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Evaluation of four scoring systems in prognostication of acute pancreatitis for elderly patients

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Research article

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Evaluation of four scoring systems in prognostication of acute pancreatitis for elderly patients

Short title : Evaluation of scoring systems for elderly patients

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Abstract

Objectives: To evaluate the four scoring systems, including Ranson, BISAP, Glasgow, and APACHE II in the prognostic assessment of acute pancreatitis (AP) for elderly patients.

Methods: A retrospective study of 918 patients presenting with AP was done at Zhongda Hospital Southeast University, from January 2015 to December 2018. The patients were divided into two groups: 368 patients who were ⩾60 years old, and 550 patients who were <60 years old. Four scoring systems were used to analyze all patients.

Results: The severity of the disease, and mortality are significantly different between the two groups (p-value <0.05), while the difference between the two groups about pancreatic necrosis is statistically insignificant (p-value =0.399). The differences of the AUCs (Area under curves) in prognostication of SAP (severe acute pancreatitis) between the two groups are statistically significant (p-value <0.05) for Ranson and APACHE II, while for BISAP and Glasgow, the differences are statistically insignificant. All the four scoring systems are effective and similar in prediction of pancreatic necrosis and death for both groups.

Conclusions: Prediction of severity, pancreatic necrosis and death in AP for elderly patients can be performed very well by using BISAP. APACHE II is more suitable for

38 younger patients when dealing with severity. Ranson and Glasgow can be used to
39 evaluate all AP patients in most cases, however, Ranson is more effective for younger
40 patients when used to assess severity.

41

42 **Keywords:** Acute pancreatitis; elderly patients; prediction; scoring system; ROC (receiver
43 operating characteristic) curve

44

Introduction

Acute pancreatitis (AP) is now one of the most common gastrointestinal conditions which causes hospitalization and becomes a significant burden for patients, their family and the health-care system[1,2]. Over the past decade, admissions show a large growth trend worldwide[3-5]. Meanwhile, many countries like the United States, Japan, and China are now facing an accelerating population aging [6]. Take China for example, according to the National Health Commission of the People's Republic of China, by 2030 the elderly population (older than 60 years) will exceed 30% of the total population. Therefore, the total number and the proportion of elderly patients among acute pancreatitis patients will increase significantly in the future.

About 80% of the acute pancreatitis cases are mild and self-limited with no sequelae. But the rest of the cases deteriorate, and necrosis arises in parts of pancreas and the ambient tissues. Although mortality associated with acute pancreatitis has continuously reduced[7], and the overall mortality of AP is now around 2%, however, when the cases become severe, it can reach to about 20–30% [8]. On the other hand, elderly patients have been taken as a subgroup of higher risk when considering the mortality related to AP[9]. Hospital acquired infections development is also considered as a reason for higher mortality. Unfortunately, elderly patients are more susceptible to nosocomial infection [10], which in turn makes the mortality even higher. Because of the higher mortality of severe acute pancreatitis (SAP) and the causes of death related to elderly patients, careful ongoing clinical evaluations, the results of routine laboratory and radiographic

testing together with multi-factorial scoring systems are necessary for the prediction of the SAP [11], especially for the elderly patients.

Several scoring systems are available, such as the Ranson criteria [12], which was the first AP scoring system and can be used in the evaluation of biliary and non-biliary pancreatitis. The Glasgow scoring system[13] is similar to Ranson criteria, which is also based on objective clinical indicators, and the assessment needs to be completed within 48 hours after admission. Acute Physiology and Chronic Health Evaluation (APACHE) II [14] was originally developed for critical patients in ICU (intensive care unit), and was used for evaluation of AP in 1989. A simple evaluation method named the bedside index of severity in acute pancreatitis (BISAP), was proposed in 2008 [15], and can be used to estimate the severity of AP in the early phase. All these scoring systems can be applied together with the ongoing evaluation by clinician and provide more accurate and rapid diagnosis.

In the past few years, many researches have been conducted to evaluate the accuracy of these scoring systems in estimating the severity of acute pancreatitis [16,17], but few researches have been done to validate these systems in the assessment of elderly AP patients. The aim of this paper was to evaluate the effectiveness of the four aforementioned scoring systems in the prediction of severity, pancreatic necrosis and death in acute pancreatitis for elderly patients.

