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Prognostic Impact of Thrombolysis in Myocardial Infarction Risk Index on Hospitalization Mortality of Patient with Acute Pulmonary Embolism

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ABSTRACT

Introduction: Acute pulmonary embolism (PE) is one of the deadly cardiovascular diseases. One of the indexes proposed in these patients for risk stratification is the Thrombolysis in Myocardial Infarction (TIMI) risk index (TRI), which includes three parameters of systolic blood pressure, age, and heart rate. This study aimed to evaluate the predictive value of TRI on in-hospital and 30-day mortality of PE patients.

Materials and Methods: This cross-sectional study included 345 patients who were diagnosed with acute PE in Madani Heart Center from January 2012 to January 2017. Demographic characteristics, hemodynamic findings upon first admission, type of treatment (i.e., thrombolytic, anticoagulant, or surgery), as well as in-hospital and 30-day outcomes were recorded for all patients. The TRI and simplified Pulmonary Embolism Severity Index (PESI) were calculated for all patients.

Results: The overall and in-hospital mortality rates were 8.7% and 8.1%, respectively. The mortality group were significantly older and had significantly higher heart rates, cardiac troponin levels, simplified PESI scores, and TRI followed by lower systolic blood pressure and O2 saturation. Moreover, the TRI obtained specificity, sensitivity, positive, and negative predictive values of 98.78%, 25.25%, 89.29%, and 76.66%, respectively, using receiver operating characteristic curves and a cut-off value of 36.73. Using the multiple logistic regression analysis we found that TRI>36.73, older age, higher heart rate and lower SBP could predict 30-day mortality.

Conclusion: The results showed that the risk of in-hospital mortality is higher with an increase in TRI. Furthermore, despite the high specificity, lower sensitivity limits its utility.

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Introduction

Acute pulmonary embolism (PE) is a common disease, which often could be fatal. The PE is related to high in-hospital or short-term mortality mostly associated with the hemodynamic instability and right ventricle (RV) dysfunction (1, 2). Moreover, it would be presented as an incidental finding on computed tomography (CT) scan or as a very severe debilitating disease (2).

The identification of the risks associated with PE outcome could help determine patients' admission to hospital or treatment as outpatients. Different risk stratification methods, biomarkers, and imaging modalities have been utilized in risk stratification of those who are at higher risk of mortality after PE, including the Pulmonary Embolism Severity Index (PESI) (3, 4). However, there are controversies on the most accurate predictor in this regard.

Recent studies have indicated that age, heart rate (HR), and systolic blood pressure (SBP) are all prognostic factors for the

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adverse outcomes of acute PE (5-7). On the other hand, the Thrombolysis In Myocardial Infarction (TIMI) Risk Index (TRI), which is usually used for the risk assessment of patients with ST-elevation myocardial infarction (STEMI), also included age, HR, and SBP (8). Therefore, it is probable that TRI could be used in evaluating the outcome of acute PE. According to two recently published studies which evaluated TRI, the in-hospital and long-term outcome could be predicted in PE patients (8, 9). However, there are few studies evaluating TRI with conflicting results and there is a need for further investigations. Therefore, this study aimed to evaluate the prognostic impact of TRI on the in-hospital mortality rate in patients with acute PE.

Materials and Methods

This cross-sectional study included 345 patients who were objectively diagnosed with acute PE based on lung CT angiography. Moreover, they were selected from those who were admitted to Madani Heart Center, in Tabriz, Iran, from January 2012 to January 2017. All patients were above 18 years of age and were subjected to transthoracic echocardiography (TTE) within the first 24 h upon admission. The exclusion criteria were: 1) uncertain diagnosis, 2) incomplete medical records regarding hemodynamic status upon admission, and/or 3) lack of echocardiographic evaluations, including Tricuspid Annular Plane Systolic Excursion (TAPSE). The study protocol was approved by the ethics committee of Tabriz University of Medical Sciences, Tabriz, Iran.

Demographic characteristics of the patient, past medical history, physical examination results, hemodynamic findings, as well as the type of treatment were recorded in this study. All patients were stratified according to PESI as the standard stratification index. The TRI was comprised of age, HR, and SBP and calculated for all patients using MedCacl software.

Furthermore, the TTE was performed on all patients using a VIVID 7 system. In addition, left ventricle (LV) ejection fraction, pulmonary arterial peak systolic pressure, and TAPSE were recorded in this study. The RV dysfunction was defined using the RV/LV ratio measured in a four-chamber view, and the ratio greater than 0.9 was considered as RV dysfunction.

In-hospital mortality was considered as the primary endpoint. The patients were followed for 30 days after discharge using the medical records along with recording in-hospital and 30-day mortality rates. It is worth mentioning that the association of mortality rate with TRI and PESI was evaluated in this study.

Statistical Analysis

All data were analyzed in SPSS software (version 20), and the results were expressed as mean±SD and percentages. Furthermore, the Chi-square test, Fischer's exact test, and/or independent t-test were used to compare data between groups. Similarly, receiver operating characteristic (ROC) curve analysis was performed to define an optimal threshold for TRI in predicting mortality. The positive and negative predictive values (PPV and NPV) were also calculated using ROC findings and area under curve and the proper cut-off value was obtained using Youden's Index. A p-value less than 0.05 was considered statistically significant.

