Int J Clin Exp Med 2019;12(8):10531-10536
www.ijcem.com /ISSN:1940-5901/IJCEM0092950

Original Article

The role of CRP or albumin with ranson scale in predicting severe acute pancreatitis mortality risk

Shanshan Han[1], Jun Ye[2], Rui Liu[2], Weiwei Chen[2], Zhiqiang Feng[1]

[1]Beijing Chaoyang Emergency Medical Center, General Surgery, Chaoyang, Beijing 100020, China; [2]Medical University of Anhui Air Force Clinical School, Haidian, Beijing 100142, China

Received February 23, 2019; Accepted June 5, 2019; Epub August 15, 2019; Published August 30, 2019

Abstract: Background: The goal of this study was to evaluate the death risk of severe acute pancreatitis (SAP) by C-reactive protein (CRP) or albumin (ALB) with Ranson score. Methods: Retrospective analysis was used in this study. A new prediction model was established by the best cut-off value of the ROC curve. Group A: CRP (> 121 mg/L); Group B: ALB (≤ 28.9 g/L); Group C: Ranson score (> 3); Group D: Ranson score (> 3) or CRP (> 121 mg/L); Group E: Ranson score (> 3) and CRP (> 121 mg/L); Group F: Ranson score (> 3) or ALB (≤ 28.9 g/L); Group G: score (> 3) and (≤ 28.9). The accuracy of predicting SAP death risk was compared among group A-G. Results: A total of 94 SAP patients were enrolled and were then divided into a survival group (n=67 cases) and a death group (n=27 cases). The area under the ROC curve of CRP, Ranson score and ALB was 0.940, 0.815 and 0.866, respectively. The optimal cut-off values were > 121 mg/L, > 3 and ≤ 28.9 (g/L), respectively. The accuracy of group A to G for predicting SAP mortality was 86.2%, 86.2%, 62.8%, 62.8%, 88.3%, 60.6% and 88.3%, respectively. Group E and group G had the highest accuracy, with their sensitivity and specificity were 81.5%, 91.1%, 66.67% and 97%, respectively. Conclusion: Two new models established by CRP or ALB combined with Ranson score could improve the accuracy in predicting the death risk in SAP compared with Ranson score alone.

Keywords: C-reactive protein, albumin, Ranson score, severe acute pancreatitis

Introduction

Acute pancreatitis (AP) is a kind of pancreatic severe inflammatory disease because of pancreatic enzymes induced by various reasons such as alcohol and cholecystolithiasis. Most AP patients only need a short term hospitalization and then recover. However, about 20% of AP patients develop into severe acute pancreatitis (SAP). In SAP patients, extensive systemic inflammatory response was found, which could cause multiple organ dysfunction syndrome (MODS) with a mortality rate as high as 20% [1]. Consequently, it is of great significance to distinguish high death risk SAP patients as soon as possible and choose treatment option, prevent complications and lower the death rate [2]. Using scores or a rating system to evaluate SAP prognosis is a complicated clinical question, however, it is very important to predict the prognosis of the patients. Although various laboratory indexes, ratios, Ranson scale, Glasgow coma scale and Acute Physiology and Chronic Health Evaluation (APACHE) II scale have been widely used to evaluate the severity of the disease and predict the death rate, these methods are still controversial. The Ranson scale is one of the earliest and most common evaluation systems and its sensitivity, specificity and accuracy have been widely discussed in the clinics [3]. C-reaction protein (CRP), generated by the liver, is a non-specific inflammatory mediator and fully investigated inflammation marker. Many researchers recommend that use CRP as a biomarker to evaluate SAP prognosis [4]. Albumin (ALB) is only generated in the liver and has been identified by the researchers its clinical value [5-7]. In the literature, several marking systems and laboratory prediction indexes have been used together to predict the severity of SAP and the death rate [8, 9]. However, this combination of indexes need further confirmation. The goal of our investigation is to evaluate the accuracy of Ranson scale in predicting

the death risk of SAP patients and use new model of CRP or ALB with Ranson scale to predict SAP death risk, providing new way to improve the prediction rate.