Methods

87 *Study design*

88 A retrospective analysis was carried out. The patients were selected complied with
89 following requirements:

90 Inclusion criteria: Primary diagnosis compliant with acute pancreatitis .

91 Exclusion criteria: (1) Information is incomplete; (2) Diagnosis is suspicious; (3)
92 Complicated with other serious diseases (include chronic pancreatitis， chronic cardiac
93 failure: New York Heart Association level IV, chronic obstructive pulmonary, chronic
94 renal insufficiency requires long-term maintenance hemodialysis, cirrhosis, and tumor);
95 (4) Died within 48 hours after admission.

96 Finally, 918 adult patients with a diagnosis of acute pancreatitis treated at Zhongda
97 Hospital Southeast University (Nanjing,China), from January 2015 to December 2018
98 were retrospectively identified.

99 The patients were further divided into two groups:Elderly group(⩾60 years old), and
100 younger group (<60 years). For both groups, four kinds of scoring systems including
101 Ranson criteria, Glasgow, APACHE-II, and BISAP were used. The BISAP, APACHE II
102 scores were assessed according to the data of the patient's admission within 24 hours, and
103 the Ranson and Glascow scores were scored at the admission and within 48 hours. All
104 scores were calculated for the most severe laboratory tests and vital signs during the
105 evaluation period (time required by the scoring system to observe). The AUCs of the
106 different scoring systems for predicting severity, pancreatic necrosis, and mortality were

107 obtained from their ROC curves. For each scoring system, the statistical differences of
108 AUCs between the two groups were analyzed.
109
110 *Diagnosis Criteria*
111 The diagnosis criteria for acute pancreatitis is determined in accordance with the 2012
112 Atlanta classification [18]. The patient should have at least two of the following three
113 diagnostic features:
114 (1) Consistent abdominal pain with acute pancreatitis.
115 (2) Serum amylase and/or lipase levels that are at least 3 times higher than the upper
116 limit of the normal range.
117 (3) Findings of acute pancreatitis on computed tomography(CT) or magnetic resonance
118 imaging (MRI).
119 According to [18], the absence of organ failure and local or systemic complications
120 is characterized as mild acute pancreatitis (MAP). The presence of local or systemic
121 complications or transient (less than 48 h) organ failure is characterized as moderately
122 severe acute pancreatitis (MSAP). Persistent (longer than 48 h) organ failure (may be
123 single or multiple organ failure) is characterized as severe acute pancreatitis (SAP).
124 Organ failure included one or more of the following :
125 (1) Shock/cardiovascular failure: Systolic blood pressure less than 90 mmHg or basal
126 systolic arterial pressure reduced more than 40 mmHg, accompanied with signs of tissue

127 hypoperfusion (lactate larger than 3 mmol/L); saturation of central venous oxygen
128 (SvcO2) less than 70%.
129 (2) Pulmonary insufficiency: Arterial PO2 less than 60 mmHg in room air or mechanical
130 ventilation required.
131 (3) Acute renal failure: Serum creatinine level >2 mg/dl after hemodialysis or
132 rehydration indicating a score no less than 2 according to modified Marshall scoring
133 system.
134 After the first week of the disease, CECT showing non-enhancement of pancreatic
135 parenchyma was defined as pancreatic necrosis.
136
137 *Treatment*
138 The following treatments were taken for the patients diagnosed as AP:
139 Abrosia, early fluid resuscitation (In the first 24 hours , the fluid resuscitation dose
140 should be 5-10 $ml \cdot kg^{-1} \cdot h^{-1}$), nutritional support (on the premise of hemodynamic stability,
141 as far as possible enteral nutrition started within 24-48 hours), pain control, application of
142 proton pump inhibitor, antibiotic, somatostatin and its analogues. Organ function support
143 in patients with organ dysfunction (such as mechanical ventilation, continuous renal
144 replacement therapy or application of vasoactive drugs).
145
146 *Statistical analysis*

SPSS version 20.0 (IBM Corp.) was used for statistical calculations: Receiver-operating curve (ROC) was used for assessing the prognostic value of each scoring system, the area under the curve (AUC) of the four scoring systems were calculated one-by-one for both groups, and the AUCs of the same system were compared between each other. A p-value <0.05 indicates statistically significant.

