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Clinical

Prediction of mortality in hospital survivors of STEMI: External validation of a novel acute myocardial infarction prognostic score☆,☆☆,★

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ABSTRACT

Introduction & objective: Recently we developed and internally-validated the Soroka Acute Myocardial Infarction (SAMI) Score for prediction of all-cause long-term mortality (c-statistic 0.83–0.94) among hospital-survivors of AMI. We aimed to perform an external-validation of the SAMI score for long-term risk-stratification of STEMI patients undergoing PCI.

Methods & settings: A prospective registry of 1273 STEMI patients treated using primary PCI and discharged alive from Rabin Medical Center in Israel between 2004 and 2014 (age 60.8 ± 12.5 years, 83% males) was utilized for the validation. Chi-square test and logistic regression were used for calibration, and c-statistic (ROC procedure) for discrimination assessment of the SAMI score.

Results: All-cause mortality following one- and 5-years post-discharge was 3.8% and 8.1%, respectively. SAMI score values ranged between (−5) and (+15) points (median 2-points). In a univariate analysis the SAMI score variables were significantly associated with 1- and 5-years mortality. Higher SAMI score was associated with increased risk for dying: a one-point increase was associated with OR of 1.33 (95%CI: 1.24–1.42, $p < 0.001$) and 1.37 (95%CI: 1.29–1.44, $p < 0.001$) for 1- and 5-years mortality respectively. No statistically significant difference was found in the currently observed mortality rates by groups of SAMI score and the expected mortality rates as per the SAMI score index. The c-statistics were 0.82 and 0.83 for 1- and 5-year mortality, respectively.

Conclusions: The SAMI score is a simple, robust and now also externally-validated prognostic tool for prediction of long-term all-cause mortality in hospital survivors of STEMI.

1. Introduction

Over the past decades, significant progress in the management of patients with ST elevation acute myocardial infarction (STEMI) led to improved survival and increased life expectancy [1,2]. However, these patients remain at increased risk for long-term mortality following hospital discharge as compared to matched general population [3]. Furthermore, signals of increasing mortality due to non-cardiovascular causes, in these patients, were reported [4]. Thus, more attention is being shifted towards understanding and improving long-term all-cause mortality of STEMI survivors.

Risk stratification following acute myocardial infarction (AMI) plays a pivotal role in identification of patients whose outcomes can be improved through specific interventions [5,6]. Various risk stratification models for different types of AMI and in specific subgroups of patients were introduced in the last decade [7–12]. However, many models have been developed from large randomized clinical trial populations, in which the generalizability and/or external validity to reliably predict the mortality risk among "all comers" STEMI patients is questionable. In addition, these models often had restricted data entry especially non-cardiovascular co-morbidity, they greatly rely on real-time evaluation hence, post-hoc assessment is often not feasible and are designed for prediction of short-term prognosis [7–12]. Thus, risk stratification tools for long-term post-discharge prognosis of hospital STEMI survivors are scarce. Furthermore, contemporary epidemiological trends in AMI were suggested to potentially compromise the validity of classical risk-stratification tools, especially for long-term prognosis [13].

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Recently, we developed and validated a new risk score: the Soroka Acute Myocardial Infarction (SAMI) Score [14]. The SAMI score is a simple assessment tool, based entirely on "real life" available and easily accessible clinical information, including non-cardiovascular comorbidities [14]. The SAMI score is a dedicated model for prediction of long-term all-cause mortality, of hospital survivors of AMI (STEMI and non-STEMI altogether). It was shown to be highly accurate for this outcome with c-statistics of 0.83–0.94 for up to10 years post discharge [14,15]. The current study was aimed to perform an external validation of the SAMI score for predicting the long-term all-cause mortality in contemporary STEMI patients undergoing primary percutaneous coronary intervention (PPCI).

