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Original Article

The predictive value of the shock index and modified shock index for the short-term mortality in patients with acute pulmonary embolism

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Abstract

Aim: The purpose of the study was to examine the relationship of shock index (SI) and modified shock index (MSI) with pulmonary embolism severity index (PESI) score in predicting short-term death in acute pulmonary embolism (APE) patients.

Material and Methods: This retrospective analysis included 104 consecutive patients whose APE was confirmed using computerized tomographic pulmonary angiography. For each patient, the PESI score, the SI, and the MSI were calculated. The main endpoint of the study was short-term mortality.

Results: Patients based on hemodynamic status or the PESI score upon admission were allocated into high risk and non-high risk groups. We noted that SI and MSI were significantly elevated in a high risk group (1.17 ± 0.17 vs. 0.77 ± 0.17 and 1.54 ± 0.29 vs. 1.05 ± 0.21, respectively, $p < 0.001$). In a correlation analysis, we showed that SI and MSI were significantly correlated with the PESI score for short-term mortality ($r = 0.491$ and $r = 0.504$, respectively, $p < 0.001$). An area under curve value of SI and MSI for short-term death were 0.66 (0.52-0.79 95% CI, $p = 0.022$) and 0.67 (0.53-0.80 95% CI, $p = 0.026$) respectively.

Conclusion: The present study findings demonstrated that the SI and MSI may be applicable in predicting short-death in patients with APE.

Keywords: Acute pulmonary embolism; modified shock index; pulmonary embolism severity index score; shock index; short-term death

INTRODUCTION

Acute pulmonary embolism (APE) is associated with significant mortality and morbidity in developed countries (1). The diagnosis of APE is often difficult due to different clinical presentations that may range from mild symptoms to sudden death (2, 3). Despite a significant advancement in diagnosis and treatment, short- and long-term death rates of patients presented with APE still remains in an undesired range. Therefore, it is an important step to stratify patients as a high or low risk in order to guide the therapeutic modalities in addition to predict possible complications. According to the current guidelines, patients presented with APE are stratified as high-risk or non-high risk depending on the presence of hypotension or shock upon admission (2). Moreover, the presence of right ventricular (RV) dysfunction in non-high risk patients is associated with higher mortality in APE patients (4-6). Pulmonary embolism severity index (PESI) score, which was introduced in 2005 by Aujesky and his colleagues, includes 11 clinical predictors with different prognostic weights (7). The PESI score has a discriminatory power to predict short-term death as well as adverse outcome events in patients with APE (8).

The shock index (SI) is calculated using heart rate (HR) and systolic blood pressure (SBP). Similarly, the modified shock index (MSI) is determined using HR and mean arterial pressure (MAP). Both indexes indicate the hemodynamic stability and are found to be useful in predicting mortality and the severity of injury in trauma patients (9-11). In this study, we hypothesized that because the PESI score includes multiple variables that are difficult to calculate, the SI and MSI as simple indexes might be used to estimate short-term death in APE patients. Therefore, the purpose of the study was to examine the correlation between admission SI and MSI with the PESI score for short-term death in APE patients.

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MATERIAL and METHODS

Study population and data collection

Between September 2017 and February 2019, 114 consecutive APE patients who were admitted to our hospital were retrospectively reviewed. After exclusion of 10 patients due to missing clinical data, the final study sample was consisted of 104 APE patients. We collected the information regarding baseline characteristics, laboratory, echocardiographic as well as computed tomographic pulmonary angiography (CTPA) findings from hospital's electronic database. In all of the patients, SBP, diastolic blood pressure (DBP), and HR were noted upon admission to the emergency service. PESI, SI and MSI were calculated for each patient. The following equation was used to calculate the SI; SI = first recorded HR/first recorded SBP. While the following equation was used to estimate the MSI; MSI=first recorded HR/first recorded MAP. The MAP was calculated using following formula; MAP = DBP+1/3(SBP-DBP). All of the patients were prescribed the standard therapy in accordance with current guidelines. The study was conducted according to the Helsinki Declaration of Principles after the approval from Local Ethic Committee (10/05/2019, no=1826).

