthermore, pleural effusion is a complication that may develop with time in SAP and may not be present at admission; hence, there is

a risk of under-scoring patients during the initial assessment. Studies have reported that BISAP does not predict mortality as well as the Ranson score [90] and for predicting SAP, it has a lower sensitivity than Ranson score within 48 hours of admission and lower specificity than Ranson score at/after 48 hours of admission [81].

It is well-established that the SIRS is associated with the development of multi-organ dysfunction and mortality in AP [99,100]. The presence of SIRS within 24 hours of admission predicts organ failure, pancreatic necrosis, ICU admission and mortality [101]. Like the APACHE II, SIRS can be reevaluated at any time point. However, SIRS does not always precede organ failure and a patient can meet the criteria for organ dysfunction without having SIRS [101]. With persistent organ failure being an important distinguishing trait between moderately severe AP and SAP, the clinical usefulness of SIRS is limited. In comparison to the Ranson score, SIRS consistently exhibits lower specificity in predicting SAP and mortality both within and at 48 hours [81,82].

The Japanese Severity Score (JSS) [102] was initially proposed to have comparable accuracy as Ranson score and APACHE II [103–105]. Despite so, it has not been adequately validated in populations outside of Japan. JSS has substantial similarities with the Ranson score, sharing six common criteria with the Ranson score. It has four additional criteria (platelet count, SIRS criteria, CRP levels and CT scan imaging features) which are not included in Ranson score and can potentially provide a more holistic assessment of the patient. However, evidence regarding the prognostic accuracy of JSS is heterogenous – JSS was found to have a much lower sensitivity than the Ranson score within 48 hours of admission [81], while another study described JSS as the most accurate score amongst the Ranson score, BISAP and Glasgow score within 24 hours of admission [106]. More data is needed to prove the generalizability of JSS for clinical use on an international scale.

The Harmless Acute Pancreatitis Score (HAPS) is a score applied within 30 minutes of admission to identify cases of mild AP and comprises three parameters (lack of rebound tenderness or guarding, normal hematocrit, normal serum creatinine) [107]. The HAPS exhibited a high predictive accuracy for mild AP [108,109]. Despite its usefulness in rapidly guiding decisions for discharging mild AP cases at the Emergency Department, the HAPS may miss out cases of seemingly mild AP that eventually progress to more severe states of the disease and thus, physicians may inadvertently discharge these patients too early. With increasing ease of access to medical facilities and greater health awareness among populations, it is expected that more patients would present much earlier on in their course of AP [110], and the risk of missing out potentially severe cases is likely to increase. In terms of its prognostic ability to predict SAP, HAPS also has a much lower specificity (0.56) compared to that of the Ranson score (0.82), which suggests that it may not be able to adequately exclude moderately severe and severe cases of AP [81].

4. The Ranson score and the Revised Atlanta Classification

The Atlanta Symposium in 1992 attempted to create a universally applicable classification system for AP [111]. The classification system was useful but was later found to be used inconsistently across institutions due to variations in interpreting the definitions of local complications [112]. Over the years, it became established that the disease course of AP is dynamic, and that the severity of AP primarily depends on the presence, duration, and severity of organ failure due to systemic inflammatory responses [100,113]. This formed the basis of the Revised Atlanta Classification in 2012 [44]. In the 2012 Revised Atlanta Classification, AP is classified into three grades of severity: Mild AP, Moderately severe AP, and Severe AP distinguished by the presence and duration of organ failure and development of local or systemic complications. The presence of organ failure is determined by the modified Marshall scoring system for organ dysfunction [99,100,114] and is described as 'transient organ failure' if the organ failure resolves within 48 hours, and as 'persistent organ failure' if organ failure persists beyond 48 hours. Moderately severe AP is defined as having transient organ failure or local or systemic complications, while Severe AP is defined as having persistent organ failure. This classification system has since formed the standard for defining the different forms of AP based on severity.