2. Methods

2.1. Study population

In the current study we analyzed STEMI patients that underwent PPCI at Rabin Medical Center in Petach Tikva, Israel between 2004 and 2014. Patients were included in a prospective STEMI registry [16]. The database included detailed demographic, clinical, angiographic and procedural data as previously described by our group [16]. Patients were excluded from the present study if admitted ≥12 h from the onset of symptoms, admitted before or after the latter period, died in-hospital or in case of missing data for SAMI score calculation. The current study was approved by the local ethics committee.

2.2. Data sources and classifications

Mortality data, obtained prospectively, were confirmed using records of the Interior Ministry of Israel. Additional parameters that are part of the SAMI Score were obtained retrospectively from the hospitals' computerized information systems. Grouping of diseases and interventions were based on ICD-9-CM discharge codes and the laboratory data according to the definitions applied in the SAMI score [14].

2.3. SAMI score and primary outcome

The SAMI risk score is comprised of 11 parameters including traditional cardiovascular risk factors, non-cardiovascular comorbidity, in-hospital evaluation and interventions, and is calculated as an arithmetic sum of the weights of all variables (Table 1). The weight of each parameter in the index is based on its' OR values in the original model [14]. Primary outcomes were: one- and 5-year post hospital discharge all-cause mortality.

2.4. Statistical analysis

Statistical analyses were performed with IBM SPSS statistics V.22. The prevalence rates of SAMI parameters were calculated. The total score for each patient was calculated based on original SAMI tool. The accuracy of the score was assessed by calculation and comparison of observed and expected (as per the SAMI score) mortality rates (calibration), and by area under the receiver operating characteristic (ROC) curve (discrimination).

3. Results

Overall 1273 STEMI patients were included, mean age 60.8 ± 12.5 years, 83% males. In-hospital mortality rate was 3.4% (patients excluded from current study). One- and 5-year post-discharge all-cause mortality rates were 3.8% and 8.1% respectively. The parameters comprising the SAMI index, their weights based on the original index and the prevalence in the current cohort are presented in Table 1. As presented in Table 2 nearly all variables comprising the SAMI score were significantly associated with 1- and 5-years mortality in the current cohort. The SAMI total score values ranged between (−5) to (+15) points, mean 3.3 ± 3.76 points and median 2 points. A total of about 35% of the cohort had a SAMI score 0 points or lower, while about 6% had a score of 11 points or greater (Fig. 1). One year mortality rate was 0.4% and 18.1%, for the former and the latter SAMI score category respectively. Similarly, five year mortality rate was 0.4% and 44.4% respectively.

Higher personal total score was associated with greater risk for post-discharge all-cause mortality: one point increase was associated with odds ratio (OR) of 1.33 (95% CI: 1.24–1.42, $p < 0.001$) and 1.37 (95% CI: 1.29–1.44, $p < 0.001$) for one- and 5-year mortality respectively. The mortality rates according to the categories of the SAMI total score were similar to the expected rates as displayed in Fig. 2. ROC curve analyses yielded c-statistics of 0.818 and 0.830 for one- and 5-year mortality, respectively.

Table 1
SAMI score parameters: original weights and prevalence in the study population.*

Parameter	Original SAMI weight	Prevalence - n (%) (n = 1273)
Age, years		
<65	0	872 (68.5)
65–75	2	222 (17.4)
>75	4	179 (14.1)
Results of echocardiography		
No results of echocardiography study	2	0
At least one of following		
Severe left ventricular dysfunction	4	120 (9.4)
Concentric or significant left ventricular hypertrophy		191 (15.0)
Moderate or severe mitral regurgitation		39 (3.1)
Moderate or severe pulmonary hypertension		10 (0.8)
Results of laboratory tests		
Plasma sodium <135 mEq/L	2	377 (29.6)
Intervention		
Conservative	0	NA
Percutaneous coronary intervention (PCI)	−3	1254 (98.5)
Coronary artery bypass grafting (CABG)	−6	19 (1.5)
Groups of diseases		
Renal diseases	2	305 (24.0)
Anemia	2	450 (35.3)
Obesity	−2	231 (18.1)
At least one of following		
Gastro-intestinal bleeding	3	8 (0.6)
Chronic obstructive pulmonary disease (COPD)		65 (5.1)
Malignant neoplasm		86 (6.8)
Alcohol or drug addiction		22 (1.7)
Schizophrenia or psychosis		12 (0.9)
Neurological disorders		119 (9.3)

* Total SAMI score for each patient is calculated as the sum of weights.