Results

In this study, 918 patients (aged from 21 to 89 years, mean age 58.4 ± 18.1) of AP were hospitalized. They were divided into two groups (Table 1): The elderly group (aged from 60 to 89 years, mean age 73.83 ± 7.78) and the younger group (aged from 21 to 59 years, mean age 42.10 ± 9.50). Of the 368 elderly patients, 27(7.3%) developed severe acute pancreatitis, 28 (7.6%) pancreatic necrosis and 11 (3%) died. While for the control group, among 550 younger patients, 25 (4.5%) developed severe acute pancreatitis, 34 (6.2%) pancreatic necrosis and 5 (0.9%) died. For both groups male patients are more than the females. The male female ratio is 201:167 and 359:191, respectively. The clinical characteristics of the two groups are also listed in Table 1. For elderly group, the proportion of severity,persistent organ failure, pancreatic necrosis, and mortality are all higher than that of the younger group. Statistically significance can be observed between the two groups with regards to the differences of severity, persistent organ failure and mortality among AP patients, while the difference of transient organ failure and pancreatic necrosis between elderly and younger AP patients is insignificant.

Table 1 Comparisons of the two groups.

Variables		Elderly patients	Younger patients	χ^2	P-value (p<0.05)
Male:Female		201:167	359:191	-	-
Mean age (years)		73.83 ± 7.78	42.10 ± 9.50	-	-
Etiology	Gall Stone	276（75.0%）	283（51.5%）	-	-
	Alcoholic	21（5.7%）	116（21.1%）		
	hyperlipemia	26（7.1%）	83 （15.1%）		
	others	45（12.2%）	68（12.3）		
Comorbi-dities	DM*	76(21.2%)	126(22.9%)	0.654	0.419
	CHD**	36(9.8%)	11(2%)	27.491	<0.01
Severity	MAP	316(85.9%)	506(92%)	8.849	<0.01
	MSAP	25(6.8%)	19(3.5%)	5.386	<0.05
	SAP	27(7.3%)	25(4.5%)	3.871	<0.05
Organ failure	transient	6(1.6%)	12(7.3%)	0.349	0.555
	persistent	27(7.3%)	25(4.5%)	3.871	<0.05
Pancreatic necrosis		28(7.6%)	34(6.2%)	0.713	0.399
Death		11(3%)	5(0.9%)	5.570	<0.05

*=Diabetes Mellitus, **=coronary heart disease

The AUCs of the four scoring systems for predicting severity of AP were obtained from their ROC curves and are listed in Table 2. For elderly group, BISAP had the largest AUC of 0.922 (95% CI, 0.890-0.947) in prediction of the severity, and was significantly higher than that of APACHE II 0.784(95% CI, 0.729-0.817, p-value <0.05). The AUCs for Ranson and Glasgow were 0.867 (95% CI, 0.828–0.900), and 0.913 (95% CI,

0.880-0.940) respectively. For younger group, in prediction of severity, Ranson had the largest AUC of 0.964 (95% CI, 0.945-0.978), while the AUC of BISAP was 0.942 (95% CI, 0.881-0.969), which was almost similar to that of APACHE II 0.951 (95% CI, 0.884-0.975, p-value>0.05), and was slightly higher than that of Glasgow 0.881 (95% CI, 0.851-0.907, p-value>0.05). Cutoffs were calculated based on the highest sensitivity and specificity achieved from ROC curves [17]. For elderly group, the cutoffs for the four scoring systems are Ranson≥4 (sensitivity 0.814, specificity 0.842), BISAP≥3 (sensitivity 0.889, specificity 0.865), APACHE II≥9(sensitivity 0.852, specificity 0.610), and Glasgow ⩾3 (sensitivity 0.852, specificity 0.842), While for younger group, the cutoffs for the four scoring systems are Ranson≥3 (sensitivity 0.920, specificity 0.928), BISAP≥2 (sensitivity 0.960, specificity 0.880), APACHE II≥8(sensitivity 0.960, 9specificity 0.930), and Glasgow≥2 (sensitivity 0.800, specificity 0.882). By using these cutoffs, the sensitivity, specificity, PPV, and NPV were calculated.

190 Table 2 Value of four scoring systems in prediction of SAP, and comparisons of ROC

191 curves between two groups.