Results

Table 1 summarizes the baseline, echocardiographic, and follow-up findings of PTE patients. The RV dysfunction was present in 55.1% of the patients, and TAPSE was abnormal in 72.5% of the cases. According to the simplified PESI, 64.9% of the patients were in the high-risk group. Overall, the mortality rate was 8.7% with most cases occurred during the admission.

Due to the lower rate of mortality in the 30-day follow-up, the different findings were compared between those with and without in-hospital mortality (Table 2). The patients in the mortality group were significantly older and had higher heart rates with lower SBP and O2 saturation followed by higher cardiac troponin levels. Regarding the echocardiographic findings, abnormal TAPSE was significantly higher in these patients; however, there was no significant difference between the groups in terms of the rate of RV dysfunction. On the other hand, the mortality group obtained higher scores in two stratifications, TRI, and simplified PESI. According to the simplified PESI, the

Mortality occurred significantly in high-risk patients.

The TRI role in predicting in-hospital mortality was evaluated using ROC curves (Figure 1). The area under the curve (AUC) was estimated at 0.918 (P<0.001), which yielded to a cut-off point of 36.73 (according to ROC curves). It was observed that TRI >36.73 had acceptable specificity (98.78%), whereas the sensitivity was low (25.25%). Moreover, PPV and NPV were determined at 89.29% and 76.66%, respectively. Additionally, a significantly positive correlation was observed between TRI and simplified PESI using Pearson's correlation (r=0.502, P<0.001).

Using the multiple logistic regression analysis considering the significant comparison between those with and without mortality, we found that TRI>36.73, older age, higher heart rate and lower SBP could predict 30-day mortality.

Table 1: The baseline, echocardiographic and follow-up findings of PTE patients

		Frequency (%) or Mean ± SD
Age (years)		59.62±16.77
Gender	Male	181 (52.6%)
	Female	163 (47.4%)
Hypertension		85 (24.63%)
Previous venous thromboembolism		
Deep vein thrombosis		17 (4.9%)
Pulmonary embolism		4 (1.15%)
Baseline hemodynamics		
Heart rate (bpm)		98.54±20.81
Systolic blood pressure (mmHg)		122.28±23.06
Oxygen saturation (%)		88.85±7.87
Echocardiographic findings		
RV diameter		38.42±8.76
LV diameter		40.43±7.05
RV/LV ratio>0.9		192 (55.1%)
TAPSE		7.84±0.52
Abnormal TAPSE (<17)		250 (72.5%)
SPAP		44.39±17.75
cTnI		0.23±0.03
Simplified PESI		0.93±0.84
Simplified PESI	Low risk	121 (35.1%)
	High risk	224 (64.9%)
TIMI risk index		31.53±19.3
Treatment type	Anticoagulation	273 (79.1%)
	Fibrinolytic	56 (16.2%)
	Surgical embolectomy	16 (4.7%)
In-hospital Mortality		28 (8.1%)
30-day Mortality		2 (0.6%)

PESI: Pulmonary Embolism Severity Index; TAPSE: Tricuspid annular plane systolic excursion; TRI: TIMI risk index; SBP: Systolic blood pressure; HR: Heart rate; SPAP: Systolic pulmonary artery pressure

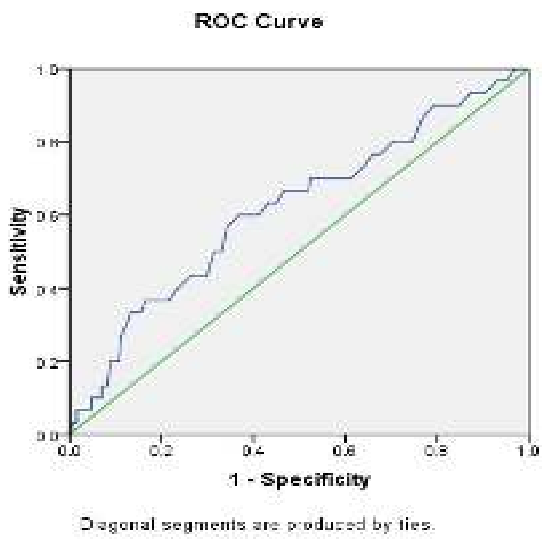

Figure 1. Receiver operating characteristic curve analysis for optimal threshold value of thrombolysis in myocardial infarction risk index.