4. Discussion

The current study comprises an external validation of a novel comprehensive risk stratification tool the SAMI risk score, in patients with STEMI that underwent PPCI and survived hospitalization. The study clearly shows that the SAMI score is highly accurate for long-term (up-to 5 years) prediction of all-cause mortality in this population. The SAMI risk score was originally developed and validated for all patients discharged-alive following AMI (i.e. STEMI and non-STEMI), albeit the current external-validation comprised only STEMI patients. Nevertheless, the score performed remarkably well, especially regarding discrimination between long-term survivors and deceased. Actually c-statistics was higher than that previously reported for most scores evaluated for such long follow-up periods [17,18]. It should however

Table 2
Relative risk for 1- and 5-year mortality by the SAMI index variables.

Variable	Values	1 year mortality		5 year mortality	
		OR (95%CI)	p	OR (95%CI)	p
Age	<65	1		1	
	65–75	2.979 (1.348–6.579)	0.007	3.856 (2.221–6.695)	<0.001
	>75	7.594 (3.832–15.049)	<0.001	10.054 (6.102–16.566)	<0.001
Results of echocardiography					
Severe LV dysfunction	No	1		1	
	Yes	8.341 (4.517–15.402)	<0.001	6.052 (3.784–9.680)	<0.001
Concentric or significant LV hypertrophy	No	1		1	
	Yes	1.169 (0.538–2.542)	0.693	1.252 (0.734–2.137)	0.409
Moderate or severe MR	No	1		1	
	Yes	9.442 (4.192–21.265)	<0.001	11.886 (6.096–23.178)	<0.001
Moderate or severe PH	No	1		1	
	Yes	6.767 (1.397–32.779)	0.050	5.095 (1.297–20.012)	0.039
No results of echo	–	NA		NA	
Results of laboratory tests					
Plasma sodium	≥135 mEq/L	1		1	
	<135 mEq/L	3.379 (1.870–6.104)	<0.001	2.125 (1.408–3.208)	<0.001
Intervention	Conservative	NA			
	PCI	1		1	
	CABG	5.156 (1.449–18.347)	0.03	3.181 (1.036–9.770)	0.057
Groups of diseases					
Renal diseases	No	1		1	
	Yes	8.267 (4.362–15.671)	<0.001	4.613 (3.041–6.997)	<0.001
Anemia	No	1		1	
	Yes	3.081 (1.691–5.612)	<0.001	3.363 (2.208–5.121)	<0.001
Obesity	No	1		1	
	Yes	1.071 (0.511–2.247)	0.856	0.906 (0.527–1.558)	0.721
Gastro-intestinal bleeding	No	1		1	
	Yes	9.037 (1.775–46.019)	0.032	3.926 (0.782–19.708)	0.127
Chronic obstructive pulmonary disease	No	1		1	
	Yes	2.313 (0.883–6.059)	0.087	5.191 (2.885–9.339)	<0.001
Malignant neoplasm	No	1		1	
	Yes	3.019 (1.364–6.682)	0.011	4.471 (2.601–7.685)	<0.001
Alcohol or drug addiction	No	1		1	
	Yes	2.680 (0.608–11.817)	0.194	2.644 (0.877–7.967)	0.09
Schizophrenia or psychosis	No	1		1	
	Yes	2.401 (0.304–18.994)	0.365	17.381 (5.412–55.817)	<0.001
Neurological disorders	No	1		1	
	Yes	3.586 (1.807–7.113)	0.001	4.842 (2.991–7.839)	<0.001

be mentioned that signals of reduced calibration especially in the intermediate categories of the score were observed. The latter could probably be explained, at least partially, by two main factors; first the focus on STEMI patients undergoing PPCI while the score was developed for both STEMI and non-STEMI, and second by potential differences in recording of some diagnoses (e.g. obesity, alcohol or drug addiction) between institutions. Mortality rates in the current study are overall consistent or possibly slightly lower compared with previous contemporary reports [1,2,17–19]. This probably suggests overall good adherence with contemporary professional guidelines.