Yet, one should be cognizant that the Revised Atlanta Classification is a set of definitions to retrospectively diagnose the severity spectrum of AP. It is not a predictor for mortality or severity of AP, and hence scoring systems are still essential for their prognostic abilities to guide clinical decisions. For a predictive tool to be effective, it should be able to predict the outcome before the diagnosis of the outcome can be made. Organ failure, the marker of severity in AP, often develops early in the course of the disease. About 30–45% of the patients who will eventually develop organ failure (either transient or persistent) will develop features of organ failure within 24 hours after admission [115–117]. The other half of patients will eventually develop features of organ failure after 24 hours of admission, and about 15% of patients have late onset organ failure which only manifests after 5–7 days of admission [116]. Since the diagnosis of mild, moderately severe or severe AP by the Revised Atlanta Classification would require first establishing the onset of organ failure and subsequently determining the duration of organ failure, a definitive diagnosis of the type of AP can only be made from at least 48–72 hours onwards after admission. Additionally, with changes in healthcare access and healthcare literacy, patients with AP are presenting earlier to hospitals [110]; thus, patients who eventually develop moderately severe or SAP may potentially require a longer time post-admission before they begin to display features of organ failure. For these reasons, any scoring system that can predict the outcomes of AP by 48 hours of admission would still be able to fulfil its role as a predictive tool, and hence scoring systems for AP such as the Ranson score, APACHE II and BISAP could still be useful in clinical practice.

Over the past few decades, some clinicians have criticized the Ranson score for requiring 48 hours for computation of the final score, quoting it as a weakness as it may affect the timeliness of initial management. However, when studied from a different perspective, this 48-hour component can be a highly valuable aspect of the Ranson score, especially for

patients where the severity grade of AP is not evident after 48 hours of admission.

The 48-hour variables in the Ranson score allows for delayed reassessment of the patient and this allows it to reflect the dynamic changes in the patient's condition, to predict the persistence and severity of multi-organ dysfunction more reliably. This is consistent with our growing understanding of the dynamic nature of AP [100,113] and the changes in the Atlanta Classification to reflect this understanding [44]. Multiple studies have reported that the 48-hour variables in Ranson score improved the score's overall prognostic accuracy and reliability. Huber et al. quoted an increase in the prognostic accuracy of the Ranson score for predicting mortality from 0.867 when used at admission to 0.971 when used 48 hours after admission [118]. The authors also reported that the Ranson score was the best predictor of mortality amongst other scoring systems such as APACHE II and BISAP at 48 hrs post-admission. In another study, the Ranson score variables calculated at 48 hours after admission proved to be superior to the variables evaluated at the time of admission in predicting the eventual severity of the condition, and the cumulative Ranson score at 48 hours after admission had better prognostic accuracy than APACHE III at 24 hours after admission in predicting mortality, prolonged ICU stays, need for operative debridement and multi-organ dysfunction [87]. Venkatesh et al. reported an increase in prognostic accuracy of the Ranson score from 57.3% at admission to 73.8% at 48 hours post-admission for predicting SAP [52]. These findings further support the use of the Ranson score for the high prognostic accuracy afforded by its 48-hour component.

While it is essential to risk stratify AP cases as early as possible, it must be noted that the clinical course of AP is dynamic and evolving, which can increase the difficulty of prognosticating cases in the initial period of presentation. Risk stratification systems with a temporal aspect, such as the Ranson score, still have a place in ensuring that physicians do not miss clinically evolving cases of SAP and do not overtreat cases of mild or moderately severe AP that may initially present with transient features of severity.

5. Prognostic accuracy of the Ranson score

In the original study, the Ranson score had a sensitivity of 65% and a specificity of 99% in predicting complications and mortality [6]. One of the main criticisms of the Ranson score was its insufficient predictive power, which was argued to offer little added value to clinical judgment [8]. The last two decades have witnessed improvements in critical care and refinements in diagnostic and interventional radiology services, impacting the quality of care and outcomes of SAP. Furthermore, an improved understanding of AP's natural history and the standardization of terminology has resulted in reduced heterogeneity of the available evidence. Thus, it is essential to review the prognostic abilities of the Ranson score and assess if it remains relevant in modern clinical practice.