Scoring system	AUC	95%CI	Cut-offs	Sensitivity	Specificity	Youden Index	PPV	NPV	Significa-nce level
elderly group/ younger group									
Ranson	0.867/0.964	0.828-0.900/ 0.945-0.978	≥4/≥3	0.814/0.920	0.842/0.928	0.613/0.809	0.289/0.377	0.983/0.996	<0.05
BISAP	0.922/0.942	0.890-0.947/ 0.881-0.969	≥3/≥2	0.889/0.960	0.865/0.880	0.754/0.764	0.343/0.276	0.990/0.998	0.383
APACHE II	0.784/0.951	0.729-0.817/ 0.884-0.975	≥9/≥8	0.852/0.960	0.610/0.930	0.462/0.899	0.147/0.429	0.981/0.998	<0.01
Glasgow	0.913/0.881	0.880-0.940/ 0.851-0.907	≥3/≥2	0.852/0.800	0.842/0.882	0.656/0.650	0.299/0.244	0.986/0.989	0.506

192

193 The comparisons of the four scoring systems in prediction of the severity in AP

194 between the two groups are also listed in Table 2. For both groups, BISAP and Glasgow

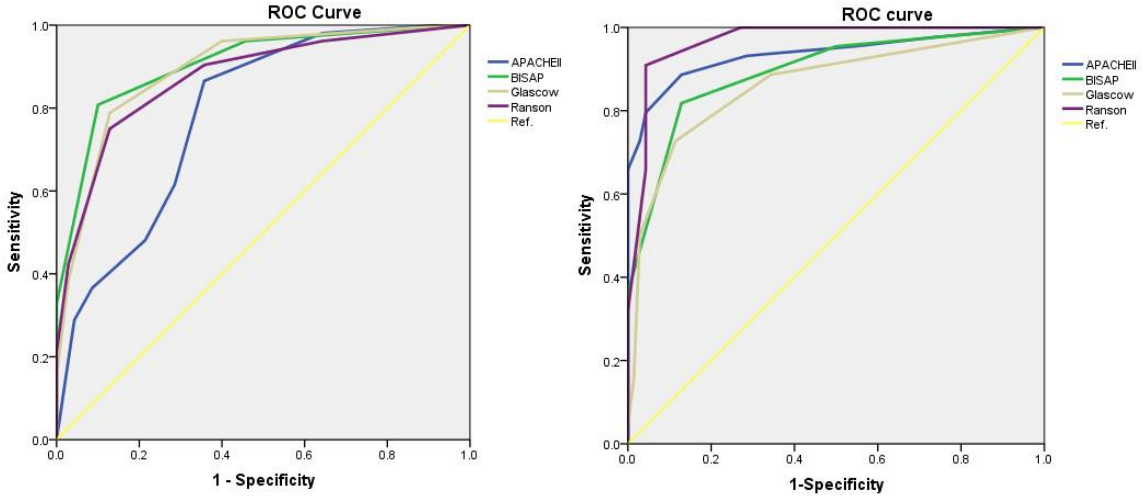
195 were with the similar effectiveness (p-value =0.383 and p-value =0.506). Whereas, the

196 accuracy of Ranson and APACHE II in assessment of severity for the younger group is

197 significantly higher than for the elderly group (p-value <0.05 and p-value <0.01). The

198 ROC curves of four scoring systems for prediction of severity of AP among elderly and

199 younger patients are shown in Fig.1(a) and (b), respectively.



(a) (b)

Fig.1 ROC curves for four scoring systems in evaluation of severity (a) elderly group (b) younger group.

The comparisons of the four scoring systems in prediction of pancreatic necrosis are listed in Table 3. The AUC of Ranson for elderly group is a little greater than for the younger group (p-value =0.105), while other three systems have larger AUCs for the younger group. However, the differences in evaluation of pancreatic necrosis between the two groups according to the four systems were insignificant. All the four scoring systems are more effective in prediction of death for younger group (Table 4), but the differences between the two groups were insignificant either.

Table 3 Comparisons of ROC curves for four scoring systems in evaluation of pancreatic necrosis between the two groups.

Scoring system	Pancreatic necrosis (AUC)		Significance
	Elderly Group	Younger Group	level
Ranson	0.931	0.866	0.105
BISAP	0.824	0.893	0.180
APACHE II	0.855	0.937	0.083
Glasgow	0.853	0.874	0.697

Table 4 Comparisons of ROC curves for four scoring systems in evaluation of death between the two groups.