Materials and methods

Basic characteristics of patients

The 94 SAP patients (Male: 53, Female: 41) of this retrospective cohort study were enrolled between January, 2015 and March, 2018. The age of these patients ranges from 18 to 81 years old. The average age was 55.57±18.279 years old. Diagnosis of AP was made according to the following two criteria: 1) continuous abdominal pain; 2) serum amylase and/or lipase 3 times higher than normal level (110 UL/L); 3) Characteristic manifestation of AP presented by abdominal ultrasound or CT scan. SAP was identified as Ranson score higher than 3 [10]. The death reason in death group is MODS. The exclusion criteria included: 1) age < 18; 2) complicated with malignant tumors; 3) complicated with chronic or acute liver disease or cholangeitis or cholecystitis; 4) severe renal failure; 5) severe anemia; 6) severe infection history within 1 month; 7) patients with incomplete clinical data such as the lack of routine blood test.

Methods

Data collection: SAP patients were retrospectively reviewed with the clinical data, including age, sex, etiology and laboratory examination (including Red Blood Cell Distribution Width (RDW), CRP, amylase, aspartate transaminase (AST), white blood cell (WBC), ALB, platelet distribution width (PDW), Superoxide Dismutase (SOD), triglycerides (TG), Fast blood glucose (FBG) and Ca^{2+}) within 48 h of admission. All enrolled patients were followed 1 month or until death.

Group analysis: Enrolled patients were divided into survival group (n=67) and death group (n=27). New prediction model was established by adapting diagnostic ROC curve and confirming best cut-off value.

Statistical analysis

The data of this study was analyzed by SPSS 21.0 software. Enumeration data use rate was presented with % and compared by x^2 analysis. Quantitative data was presented with X ± s and compared by t test. Abnormal distribution data was presented with median quarterback spacing and analyzed by Mann-Whitney U test. Binary logistic regression analysis was used to confirm the factor of SAP patients' death within the hospital. Regression coefficient was analyzed by word test. The influencing factors of death were calculated by ROC curve and grouped according to the best cut-off value. The positive predictive value, negative predictive value and accuracy were calculated by four-grid test. GraphPad Prism 7.00 was used for figures. P < 0.05 indicates that the difference has statistical significance.

Results

Basic characteristics of patients

Among the retrospectively reviewed 94 SAP patients, there were 41 males and 26 females in survival group. The etiology included biliary tract related diseases (n=49), alcoholism (n=8), high fat diet (n=7), drugs (n=2) and others (n=1). There were 12 males and 15 females in death group. The etiology included biliary tract related diseases (n=23), alcoholism (n=2), high fat diet (n=1) and drugs (n=1). There is no significant difference between the gender and etiology (p > 0.05).

Univariate analysis of clinical data

There was no significant difference between gender, RDW, AMY, WBC, AST, Ca^{2+}, PDW, and TG between the 2 groups (p > 0.05). Significant differences were found in CRP, Ranson scale, ALB, FBG and SOD between the 2 groups (p > 0.05) (**Table 1**). The levels of CRP and ALB were shown in **Figures 1** and **2**.

Binary logistic regression analysis

Five differential clinical indexes (CRP, Ranson scale, ALB, FBG and SOD), obtained from the univariate analysis of clinical data from the two groups, were performed stepwise regression analysis according to the inclusion criteria (α= 0.05) and exclusion criteria (β=0.10). Finally, CRP, Ranson scale, ALB and SOD were considered as significant clinical indexes. Binary logistic regression analysis showed that CRP, Ranson scale, and ALB were independent risk factor for the death of SAP patients (p < 0.05, **Table 2**).