A literature search was undertaken to identify systematic reviews that compared the Ranson score's effectiveness and other scoring systems in prognosticating AP. The search was conducted on 30 September 2020 on PubMed (Medline), Embase, Scopus, and Cochrane Library databases, using keywords: pancreatitis, pancreat*, prognos*, predict*, mortality, severity, outcome, scor*, criteria, Ranson; with appropriate Boolean operators. In total, five systematic reviews fulfilled the above criteria. Three systematic reviews compared Ranson score and other scoring systems for stratifying the severity of AP, and four systematic reviews compared Ranson score and other scoring systems for the prediction of mortality in AP (Table 2). The studies evaluated the accuracy of each scoring system in stratifying severity and predicting mortality of AP via Receiver Operating Characteristic curves, from which measurements including Area under Curve (AUC), sensitivity, specificity, diagnostic odds ratio (DOR) was calculated. Yang et al. was the only study which examined the accuracy of each scoring system at two different timepoints for the prediction of severity – within 48 hours of admission and at/after 48 hours of admission; while all other studies evaluated each scoring system at the timepoints defined by their original study.

Based on the systematic reviews (Tables 3 and Tables 4), the Ranson score is shown to have comparable, if not superior, levels of accuracy as other commonly used scoring systems such as APACHE II, BISAP, CTSI, and Glasgow score in stratifying severity of AP and predicting mortality.

5.1. Prognostic accuracy of the Ranson score in stratifying severity

In Mikó et al., the Ranson score had the second highest AUC for stratifying severity (0.81). The Ranson score outperformed APACHE II, BISAP, CTSI and CRP, and was second only to mCTSI (Table 3) [88]. There was, however, no statistical difference between the severity prediction values of the Ranson score and other scoring systems. The Ranson score, together with CTSI and mCTSI, was amongst the highest in terms of sensitivity for stratifying severity. These findings suggest that the Ranson score can be as valuable as APACHE II, BISAP, CTSI, mCTSI and CRP for stratifying severity of AP.

In Gao et al., the Ranson score had a reasonably high AUC (0.83) and DOR (13.35) for identifying SAP, which was comparable to both APACHE II and BISAP (Table 3) [90]. The Ranson score also had a higher sensitivity (0.66) than BISAP, and a higher specificity (0.78) than APACHE II.

In Yang et al., the Ranson score was found to be comparable to BISAP, CRP and the HAPS for stratifying severity in AP (Table 3) [81]. Within 48 hours of admission, the Ranson score exhibited moderate sensitivity (0.66) that was higher than that

Table 2. Overview of studies included.

	References		Study Period (of Included Studies)	No. of Studies included	Clinical Outcome Evaluated
1	Mikó et al., 2019	[88]	1992–2016	30	Mortality, Severity
2	Di et al., 2016	[82]	1971–2014	94	Mortality
3	Gao et al., 2015	[90]	2000–2013	10	Mortality, Severity
4	Yang et al., 2014	[81]	2003–2012	7	Severity
5	Gravante et al., 2009	[89]	1974–2007	56	Mortality

Table 3. Comparison of studies for stratifying severity of Acute Pancreatitis.