Echocardiography and CTPA imaging

All of the patients underwent a standard echocardiographic examination by using the Philips EPIQ 7 device (Philips Healthcare, Andover, USA) and a 2.5 MHz probe after admission to hospital. The left ventricular ejection fraction (LVEF) was obtained using the modified Simpson method (12). The simplified Bernoulli equation was used to determine pulmonary arterial systolic pressure (PASP) (13).

In the present study, the diagnosis of APE was confirmed using multi-slice spiral CTPA (Toshiba Medical Systems Corporation, Tochigi, Japan) in all patients. An experienced radiologist confirmed the diagnosis of APE in case of complete or partial luminal filling defect was present in the main pulmonary arteries or its branches.

Laboratory analysis

All blood samples were collected from the antecubital vein upon admission to the emergency service. Hematologic parameters were measured as part of the automated complete blood count using the Sysmex hematology analyzers (Sysmex Corporation, Kobe, Japan). Plasma D-dimer levels were measured using an immunoturbidimetric assay. Biochemical measurements were performed using Beckman Coulter kits and calibrators. Creatinine kinase myocardial band (CK-MB) and troponin I levels were measured using a chemiluminescence immunoassay method (Access 2 Immunoassay System; Beckman Coulter, Inc.).

Definitions and short-term follow-up

Patients were classified as high risk if they presented with hemodynamic instability such as shock or hypotension regardless of the calculated PESI score (2, 7). Hemodynamically stable patients were classified as intermediate or low risk based on the PESI score or whether had a RV dysfunction in imaging tests or elevated cardiac myocardial injury markers (2). The main endpoint of the study was the short-term mortality within 30 days. Short-term mortality was accepted as death from any cause during first 30 days. All short-term events were evaluated and confirmed by a trained study coordinator.

Statistical analyses

Mean ± SD was used to express quantitative variables. To test the normality of the data, the Kolmogorov-Smirnov test was used. The categorical variables were expressed as numbers and percentages. Two-group comparisons were made by independent t test when numerical variables provided normal distribution condition, while the Mann Whitney U test was used when it was not provided. The chi-square test or Fisher exact test was used to evaluate the differences of the categorical variables. Correlation analyzes were calculated using Pearson's or Spearman's correlation tests. The effect size (Cohen's d) and power value (1-β) of the SI and MSI for short-term mortality were calculated using G*Power software (version 3.1.9.2). The effect size and power value were 2.352 and 0.985, respectively. A p-value of < 0.05 indicated statistical significance. All analyses were performed using SPSS version 22.0 (IBM, Chicago, Illinois).

RESULTS

Baseline Characteristics

Table 1 is a presentation of baseline characteristics of all patients. The study population mean age was 62.9±17.2 years, and 63 patients (60%) were female. We divided study population into two groups as; patients with a high risk APE and those without high risk APE. The high-risk group was older compared to the other group ($p < 0.05$). Predisposing factors including a previous coronary artery disease, diabetes mellitus, hyperlipidemia, etc. were similar between the two groups. On admission, high risk group had significantly elevated PESI score, SI, and MSI ($p < 0.05$ for each). As expected, SBP, DBP, and MAP were significantly lower in the high-risk group ($p < 0.05$ for each). Notably, the mortality was significantly elevated in the high-risk group ($p = 0.006$).

Laboratory and echocardiographic findings

Table 2 presents laboratory and echocardiographic findings of all patients. Comparison of laboratory parameters showed that there were no statistically differences between groups. In terms of echocardiographic findings, high-risk group had a lower LVEF and RV tricuspid annular plane systolic excursion (TAPSE) ($p = 0.048$ and $p = 0.018$, respectively) and higher RV diameter ($p = 0.03$). Other echocardiographic findings were similar between the groups.