Table 2: Baseline and in-hospital findings between patients with and without in-hospital mortality

			Mortality group	Alive group	P value
Age (years)			77.21±10.11	58.07±16.35	<0.001*
Gender	Male		16 (57.1%)	165 (52.1%)	0.6
	Female		12 (47.9%)	152 (47.9%)	
HR			108.14±22.55	97.69±20.47	0.01*
SBP			109.39±21.54	123.42±22.87	0.002*
Oxygen saturation (%)			84.28±8.04	89.25±7.74	0.001*
SPAP			47.32±13.24	44.13±18.09	0.36
cTnI			0.47±0.22	0.20±0.02	0.01*
RV dysfunction			19 (67.9%)	171 (53.9%)	0.15
Abnormal TAPSE			26 (92.9%)	224 (70.7%)	0.01*
TRI			61.47±21.52	26.93±15.47	<0.001*
Simplified PESI			1.67±0.86	0.86±0.81	<0.001*
Simplified PESI		Low risk	3 (10.7%)	118 (37.2%)	0.005*
		High risk	25 (89.3%)	199 (62.8%)	

* p is two sided-significant. PESI: Pulmonary Embolism Severity Index; TAPSE: Tricuspid annular plane systolic excursion; TRI: TIMI risk index; SBP: Systolic blood pressure; HR: Heart rate.

Table 3: Multiple logistic regression analysis evaluating the predictive factors on mortality

	Odds ratio	Confidence interval 95%		P value
		Lower limit	Upper Limit	
Age	0.901	0.849	0.955	<0.001
Systolic blood pressure	1.033	1.009	1.058	0.007
Heart rate	0.978	0.957	0.999	0.04
O2 Saturation	1.051	0.994	1.111	0.08
Simplified PESI	0.691	0.148	3.225	0.63
TRI	4.140	1.023	16.526	0.04
TAPSE	1.039	0.975	1.107	0.23
CTNI	0.790	0.457	1.365	0.39

* p is two sided-significant. PESI: Pulmonary Embolism Severity Index; TRI: TIMI risk index

Discussion

The obtained findings in this study showed that patients who died in hospital were older with unstable hemodynamics upon admission; moreover, they obtained higher scores in terms of troponin, TRI, and simplified PESI. Additionally, the TRI had significant specificity followed by very low sensitivity in predicting in-hospital mortality.

It is important to stratify PE patients who are at the risk of adverse outcomes and mortality. Different stratifying methods have been recommended in recent years; however, there is still a need for a standard method. Previous studies have revealed that age is an important determinant of PE severity (6, 9, 10). Among hemodynamic variables, lower SBP and oxygen saturation, as well as higher HR are the other factors affecting the patients' outcome. Moreover, some or all of them are usually utilized in different stratification methods, such as TRI, PESI, and simplified PESI (8-11). Cardiac troponin-I has also been evaluated in previous studies, and it was shown that its elevated levels are associated with an increased risk of mortality in the first three months after acute PE (11, 12). These results are in line with the findings in this study.

The in-hospital mortality rate was determined at 8.1% in this study. The reported rate of in-hospital and overall mortality varies in different studies ranging from 2.3%-5.4% to as high as 50.5% (4, 9-14); nonetheless, the most recent studies similar to the present study reported mortality rate to be lower than 10%. The reason for this variation could be attributed to the study population, older age, and inclusion of more high-risk patients.

The TRI has been previously proven to predict in-hospital and 30-day mortality rates among STEMI patients (15). The variables in TRI include age, SBP, and HR, which have a prognostic role in PE severity; therefore, it seems feasible to employ this index for risk stratification of patients who are at high risk of mortality. Zuin et al. (9) indicated that TRI had the ability to predict

30-day mortality and adverse outcomes in PE patients. Moreover, they calculated a cut-off of >45 for TRI which had high AUC (0.91), as well as PPV and NPV of 8.3% and 96%, respectively. However, they mentioned no sensitivity and specificity for TRI>45. In another study conducted by Keskin et al. (8), they demonstrated the AUC of 0.77 for TRI>38, which had the sensitivity and specificity of 68% and 70%, respectively; however, they reported no PPV and NPV in their results.

In the present study, considering a cut-off TRI>36.73, sensitivity, specificity, PPV, and NPV were 25.25%, 98.78%, 89.29%, and 76.66%, respectively. Furthermore, the highest specificity and PPV were obtained in this study, compared to previous studies, whereas the low sensitivity was its limitation. When the AUC is between 0.75 and 0.92 in a study, it has good accuracy, and the results are feasible (16). Given that the AUC is 0.918 in the current study, it can be claimed that the results have good accuracy.

We observed that TRI>36.73, older age, higher heart rate and lower SBP could predict 30-day mortality in PE patients. Similarly, Keskin et al. (8) reported TRI could predict short term and long-term outcome in PE patients. Zuin et al. (9) also reported that TRI>45 could predict 30-day mortality.

Limitations of the Study

The retrospective design of this study is considered a major limitation in the research process leading to missing some variables; therefore, there was no possibility to evaluate all parameters. Moreover, the small sample size, compared to previous studies, which yielded a lower rate of mortality was another limitation that limited the interpretation of our findings. In addition, this study evaluated 30-day follow-up outcomes; accordingly, further studies are recommended to assess long-term outcomes.

Conclusion

The results showed that an increase in TRI leads to a higher risk of in-hospital mortality. Moreover, despite its high specificity to exclude those at a lower risk of mortality, it is not sensitive enough to predict mortality. However, since this study is among the few studies that have evaluated the TRI role in mortality among PE patients, the findings should be interpreted cautiously. Further studies are necessary to confirm these findings.

Conflicts of Interest

The authors declare that they have no competing interest regarding the publication of this study.

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