	Reference		Definition of SAP (No. of Studies)	Scoring Systems compared	Pooled AUC (95% CI) ◊	Sensitivity (95% CI)	Specificity (95% CI)	Diagnostic Odds Ratio (95% CI)	Positive Likelihood Ratio (PLR) (95% CI)	Negative Likelihood Ratio (NLR) (95% CI)
1	Mikó et al., 2019	[88]	2012 Revised Atlanta (8) 2009 Atlanta (3) 2008 Atlanta (2) 1992 Atlanta (4) Organ Failure (4) Others or Unspecified (9)	Ranson Score	0.81 (0.75–0.87)	0.79 (0.69–0.86)	0.78 (0.71–0.84)	13.32 (7.33–24.24)	-	-
				APACHE II	0.80 (0.77–0.83)	0.71 (0.60–0.79)	0.80 (0.71–0.88)	9.94 (6.45–15.30)	-	-
				BISAP	0.79 (0.72–0.86)	0.73 (0.53–0.87)	0.80 (0.72–0.88)	11.71 (4.49–30.61)	-	-
				CRP	0.73 (0.64–0.83)	0.71 (0.59–0.81)	0.87 (0.66–0.96)	16.75 (3.49–80.48)	-	-
				CTSI	0.80 (0.76–0.85)	0.81 (0.73–0.87)	0.82 (0.73–0.88)	19.10 (10.29–35.45)	-	-
				mCTSI	0.83 (0.75–0.91)	0.88 (0.47–0.98)	0.80 (0.56–0.92)	29.07 (3.36–251.91)	-	-
2	Gao et al., 2015	[90]	2012 Revised Atlanta (6) 1992 Atlanta (3) Unspecified (1)	Ranson Score	0.83 (SE 0.08)	0.66 (0.59–0.72)	0.78 (0.76–0.81)	13.35 (4.53–39.36)	4.05 (2.26–7.27)	0.36 (0.22–0.60)
				APACHE II, cutoff 8	0.82 (SE 0.03)	0.83 (0.77–0.88)	0.59 (0.56–0.63)	10.77 (6.80–17.07)	2.54 (1.72–3.73)	0.26 (0.18–0.40)
				BISAP, cutoff 3	0.87 (SE 0.06)	0.51 (0.43–0.60)	0.91 (0.89–0.92)	18.08 (8.27–39.55)	7.23 (4.21–12.42)	0.56 (0.44–0.71)
				BISAP, cutoff 2	0.88 (SE 0.04)	0.63 (0.55–0.70)	0.82 (0.79–0.84)	8.45 (3.46–20.65)	3.51 (2.24–5.52)	0.44 (0.27–0.73)
3	Yang et al., 2014	[81]	Persistent Organ Failure (7)	**Within 48 hours of Admission**						
				Ranson Score	-	0.66 (0.58–0.74)	0.82 (0.78–0.84)	9.84 (2.72–35.6)	3.82 (1.94–7.51)	0.41 (0.22–0.75)
				APACHE II	-	0.84 (0.78–0.89)	0.58 (0.55–0.62)	13.7 (5.80–32.4)	2.67 (1.55–4.62)	0.22 (0.11–0.44)
				BISAP	-	0.54 (0.46–0.63)	0.82 (0.78–0.84)	6.08 (4.06–9.12)	3.24 (2.21–4.75)	0.58 (0.41–0.82)
				Glasgow Score	-	0.78 (0.69–0.86)	0.82 (0.790–0.86)	15.4 (4.60–51.8)	4.27 (3.06–5.95)	0.28 (0.11–0.70)
				SIRS	-	0.69 (0.59–0.78)	0.63 (0.59–0.67)	4.16 (2.20–7.87)	1.97 (1.33–2.92)	0.48 (0.35–0.64)
				HAPS	-	0.71 (0.61–0.80)	0.56 (0.521–0.61)	2.98 (1.84–4.83)	1.61 (1.35–1.90)	0.53 (0.39–0.74)
				JSS		0.53 (0.43–0.63)	0.90 (0.87–0.92)	9.71 (3.39–27.8)	5.19 (2.66–10.1)	0.54 (0.36–0.81)
				CRP		0.66 (0.51–0.79)	0.88 (0.78–0.94)	11.6 (4.43–30.1)	4.85 (2.45–9.59)	0.41 (0.21–0.82)
				At/After 48 hrs of Admission						
				Ranson Score	-	0.59	0.93	-	2.81	0.52
				APACHE II	-	0.84 (0.73–0.87)	0.62 (0.58–0.66)	8.58 (5.36–13.7)	2.35 (1.71–3.24)	0.31 (0.21–0.45)
				BISAP	-	0.68 (0.57–0.77)	0.82 (0.78–0.85)	9.00 (4.30–18.8)	3.64 (2.64–5.02)	0.41 (0.27–0.63)
				Glasgow Score	-	0.72 (0.62–0.81)	0.80 (0.77–0.84)	8.52 (4.78–15.2)	2.98 (1.96–4.53)	0.38 (0.13–1.12)
				SIRS	-	0.71 (0.61–0.80)	0.72 (0.68–0.76)	6.54 (4.00–10.5)	2.60 (2.10–3.14)	0.40 (0.29–0.55)
				HAPS	-	0.57 (0.47–0.67)	0.88 (0.85–0.90)	8.51 (2.73–26.6)	4.48 (1.40–14.3)	0.52 (0.41–0.66)
				JSS	-	0.73 (0.63–0.82)	0.91 (0.89–0.94)	26.1 (15.0–42.2)	8.01 (5.88–10.9)	0.31 (0.20–0.47)

APACHE II: Acute Physiology and Chronic Health Evaluation II, BISAP: Bedside Index of Severity in Acute Pancreatitis, CRP: C-Reactive Protein, CTSI: CT Severity Index, HAPS: Harmless Acute Pancreatitis Score, JSS: Japanese Severity Score, mCTSI: Modified CT Severity Index, SIRS: Systemic Inflammatory Response Syndrome

◊ For Pooled AUC, Gao et al. evaluated the Standard Error (SE) instead of 95% CI

Table 4. Comparison of studies for predicting mortality in Acute Pancreatitis.