Correlation of PESI score with echocardiographic findings, SI and MSI

Correlation of SI and MSI with baseline characteristics, echocardiographic findings and PESI score are shown

Table 1. Baseline demographic characteristics findings of all patients

	High risk group (n=27)	Non-High risk group (n=77)	P value
Age, years	67.67 ± 14.46	61.23 ± 17.86	0.108
Female gender, n (%)	14 (51.9)	49 (63.6)	0.284
Body mass index, kg/m^2	28.05 ± 5.59	28.99 ± 5.72	0.47
Coronary artery disease, n (%)	5 (18.5)	12 (15.6)	0.466
Hypertension, n (%)	18 (66.7)	44 (57.1)	0.382
Diabetes mellitus, n (%)	10 (37)	24 (31.2)	0.578
Current smoking status, n (%)	10 (37)	25(32.5)	0.667
Hyperlipidemia, n (%)	8 (29.6)	14 (18.2)	0.222
DVT history, n (%)	7 (25.9)	21 (27.3)	0.892
Operation history, n (%)	8 (29.6)	21 (27.3)	0.815
Immobilization, n (%)	13 (48.1)	24 (31.2)	0.117
Cerebrovascular disease, n (%)	3 (11.1)	7 (9.1)	0.508
Cancer, n (%)	8 (29.6)	17 (22.1)	0.436
On admission			
PESI score	130.63 ± 26.02	91.52 ± 33.02	<0.001
Systolic blood pressure, mmHg	85.56 ± 9.14	129.25 ± 18.23	<0.001
Diastolic blood pressure, mmHg	56.22 ± 10.66	76.53 ± 10.85	<0.001
Mean arterial pressure, mmHg	66 ± 9.26	94.23 ± 11.50	<0.001
Heart rate, beats per minute	99.70 ± 15.23	98.08 ± 16.93	0.646
Shock index	1.17 ± 0.17	0.77 ± 0.17	<0.001
Modified shock index	1.54 ± 0.29	1.05 ± 0.21	<0.001
Short-term mortality, n (%)	11 (40.7)	11 (14.3)	0.006

Continuous variables are presented as mean ± SD, nominal variables presented as frequency (%).
DVT: Deep Vein Thrombosis; PESI: Pulmonary Embolism Severity Index

Table 2. Laboratory and echocardiographic findings of all patients

	High risk group (n=27)	Non-High risk group (n=77)	P value
Laboratory variables			
D-dimer, ng/mL	9.23 ± 12.32	5.23 ± 3.84	0.292
Troponin I, pg/mL	29.69 ± 95.20	30.22 ± 126.94	0.763
Creatine kinase myocardial band, ng/dL	6.56 ± 7.20	3.19 ± 3.47	0.133
Blood urea nitrogen, mg/dL	39.91 ± 18.26	45.78 ± 26.11	0.207
Creatinine, mg/dL	0.93 ± 0.24	1.17 ± 1.35	0.792
Glomerular filtration rate, ml/L	74.03 ± 22.54	76.08 ± 23.86	0.742
Glucose, mg/dL	182.36 ± 92.60	151.47 ± 62.86	0.13
ALT, U/L	29.24 ± 31.05	36.57 ± 45.01	0.083
AST, U/L	33.88 ± 33.31	34.51 ± 28.99	0.957
White blood cell, cells/µL	10.24 ± 4.35	10.37 ± 4.56	0.892
Hemoglobin, g/dL	11.48 ± 1.79	11.88 ± 1.93	0.331
Platelets, cells/µL	220.65 ± 77.63	253.63 ± 89.64	0.079
Echocardiography parameters			
LVEF, %	52.77 ± 9.66	56.29 ± 7.71	0.048
LV end-systolic diameter, mm	2.98 ± 0.86	2.89 ± 0.59	0.6
LV end-diastolic diameter, mm	4.66 ± 0.60	4.66 ± 0.53	0.965
LA diameter, mm	3.77 ± 0.47	4.25 ± 3.97	0.661
RV TAPSE	1.63 ± 0.37	2.01 ± 0.37	0.018
RV diameter, mm	4.83 ± 0.51	3.95 ± 1.25	0.03
PASP, mmHg	39.04 ± 12.96	36.43 ± 12.27	0.401