Over the last 10–15 years, multiple methods aiming to stratify STEMI patients according to their risk of mortality were developed. The most widely evaluated and applied scores include the TIMI risk score [8], the dynamic TIMI risk index [20], CADILLAC risk score [9], GRACE risk

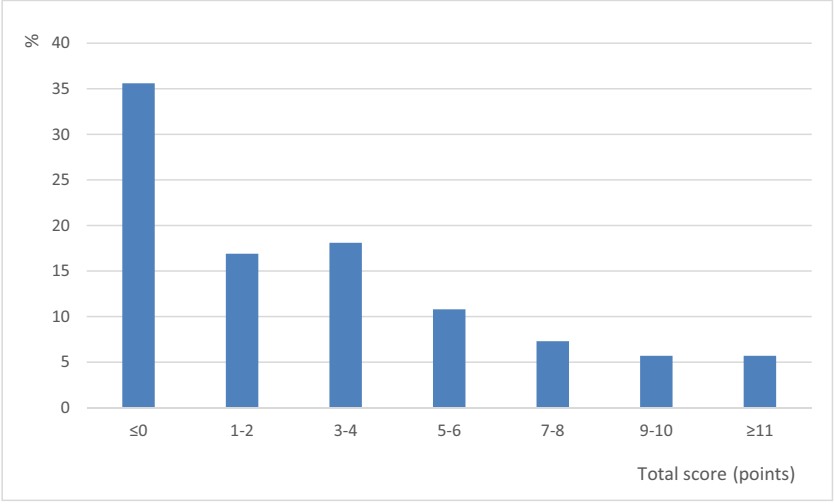
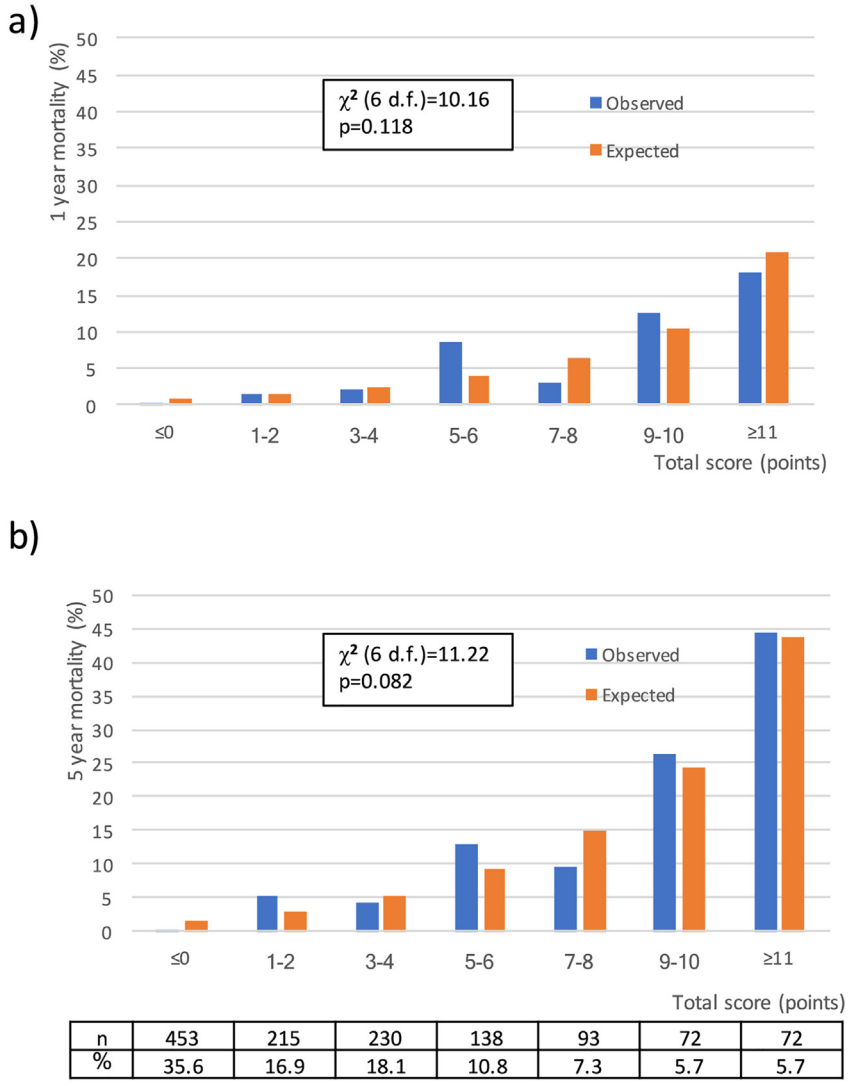