	Reference		Scoring Systems compared	Pooled AUC (95% CI) ◊	Sensitivity (95% CI) *	Specificity (95% CI) *	Diagnostic Odds Ratio (DOR) (95% CI)	Positive Likelihood Ratio (PLR) (95% CI) ¶	Negative Likelihood Ratio (NLR) (95% CI) ¶
1	Mikó et al., 2019	[88]	Ranson Score	0.87 (0.81–0.92)	0.91 (0.70–0.98)	0.72 (0.66–0.79)	28.72 (7.57–109.05)	-	-
			APACHE II	0.91 (0.88–0.93)	0.92 (0.70–0.98)	0.79 (0.66–0.88)	45.08 (11.4–178.2)	-	-
			BISAP	0.87 (0.83–0.90)	0.88 (0.71–0.96)	0.77 (0.70–0.83)	24.74 (9.44–64.81)	-	-
			CRP	0.73 (0.66–0.81)	-	-	-	-	-
			CTSI	0.79 (0.73–0.86)	0.88 (0.69–0.97)	0.61 (0.52–0.70)	12.84 (4.19–39.41)	-	-
			mCTSI	0.80 (0.72–0.89)	0.95 (0.76–0.99)	0.36 (0.16–0.63)	10.32 (2.11–50.53)	-	-
2	Di et al., 2016	[82]	Ranson Score	-	0.900 (0–1.000)	0.674 (0.136–0.970)	-	-	-
			APACHE II	-	1.000 (0.677–1.000)	0.634 (0.214–0.959)	-	-	-
			BISAP	-	0.714 (0.333–1.000)	0.876 (0.629–0.976)	-	-	-
			Glasgow Score	-	0.500 (0.294–1.000)	0.786 (0.270–0.969)	-	-	-
			JSS (revised 2009)	-	0.504 (0–1.000)	0.873 (0.696–0.990)	-	-	-
			SAPS	-	1.000 (1.000–1.000)	0.354 (0.354–0.354)	-	-	-
			SIRS	-	1.000 (0.333–1.000)	0.596 (0.155–0.782)	-	-	-
3	Gao et al., 2015	[90]	Ranson Score	0.92 (SE 0.05)	0.93 (0.78–0.99)	0.69 (0.65–0.73)	23.44 (6.91–79.47)	3.27 (2.03–5.26)	0.15 (0.05–0.45)
			APACHE II, cutoff 8	0.83 (SE 0.16)	0.95 (0.77–1.00)	0.68 (0.63–0.73)	20.92 (4.72–92.67)	2.74 (2.26–3.33)	0.15 (0.04–0.54)
			BISAP, cutoff 3	0.87 (SE 0.03)	0.56 (0.53–0.60)	0.91 (0.90–0.91)	13.72 (9.82–19.18)	5.65 (4.23–7.55)	0.48 (0.41–0.56)
			BISAP, cutoff 2	0.82 (SE 0.02)	0.81 (0.78–0.84)	0.70 (0.70–0.71)	10.18 (8.33–12.45)	2.72 (2.44–3.04)	0.27 (0.23–0.32)
4	Gravante et al., 2009	[89]	Ranson Score	-	0.65	0.70	-	PPV = 20–63	NPV = 86–94
			APACHE II	-	0.65–0.81	0.77–0.91	-	PPV = 23–69	NPV = 86–99
			Glasgow Score	-	0.94	0.28	-	PPV = 18–66	NPV = 86–100

APACHE II: Acute Physiology and Chronic Health Evaluation II, BISAP: Bedside Index of Severity in Acute Pancreatitis, CRP: C-Reactive Protein, CTSI: CT Severity Index, JSS: Japanese Severity Score, SAPS: Simplified Acute Physiology Score, mCTSI: Modified CT Severity Index, SIRS: Systemic Inflammatory Response Syndrome

* For Sensitivity and Specificity, Di et al. presented the data as Sensitivity (Range) and Specificity (Range)