Table 1. Univariate analysis of the clinical data in 2 groups

Variate	Survival group (67)	Death group (27)	*t*/*Z* value	*P* value
Age (year)	55.12±17.31	56.70±20.78	0.379	0.706
RDW (%)	14.49±1.35	14.84±1.57	1.068	0.288
CRP (mg/L)	71.70±37.50	164.22±41.61	10.486	< 0.001
Ranson score	4 (3, 4)	5 (4, 5)	5.073	< 0.001
AMY (U/L)	630 (487, 1350)	973 (578, 1300)	0.184	0.854
WBC (10^9/L)	14.79±5.01	16.52±5.14	1.504	0.136
AST (U/L)	53 (33,200)	43 (25, 65)	1.406	0.160
ALB (g/L)	34.86±4.19	27.20±4.91	7.615	< 0.001
FBG (mmol/L)	9.25±4.51	11.49±5.17	2.088	0.039
Ca^{2+} (moL/L)	1.55±0.55	1.33±0.48	1.817	0.073
PDW (%)	15.7 (14.5, 16.2)	15.9 (13.3, 19.6)	1.306	0.192
TG (mmol/L)	1.55 (0.7, 4.7)	1.98 (1.0, 5.6)	0.117	0.907
SOD (IU/G)	92.02±24.68	68.70±24.74	4.140	< 0.001

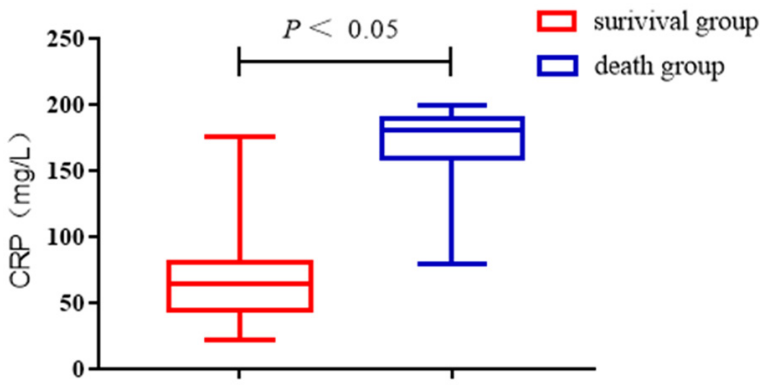

Figure 1. CRP level in 2 groups.

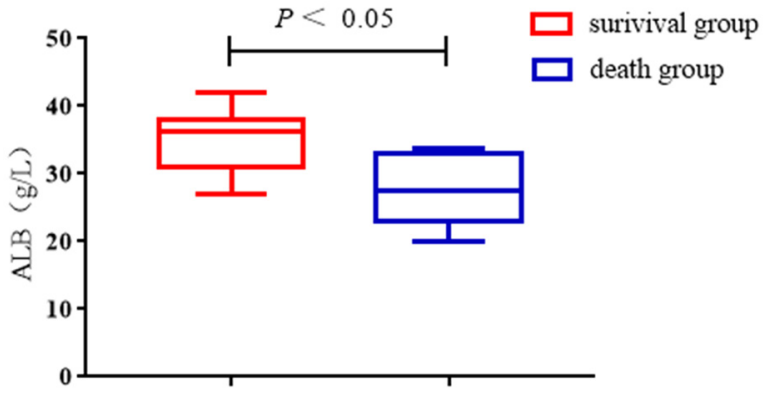

Figure 2. ALB level in 2 groups.

The analysis of ROC curve

The area under ROC curve of CRP, Ranson scale and ALB was 0.940, 0.815 and 0.866, respectively. The best cut-off value was > 121, > 3, ≤ 28.9, respectively and sensitivity was 81.48%, 96.30%, 70.37%, respectively (**Table 3**, **Figure 3**).