Scoring system	Death (AUC)		Significance level
	Elderly Group	Younger Group	
Ranson	0.870	0.944	0.138
BISAP	0.891	0.919	0.625
APACHE II	0.918	0.919	0.986
Glasgow	0.899	0.951	0.258

Discussion

In this study, 918 AP patients were divided into two groups: the elderly group and the younger group. As summarized in Table1, both groups of AP patients with diabetes are statistically insignificant , which is similar to a recent research in China[19], and indicates that diabetes may be not relevant to the age factor of AP patients. Statistical difference can be observed between the two groups of AP patients with coronary heart disease, because the incidence of coronary heart disease increases with age. Significantly higher risk of severe pancreatitis (MSAP and SAP), persistent organ failure and death can also be found in the elderly patients group. This is probably because in the process of human aging, the function of various organs gradually decreases[20], so elderly patients are more likely to face organ failure. Besides of severity and older age [9], nosocomial infection can also increase the mortality of AP patients [21]. Meanwhile, elderly patients are susceptible to infection, which further increase the risk of mortality. Pancreatic necrosis is similar for both groups in our study, however, highest mortality is related with infected pancreatic necrosis [22], special attention and treatment are necessary for elderly patients.

236 For the four scoring systems, age contributes to the scores (Ranson: +1 point for
237 age>55; Glasgow: +1 point for age>55; APACHEII: +1 point for age between 45-54, +2
238 points for age between 55-64, +3 points for age between 65-74, +4 points for age ≥75;
239 BISAP: +1 point for age>60;). According to Table 2-4, in prediction of severity, Ranson
240 for elderly patients is less useful than it is for younger patients. But Ranson scoring
241 system is equally effective when applied to evaluate pancreatic necrosis and death for
242 both groups. Among the four systems, Ranson shows the best performances in prediction
243 of pancreatic necrosis for elderly patients. When use Ranson to predict SAP for elderly
244 group, the score should be≥4, and is similar to [23]. While for younger group, the score
245 is≥3, which is the same as the criterion [24].

246 Glasgow score is calculated based on objective clinical indicators, the evaluation were
247 mostly used in Europe [16]. The results in our hospital suggest that good and similar
248 predictive ability for severity,pancreatic necrosis and death can be observed for both
249 groups of AP patients. And the prediction ability of Glasgow is similar to Ranson score
250 [23]. In [24] Glasgow≥3 was used to diagnose SAP. And in our research, Glasgow≥3 and
251 Glasgow≥2 are the criterion for deciding SAP among the AP patients in elderly group and
252 younger group, respectively.

253 Through many years of practice, APACHE II is recognized as the most widely used
254 AP scoring system, and is recommended by a number of guidelines[25,26]. However, this
255 scoring system is complex and cumbersome[9], and according to our research, for elderly
256 patients, it is not as effective in prediction of severity as for younger AP patients. For

257 APACHE II, the cut-off≥8 is generally accepted as the criteria for diagnosis of SAP[24].
258 While in [27] and [28], APACHE II ≥6 and APACHE II≥5 were used as cut-offs,
259 respectively. According to this study, in order to assess severe AP patients, APACHE II
260 ≥9 is for elderly group, and APACHE II≥8 is for younger patients group.

261 BISAP is a simple scoring system. The required data can easily be achieved at the
262 time of admission. The in hospital death can be predicted in early stages of AP [29]. Also
263 organ failure can be predict accurately by using this scoring system [8]. In our study, for
264 prediction of severity, pancreatic necrosis and death, BISAP is useful for both elderly
265 patients and younger patients. While for elderly patients, BISAP shows the best ability in
266 prediction of severity. According to [28,30], when BISAP≥2, the patient should be treated
267 as SAP. While in [31-34], BISAP≥3 is used to determine patients with SAP. In this
268 research, the criterion for predict SAP is also different for the two groups: (elderly group:
269 BISAP≥3, younger group: BISAP≥2).

270 For elderly group, even if the condition is mild, the score is still likely to be higher
271 than the younger group. In this research, the scoring cut-offs for the elderly group are one
272 point higher than for the younger group, these changes can increase the specificity while
273 slightly reducing the sensitivity of the four scoring systems.

274

275 ## Conclusions

276 Elderly AP patients are more prone to develop severe disease, organ failure and die
277 while in hospital. More attention, appropriate triage and early prevention should be taken.