¶Gravante et al. compared Positive Predictive Value (PPV) (%) and Negative Predictive Value (NPV) (%) instead of Positive Likelihood Ratio and Negative Likelihood Ratio

◊ For Pooled AUC, Gao et al. evaluated the Standard Error (SE) instead of 95% CI

of BISAP (0.54) and JSS (0.53) and had much better specificity (0.82) than APACHE II (0.58) and SIRS (0.63). This is a particularly interesting finding. Many critics of the Ranson score claim that the Ranson score is less useful for advising early decision-making because of the need to wait for complete computation of the score. However, this finding shows that the Ranson score variables computed at admission already has relatively high specificity and can be useful for discriminating severe and non-severe AP for guiding the disposition and initial management of patients. At/after 48 hours of admission, the Ranson score performed better than the APACHE II in terms of its positive and negative likelihood ratios. The Ranson score also had the highest specificity (0.93) amongst all scoring systems at this time point. At 48 hours of admission, this is usually the transitional time point of clinical care where most clinicians would have to make decisions regarding which patients can be safely discharged or transferred to receive different intensity of care, and the high specificity of the Ranson score at 48 hours allows clinicians to safely exclude SAP at this time point.

5.2. Prognostic accuracy of the Ranson score for predicting mortality

Mikó et al. found that the Ranson score had a better AUC (0.87) than all systems except APACHE II (0.91) for predicting mortality (Table 4) [88]. The Ranson score also had the third-best sensitivity (0.91) for the prediction of mortality, which was slightly lower than that of mCTSI (0.95) and APACHE II (0.92). However, the Ranson score had a relatively high specificity (0.72) which was comparable to that of APACHE II (0.79) and BISAP (0.77), and much higher than that of mCTSI (0.36).

Di et al. evaluated the Ranson score against other scoring systems for the prediction of mortality in AP based on the sensitivity and specificity levels of each scoring system (Table 4) [82]. The Ranson score had a relatively high sensitivity (0.900) which was just slightly lower than that of the APACHE II (1.0) and SAPS (1.0). However, the Ranson score had a higher specificity level (0.674) compared to that of APACHE II (0.634) and SAPS (0.354).

Gao et al. found that the Ranson score had the highest AUC (0.92), second highest sensitivity (0.93) and highest DOR (23.44) for predicting mortality, among the other scoring systems compared – APACHE II and BISAP (Table 4) [90].

Gravante et al. compared the Ranson score, APACHE II and Glasgow score for the prediction of mortality (Table 4) [89]. The Ranson score was found to have lower sensitivity (0.65) than APACHE II (0.65–0.81), and its specificity (0.70) was lower than APACHE II (0.77–0.91) but higher than the Glasgow score (0.28). Despite this, the Ranson score had a positive predictive value (20–63%) and negative predictive value (86–94%) that was equivalent to that of APACHE II (23–69% and 86–99%) and Glasgow score (18–66% and 86–100%).

5.3. Summary of findings and Discussion

These five studies highlight that the Ranson score is indeed a valuable tool in modern clinical practice for prognosticating AP and is by no means inferior to other newer scoring systems for severity stratification and mortality prediction. The studies also underline that no one scoring system consistently stands out among the rest at predicting mortality and stratifying severity in AP patients. Each score has inherent strengths and weaknesses, and variations in study findings can be attributed to the differences in population demographics, etiology of AP, and heterogeneity in clinical care.

Di et al. reported that the serial usage of Ranson score improved the specificity of the SAPS with similarly high sensitivity levels [82]. Gao et al. found that employing both Ranson score and APACHE II to predict mortality yielded a very low negative likelihood ratio of 0.15, indicating that a low score of both scoring systems was highly reliable in identifying patients at low risk of mortality [90]. In other studies, combinations of scores such as APACHE II with CRP, CRP with BISAP, and interleukin-10 with serum calcium was found to predict SAP more accurately than when either score was used alone [117,119,120]. These findings emphasize that while the search for a single holistic predictor continues, it is possible that scoring systems used complementarily with each other, can achieve higher levels of prognostic accuracy. Future studies can further explore how various scoring systems can be combined to optimize their prognostic abilities.