Death risk prediction of SAP patients by new model

The best cut-off value of CRP, Ranson scale and ALB was > 121, > 3, ≤ 28.9, respectively. We defined cut-off value as follows: Group A: CRP > 121 mg/L; Group B: ALB ≤ 28.9 g/L; Group C: Ranson scale > 3; Group D: Ranson scale > 3 or CRP > 121 mg/L; Group E: Ranson scale > 3 and CRP > 121 mg/L; Group F: Ranson scale > 3 or ALB ≤ 28.9 g/L; Group G: Ranson scale > 3 and ALB ≤ 28.9 g/L. The accuracy of the death risk prediction in group A-G was 86.2, 86.2, 62.8, 62.8, 88.3, 60.6 and 88.3 percent respectively. Therefore, the accuracy of death prediction in SAP patients was the highest in group D (OR 44.7, 95% CI: 12.4-161.4) and group F (OR 65.0, 95% CI: 12.9-328.0) (**Table 4**).

Discussion

The digestive enzyme secreted by the pancreas in AP patients could destroy the pancreas itself and its surrounding tissues, which formed acute inflammation and tissue damage, and this damage would further lead to enzyme release and a vicious cycle. Although advances of medical technology have significantly improved the prognosis of AP patients, some severe patients had a bad treatment effect which lead to the death of the patients. SAP has been widely investigated in the clinics, the prediction of SAP death risk has remained a great challenge. Many scoring systems or laboratory indexes are used to predict SAP prognosis, but the accuracy of these pre-

Table 2. Binary logistic regression analysis between the groups

Variate	B	S.E	Wals	*P* value	OR	95% CI
CRP	0.018	0.009	3.979	0.046	1.019	1.000~1.037
Ranson scale	2.247	1.011	4.939	0.026	9.460	1.304~68.638
ALB	-0.524	0.250	4.395	0.036	0.592	0.363~0.966
SOD	0.029	0.023	1.683	0.195	1.030	0.985~1.077

Table 3. Comparison of indexes in ROC curve

Variate	AUC	Youden index	Cut-off value	*P* value	95% CI	Sensitivity (%)	Specificity (%)
CRP	0.940	0.725	> 121	< 0.001	0.871~0.979	81.48	91.04
Ranson score	0.815	0.456	> 3	< 0.001	0.722~0.888	96.30	49.25
ALB	0.866	0.629	≤ 28.9	< 0.001	0.780~0.927	70.37	92.54

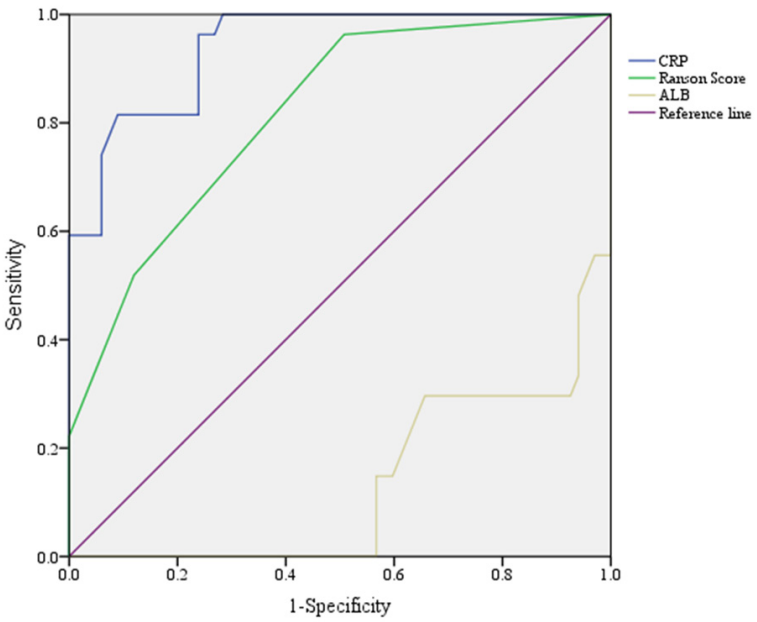

Figure 3. ROC curve of CRP, Ranson scale and ALB.