Continuous variables are presented as mean ± SD, nominal variables presented as frequency (%). ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, LVEF: Left Ventricular Ejection Fraction, LV: Left Ventricle, LA: Left Atrium, RV: Right Ventricle, TAPSE: Tricuspid Annular Plane Systolic Excursion, PASP: Pulmonary Artery Systolic Pressure

Table 3. Correlation of shock index and modified shock index with baseline characteristics, echocardiographic findings and PESI score

	Shock index		Modified shock index	
Correlation between	R value	P value	R value	P value
PESI Score	0.491	<0.001	0.504	<0.001
Systolic blood pressure	-0.767	<0.001	-0.683	<0.001
Diastolic blood pressure	-0.561	<0.001	-0.667	<0.001
Mean arterial pressure	-0.714	<0.001	-0.733	<0.001
Heart rate	0.588	<0.001	0.618	<0.001
RV TAPSE	-0.598	<0.001	-0.525	<0.001
LVEF	-0.245	0.018	-0.259	0.013
PASP	0.319	0.002	0.319	0.002

PESI: Pulmonary Embolism Severity Index; RV: Right Ventricle, TAPSE: tricuspid Annular Plane Systolic Excursion, LVEF: Left Ventricular Ejection Fraction, PASP: Pulmonary Artery Systolic Pressure

in Table 3. We observed that PESI score was positively correlated with SI (r = 0.491, p < 0.001) and MSI (r = 0.504, p < 0.001).

ROC curve analysis

A ROC analysis demonstrated that area under curve values of SI and MSI for short-term death were 0.66 (0.52-0.79 95% CI, p = 0.022) and 0.67 (0.53-0.80 95% CI, p = 0.026), respectively (Figure 1). The best cut-off value for SI obtained by the ROC curve analysis was 0.87 for the prediction of short-term death (sensitivity: 68.2%, specificity: 60.0%). The best cut-off value for MSI obtained by the ROC curve analysis was 1.16 for the prediction of short-term death (sensitivity: 68.2%, specificity: 60.8%).

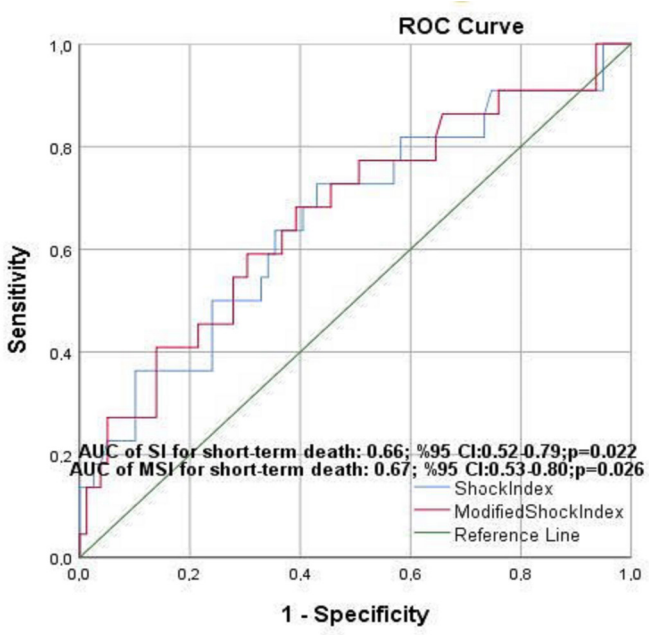

Figure 1. Area under curve values of SI and MSI for short-term death with ROC analysis

DISCUSSION

In this study, we were able to show that the SI and MSI, calculated in a simple way, were correlated with the PESI in predicting short-term death in APE patients. Patients within the high risk group had significantly elevated short-term mortality in addition to higher admission PESI score, SI and MSI.