6. Conclusion

Despite being the oldest scoring system available, the Ranson score still retains its clinical validity over the years. It is shown to have consistently high prognostic accuracy. The Ranson score incorporates the best of both worlds. It has components measured at admission to provide early assessment of the patient – the Ranson score used at admission has a high level of specificity and this can be useful in discriminating severe and non-severe AP to guide the initial management of patients. It also has components which consider the dynamism of the disease by evaluating the patient at 48 hours post-admission. The 48-hour component is an inherent advantage that is supported by the Revised Atlanta Classification and has been shown in multiple studies to raise its cumulative prognostic accuracy significantly. These aspects, coupled with its relative ease of use and practicality in resource and time-limited settings, are strong reasons for the Ranson score to remain a relevant and valuable tool in current clinical practice.

7. Expert opinion

Acute pancreatitis (AP) is a disease in evolution and can present in a wide spectrum of forms in terms of severity and risk of mortality. The use of multiple risk stratification tools can supplement clinical judgment, thus improving the quality of care and clinical outcomes of the patient. Many scoring systems have been introduced over the past few decades, and it is important that pancreatologists critically appraise the available evidence to enhance our understanding of AP and its clinical management. In our opinion, there is no one perfect prognostic tool to risk stratify and predict mortality in AP. Each scoring system has inherent strengths and weaknesses. Clinicians must do local audits to evaluate the utility of

existing well-validated scoring systems to determine which scoring system would perform the most optimally and can be most feasibly implemented in the local context. In addition, other factors such as patient demographics, disease etiology, personal experience of the clinician, and local resources are important determinants that impact the delivery of care and should be considered in tandem with scoring systems. This literature review proposes that the Ranson score is an effective prognostication tool for AP and advocates that the 48-hour time frame is its inherent strength and not a weakness.

In the era of technological advancements, there is increased attention on the use of digital tools to aid clinical decisions. Machine learning algorithms and other intelligent database systems have been developed over the years to predict various outcomes in AP, including severity of AP and length of hospital stay [121]. There are several types of machine learning algorithms proposed for the evaluation of acute pancreatitis, including artificial neural network (ANN), support vector machine (SVM) and logistic regression analysis (LRA). These machine-learning algorithms can store and interpret large amounts of data from multiple sources to construct an electronic tool for prognosticating AP and guiding clinical decisions. Of these three, ANN is the most well-researched and ANN models have been found to perform better than APACHE II, modified Glasgow score and Ranson score in predicting SAP in terms of prognostic accuracy and speed [78,119,122,123]. ANN, SVM and LRA have been found to be efficient prognostic tools for predicting SAP, with accuracy levels consistent with APACHE II [124].

Radiomics, the electronic process of translating features on imaging into quantitative data, can potentially overcome some of the existing limitations in radiologic scoring systems. Standardized processes for identifying pancreatic morphological changes can be developed, thus reducing interobserver variability. Furthermore, these electronic systems may be more adept than the human eye at detecting minute abnormalities on imaging scans in very early phases of AP. One study crafted a radiomics model for predicting SAP and it was found to have higher predictive accuracy than APACHE II, BISAP and MRSI [125]. Another study found radiomics useful in predicting the risk of recurrent acute pancreatitis [126].

There are also ongoing efforts to create intelligent systems that improve the efficiency of calculating scoring systems and can rapidly advise clinical decisions. The Ariel Dynamic Acute Pancreatitis Tracker was developed to incorporate information of patients to calculate the severity scores for SIRS, Panc 3, BISAP and HAPS [127]. It is shown to be highly accurate in identifying mild AP where the intensity of care can be downgraded safely.

While these intelligent computer-based systems present a hopeful future for improvements in the management of AP, there are criticisms that these systems fail to consider real-life clinical challenges such as incomplete clinical parameters and patient circumstances [121]. Besides difficulties in ensuring technological access, there may also be concerns related to data governance with potential direct impacts on patient confidentiality.

With these ongoing efforts to develop and evaluate new predictive tools, other logistical and ethical challenges may arise which can affect the feasibility of implementation in standard clinical practice. It is safe to say that traditional tried and tested scoring systems such as the Ranson score will remain a key part of clinical practice in the present time. As the search for a single most accurate predictive tool continues, clinical judgment should remain absolute in the assessment of AP, and any scoring system and predictive tool should be supplemented by clinical wisdom.

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