Research has shown that CRP has been used to evaluate SAP prognosis. Ajay K. Khanna [16] reported that the accuracy of CRP in evaluating AP severity was 93.3%, the accuracy of CRP in evaluating the risk of organ failure was 83.3% and the accuracy of CRP in predicting death risk was 63.3%. FatihBaşak [17] reported that the accuracy of CRP in evaluating AP severity was 80.1% and the accuracy in predicting death risk was 70.7%. In this study, the ROC curve showed that CRP (> 121 mg/L) was a relatively accurate index in evaluating SAP death risk and the accuracy was 86.2% (OR 29.5, 95% CI 8.6-100.7).

diction system need to be improved. The establishment of many prediction models has been based on laboratory examinations and imaging evidence, such as BISAP scale (≥ 3), Ransonscale (≥ 3), CT index (≥ 3) [11], CRP/ALB (> 16.28) [12], BMI (> 26 kg/m^2) [13]. SAP is defined as acute pancreatitis with consistent organ dysfunction and SAP in this study were the patients with Ranson score ≥ 3 defined by Atlantic conference in 2012.

CRP is an important acute phase inflammatory biomarker and reach at its peak level at 24-48 h of the disease. It is very simple and easy to measure CRP level in the serum [14, 15].

The reasons that SAP patients had hypoalbuminemia are as follows: 1) the inflammatory process could cause insulin resistance during infection and cause metabolic dysfunction. Consequently, the utilization rate of glucose decreases which lead to more degradation of ALB. 2) the stimulation of inflammation could cause decreased ALB generation in the liver. 3) during the process of stress, the vasopermeability was increased and ALB would penetrate into interstitial space, which lead to the loss of serum ALB. There are many physiological roles of ALB, including osmotic pressure maintenance, protect microvascular system, reduce vasopermeability, anticoagulation, acid-base neutr-

Table 4. Accuracy of death risk prediction

Group	Survival group (n=67)	Death group (n=27)	χ^2	*P*	OR (95% CI)	Sen (%)	Spec (%)	PPV (%)	NPV (%)	Accuracy (%)
A	5 (7.5)	19 (70.4)	40.056	< 0.001	29.5 (8.6~100.7)	70.4	92.5	79.2	88.6	86.2
B	5 (7.5)	19 (70.4)	40.056	< 0.001	29.5 (8.6~100.7)	70.4	92.5	79.2	88.6	86.2
C	34 (50.7)	26 (96.3)	17.295	< 0.001	25.2 (3.2~196.8)	92.3	49.25	43.3	97.6	62.8
D	34 (50.7)	26 (96.3)	17.295	< 0.001	25.2 (3.2~196.8)	92.3	49.25	43.3	97.6	62.8
E	6 (9.0)	22 (81.5)	48.401	< 0.001	44.7 (12.4~161.4)	81.5	91.1	78.6	92.4	88.3
F	37 (55.2)	27 (100.0)	17.757	< 0.001	1.7 (1.4~2.1)	100.0	44.8	42.12	100.0	60.6
G	2 (3.0)	18 (26.9)	46.594	< 0.001	65.0 (12.9~328.0)	66.7	97.0	90.0	87.83	88.3

alization, anti-infection, etc. [18, 19]. Li S et al. suggested that serum ALB is a good clinical prediction index of consistent organ failure of AP [20]. Therefore, hypoalbuminemia may have a cause-effect relationship with consistent organ failure of SAP, not just a marker of SAP severity. In this study, the ROC curve showed that ALB ≤ 28.9 mg/L is a relatively accurate index to evaluate SAP death risk and the accuracy rate is 86.2% (OR 29.5, 95% CI: 8.6-100.7). The accuracy rate of ALB and CRP in predicting SAP death risk was similar, which suggested that both the 2 indexes could predict SAP death risk.