Fig. 1. Distribution of the SAMI total score.



n	453	215	230	138	93	72	72
%	35.6	16.9	18.1	10.8	7.3	5.7	5.7

Fig. 2. Observed and expected mortality rates by the groups of SAMI total score: a) for one-year mortality; b) for 5-year mortality. *The table below presents the number and percent of patients in each group.

index [11], Zwolle score [12] and the PAMI [10] risk score. Although some of these means were designed (PAMI and CADILLAC) or validated (TIMI) for patients treated with invasive procedures (i.e. primary PCI), they were all originally conceived for relatively short-term risk stratification; 30-days-1-year. Furthermore, although subsequent evaluations for longer periods were performed, it often yielded lower performance by these scores [17,18]. Importantly the dynamic TIMI risk model which is an upgrade of the classic TIMI risk score, was designed for reassessment of the risk of patients discharged from hospital [20]. However, since this score was derived from phase 3 clinical trials with highly selective inclusion criteria, its generalizability for real-life patients is questionable. Additionally, it is based to a great extent on bedside real time information (e.g. Killip score and heart rate), hence intricate for calculation retrospectively or by others rather than in-hospital treating physicians [18,20].

Thus the SAMI score, being a risk stratification tool designed and dedicated for hospital survivors, outstands for being based entirely on easily accessible (including retrospectively) clinical information including non-cardiovascular co-morbidity and validated for long-term (at least 5 years) all-cause mortality. It therefore could be a meaningful risk stratification tool for post-discharge treating physicians contemplating risk benefit ratio of different interventions as well as decision makers steering cost-effectiveness in allocation of resources for secondary prevention programs. Furthermore, it can greatly assist researchers in large scale epidemiological monitoring on one hand or in selection of appropriate populations for evaluation of new treatments on the other.

4.1. Limitations

Several limitations of the current study and the SAMI score should be addressed. First, the validation cohort used in the current study is from only one hospital and was of relatively medium size (N = 1273). However, patients were followed-up prospectively, which ensured an adequate detection of long-term mortality events. Second, since the score is based, to a large extent, on recorded diagnoses of STEMI patients, recording bias, especially of non-cardiovascular risk factors and co-morbidity could be a significant shortcoming. Third, evaluation regarding the cause of death, especially differentiating cardiac from non-cardiac cause was not performed.

5. Conclusions

The SAMI risk score is a simple, robust and validated prognostic tool for up-to 5-years all-cause mortality in hospital survivors of STEMI that

underwent PPCI. Additional multi-center studies with larger diverse cohorts are warranted to further validate and generalize this risk score.

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