APE is a life-threatening but potentially reversible disease which occurs as a result of the obstruction of the main pulmonary artery or its branches (4,14). Acute increase in the RV outflow resistance causes acute RV dilation and dysfunction which leads to decrease in the preload of the LV. In addition, due the ventricular interdependence, LV diastolic compliance is decreased, which may ultimately lead to acute cardiogenic shock and death (5,15).

In recent years, several studies have investigated the potential utility of different risk scores, imaging techniques, and some biomarkers to estimate the risk of death in APE patients. For example, some biomarkers including brain natriuretic peptide, cardiac troponins, and CK-MB have been shown to be useful to predict the myocardial damage, the RV dysfunction as well as hemodynamic impairment and short-term mortality among APE patients (6,16-18). Also, Khemasuwan et al. examined the relationship between some RV echocardiographic parameters and short-term death in patients with APE and demonstrated that some parameters independently related to short-term death (19). In a recent meta-analysis, the RV dysfunction marked by CTPA is found to be related with elevated risk of mortality in hemodynamically stable APE patients (20).

Thus far, several scoring systems have been investigated and found to be useful in APE patients. For example, the PESI score is the most well-known risk scoring system. The PESI score determine the risk of death by including several variables such as gender, age, pulse rate, chronic heart failure etc. The PESI score has been mainly developed to identify low risk APE patients. In addition, this index has been shown to be powerful in demonstrating short-term of death in APE patients (21-23). However, despite its serious power, the calculation can sometimes be problematic due to the presence of several parameters.

The SI and MSI represent the hemodynamic status of the

patient. Admission HR, SBP, and MAP, all of which can be obtained at the first medical contact, are sufficient to calculate the SI and MSI. Initially, the predictive value of the SI for mortality was demonstrated in traumatic patients. Also, the SI has been shown to be useful in evaluating the acute critical disease in emergency department (9,24). Although a study conducted by Liu showed that the MSI is more valuable than SI in predicting mortality in traumatized adult patients (10), both indexes are shown to be good in predicting massive bleeding. Moreover, both indexes were also associated with the increase risk of mortality, the severity of injury, and days of stay in intensive care units (25).

In the present study, we demonstrated that the SI and MSI can be used to estimate short-term mortality in APE patients because both indexes are positively correlated with PESI score. We also considered that the SI and MSI may be an indicator of severity of disease in APE patients because as the severity of APE increases, the presence of tachycardia and hypotension becomes prominent, thus leading to high index scores.

Our study findings may be useful and valuable in terms of clinical applicability. Both index depends on the hemodynamic parameters that can be easily obtained at the emergency service. Of note, patients with a high SI and MSI should be closely followed-up since these patients may have elevated mortality rates.

LIMITATIONS

If we talk about the limitations of the study; first, our study had a cross-sectional and retrospective design. However, we tried to enroll all consecutive APE patients. Second, we were not to be able to evaluate the main cause of mortality since we focused only on all-cause mortality in the study. Third, since the number of high-risk patients included in the study was small, this might be another reason why some of the parameters in our correlation analysis showed a weak correlation. Fourth, multivariate analysis was not used in the study because we had a limited number of event, which may cause overfitting in the model. Finally, there is a need to validate our study findings with larger scale and prospective studies.

CONCLUSION

Based on the study findings, the SI and MSI were significantly higher in high-risk APE patients, and these indexes were positively correlated with PESI score for 30 days mortality. Therefore, these simple indexes may be used in predicting short-term death in APE patients.

Competing interests: The authors declare that they have no competing interest.

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