There have been a lot of studies investigating the grade systems in predicting SAP prognosis. However, each grade system has its disadvantages, such as complexity, difficulty in application or low accuracy. The Ranson system was used in this study. Başak F [17] reported that the accuracy of Ranson scale (≥ 3) in predicting SAP death risk was 79.9%. Ranson [21] reported that the accuracy of Ranson scale (≥ 5) in predicting SAP death risk was 65%. This study showed that the accuracy of Ranson scale (> 3) in predicting SAP death risk was 62.8% (OR 25.2, 95% CI: 3.2-196.8). The purpose of our study was to design new model of CRP or ALB with Ranson scale in predicting SAP death risk and increase the accuracy of Ranson scale.

Furthermore, in this study sensitivity of predicting SAP death risk was 81.5%, the specificity was 91.1% and the accuracy was 88.3% (OR 44.7, 95% CI: 12.4-161.4) in group E (Ranson scale > 3 and CRP > 121) and 66.7%, 97.0 and 88.3 (OR 65.0, 95% CI: 12.9-328.0) in group G (Ranson scale > 3 and ALB ≤ 28.9). Both the 2 new models improved the accuracy of SAP death risk prediction with a similar accuracy rate. Therefore, SAP patients who are qualified in these 2 models should be intensively monitored, which could reduce mortality rate. There are several limitations in our study. First, CRP itself is a limited factor. Although we excluded reasons that might cause CRP elevation through exclusion criteria, there are to some extent several factors that might be neglected. Second, there are many factors that are associated with decreased ALB. Large scale prospective studies are also needed in the future. In conclusion, both CRP and ALB could improve the accuracy of SAP death risk prediction with Ranson scale.

Disclosure of conflict of interest

None.

Address correspondence to: Zhiqiang Feng, Beijing Chaoyang Emergency Medical Center, General Surgery, No. 27 Dongli, Zhouzhuang Jiayuan, Hongyannan Road, Chaoyang District, Beijing 100020, China. Tel: 86 18755252970; E-mail: fengzhiqiang187@163.com

References

[1] Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, Tsiotos GG, Vege SS; Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013; 62: 102-111.

[2] Harshit Kumar A, Singh Griwan M. A comparison of APACHE II, BISAP, Ranson's score and modified CTSI in predicting the severity of acute pancreatitis based on the 2012 revised Atlanta classification. Gastroenterol Rep (Oxf) 2018; 6: 127-131.

[3] Hirth M, Vujasinovic M, Münch M, Weiss C, Löhr M, Ebert MP, Schneider A. Monitoring and predicting disease activity in autoimmune pan-