For prediction of severity, BISAP is the most appropriate scoring system. Ranson and APACHE II for elderly patients are not as useful as they for younger patients. All the four scoring systems show similar performances when predict the pancreatic necrosis and mortality between elderly and younger patients. Either score of the four scoring systems used to decide whether the patients are with SAP is different between two groups. The results suggest us to distinguish between younger and the elderly patients when using these scoring systems to determine if they are SAP. However, in this research, we use sixty as a cut-off age[35] to divide the patients into two groups. Change in age selection has an impact on grouping and may affect the final outcome, so for some area with different age distribution from China (for example: where people tends to live longer), change of the cut-off age and further research are necessary.

Abbreviations

AP:Acute pancreatitis; SAP: severe acute pancreatitis; MAP: mild acute pancreatitis; MSAP: moderately severe acute pancreatitis; BISAP: bedside index of severity in acute pancreatitis; APACHE: Acute Physiology and Chronic Health Evaluation;

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Authors' contributions

Yajie Li: study concept and design, data collection, data analysis, and writing of the draft manuscript; Jun Zhang: measurement of the samples and study co-design; Jihong Zou: data collection and review of the manuscript. All authors have approved the final version of the article.

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Conflict of interests

All the authors declare that they have no conflicts of interest.

Data Availability

The [SPSS data file] data used to support the findings of this study are available from the first author (Ms. Li Yajie) upon request.

Anyone need the data can contact the following address:

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Ethics approval and consent to participate

319 This study was approved by the Ethics Committee for Clinical Research of Zhongda
320 Hospital, Affiliated to Southeast University. The use of the patients' medical records were
321 for research purposes only.
322

323 ## Consent for publication

324 Not available.
325

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Figures

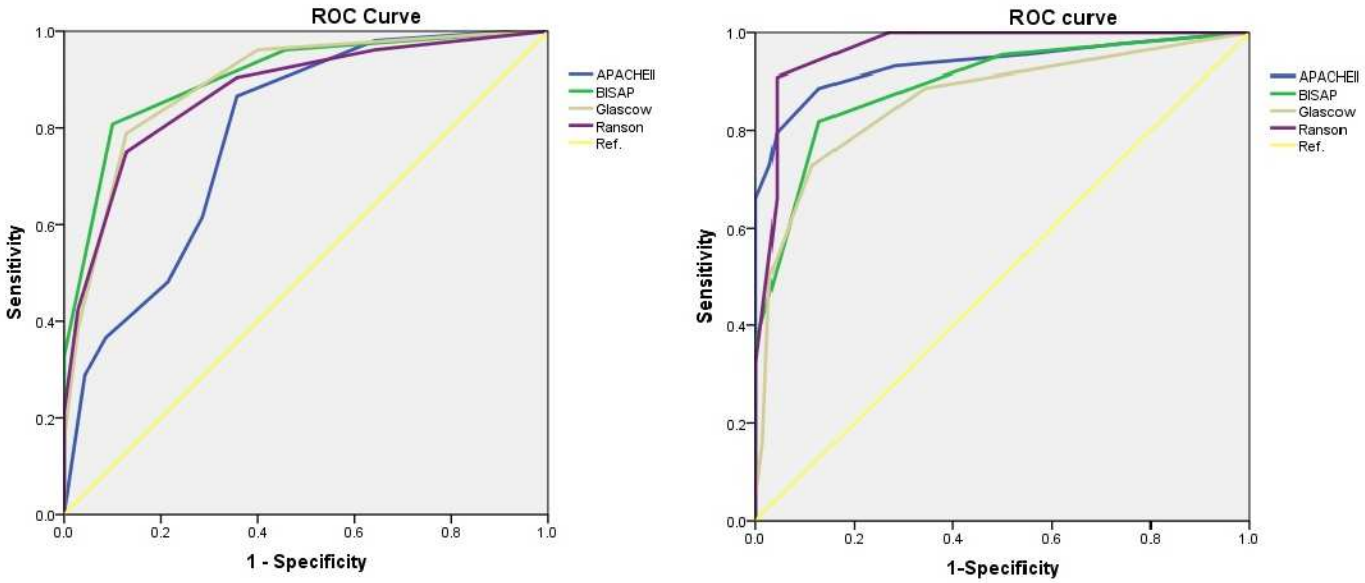

Figure 1

ROC curves for four scoring systems in evaluation of severity (a) elderly group (b) younger group.