creatitis with the M-ANNHEIM-AiP-Activity-Score. Pancreatology 2018; 18: 29-38.
[4] Gomatos IP, Xiaodong X, Ghaneh P, Halloran C, Raraty M, Lane B, Sutton R, Neoptolemos JP. Prognostic markers in acute pancreatitis. Expert Rev Mol Diagn 2014; 14: 333-346.
[5] Gonzálvez-Gasch A, de Casasola GG, Martín RB, Herreros B, Guijarro C. A simple prognostic score for risk assessment in patients with acute pancreatitis. Eur J Intern Med 2009; 20: e43-8.
[6] Hong W, Lin S, Zippi M, Geng W, Stock S, Basharat Z, Cheng B, Pan J, Zhou M. Serum albumin is independently associated with persistent organ failure in acute pancreatitis. Can J Gastroenterol Hepatol 2017; 2017: 5297143.
[7] Jin M, Zhang H, Lu B, Li Y, Wu D, Qian J, Yang H. The optimal timing of enteral nutrition and its effect on the prognosis of acute pancreatitis: a propensity score matched cohort study. Pancreatology 2017; 17: 651-657.
[8] Johnson CD, Toh SK, Campbell MJ. Combination of APACHE-II score and an obesity score (APACHE-O) for the prediction of severe acute pancreatitis. Pancreatology 2004; 4: 1-6.
[9] Li Y, Zhao Y, Feng L, Guo R. Comparison of the prognostic values of inflammation markers in patients with acute pancreatitis: a retrospective cohort study. BMJ Open 2017; 7: e013206.
[10] Shah AP, Mourad MM, Bramhall SR. Acute pancreatitis: current perspectives on diagnosis and management. J Inflamm Res 2018; 11: 77-85.
[11] Yadav J, Yadav SK, Kumar S, Baxla RG, Sinha DK, Bodra P, Besra RC, Baski BM, Prakash O, Anand A. Predicting morbidity and mortality in acute pancreatitis in an Indian population: a comparative study of the BISAP score, Ranson's score and CT severity index. Gastroenterol Rep (Oxf) 2016; 4: 216-220.
[12] Kaplan M, Ates I, Akpinar MY, Yuksel M, Kuzu UB, Kacar S, Coskun O, Kayacetin E. Predictive value of C-reactive protein/albumin ratio in acute pancreatitis. Hepatobiliary Pancreat Dis Int 2017; 16: 424-430.
[13] Türkoğlu A, Böyük A, Tanrıverdi MH, Gündüz E, Dusak A, Kaplan I, Gümüş M. The potential role of BMI, plasma leptin, nesfatin-1 and ghrelin levels in the early detection of pancreatic necrosis and severe acute pancreatitis: a prospective cohort study. Int J Surg 2014; 12: 1310-1313.
[14] Johnsen E, Fathian F, Kroken RA, Steen VM, Jørgensen HA, Gjestad R, Løberg EM. The serum level of C-reactive protein (CRP) is associated with cognitive performance in acute phase psychosis. BMC Psychiatry 2016; 16: 60.
[15] Brasselet C, Garnotel R, Pérotin S, Vitry F, Elaerts J, Lafont A, Metz D, Gillery P. Percutaneous coronary intervention-induced variations in systemic parameters of inflammation: relationship with the mode of stenting. Clin Chem Lab Med 2007; 45: 526-530.
[16] Khanna AK, Meher S, Prakash S, Tiwary SK, Singh U, Srivastava A, Dixit VK. Comparison of Ranson, Glasgow, MOSS, SIRS, BISAP, APACHE-II, CTSI Scores, IL-6, CRP, and procalcitonin in predicting severity, organ failure, pancreatic necrosis, and mortality in acute pancreatitis. HPB Surg 2013; 2013: 367581.
[17] Başak F, Hasbahçeci M, Şişik A, Acar A, Tekesin K, Baş G, Alimoğlu O. Can C-reactive protein levels increase the accuracy of the Ranson score in predictin the severity and prognosis of acute pancreatitis? A prospective cohort study. Turk J Gastroenterol 2017; 28: 207-213.
[18] Viasus D, Garcia-Vidal C, Simonetti A, Manresa F, Dorca J, Gudiol F, Carratalà J. Prognostic value of serum albumin levels in hospitalized adults with community-acquired pneumonia. J Infect 2013; 66: 415-23.
[19] Vincent JL, Russell JA, Jacob M, Martin G, Guidet B, Wernerman J, Ferrer R, McCluskey SA, Gattinoni L. Albumin administration in the acutely ill: what is new and where next? Crit Care 2014; 18: 231.
[20] Li S, Zhang Y, Li M, Xie C, Wu H. Serum albumin, a good indicator of persistent organ failure in acute pancreatitis. BMC Gastroenterol 2017; 17: 59.
[21] Yang L, Liu J, Xing Y, Du L, Chen J, Liu X, Hao J. Comparison of BISAP, Ranson, MCTSI, and APACHE II in predicting severity and prognoses of hyperlipidemic acute pancreatitis in Chinese patients. Gastroenterol Res Pract 2016; 2016: 1834256.