Influence of the Danish Co-morbidity Index Score on the Treatment and Outcomes of 2.5 Million Patients Admitted With Acute Myocardial Infarction in the United States

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This study aimed to determine the association between the Danish Co-morbidity Index for Acute Myocardial Infarction (DANCAMI) and restricted DANCAMI (rDANCAMI) scores and clinical outcomes in patients hospitalized with AMI. Using the National Inpatient Sample, all AMI hospitalizations were stratified into four groups based on their DANCAMI and rDANCAMI score (0; 1 to 3; 4 to 5; ≥6). The primary outcome was all-cause mortality, whereas secondary outcomes were major adverse cardiovascular/cerebrovascular events, major bleeding, ischemic stroke, and receipt of coronary angiography or percutaneous coronary intervention. Multivariate logistic regression was used to determine adjusted odds ratios (aOR) with 95% confidence intervals (95% CIs). Patients with DANCAMI risk score ≥6 were more likely to suffer mortality (aOR 2.30, 95% CI 2.24 to 2.37) and bleeding (aOR 5.85, 95% CI 5.52 to 6.21) and were less likely to receive coronary angiography (aOR 0.34, 95% CI 0.33 to 0.34) and percutaneous coronary intervention (aOR 0.29, 95% CI 0.28 to 0.29) compared with patients with DANCAMI score of 0. Similar results were observed for the rDANCAMI score. In conclusion, increased DANCAMI and rDANCAMI scores were associated with worse in-hospital outcomes in patients with AMI and lower odds of invasive management. The use of co-morbidity scores identifies patients at high risk of adverse outcomes and highlights disparities in care. **(Am J Cardiol 2022;00:1−10)**

Co-morbidities among patients with acute myocardial infarction (AMI) are common and associated with a poor prognosis.[1] Co-morbidity prediction models have previously been used in research to predict the prognosis of AMI, reflected by the co-morbidity burden of patients. Such examples include the Charlson Co-morbidity Index (CCI), the Elixhauser Co-morbidity Index (ECI), and more recently the Danish Co-morbidity Index for Acute Myocardial Infarction (DANCAMI).[2−5]

Although CCI and ECI have been studied in different populations, the performance of novel co-morbidity risk scores such as DANCAMI and restricted DANCAMI (rDANCAMI) is not well defined in large populations.[3,6,7] The DANCAMI score was developed and validated to predict 1-year mortality post myocardial infarction in a cohort of Danish and New Zealand patients admitted for AMI including 24 cardiovascular and non-cardiovascular co-morbidities.[3] The rDANCAMI score includes 17 non-cardiovascular co-morbidities only.[3]

This study aimed to investigate the use of the DANCAMI and rDANCAMI scores for the prognosis of patients admitted with AMI using a national cohort of the US hospitalizations and to compare the performance of these scores in predicting the in-hospital mortality.

Methods

The National Inpatient Sample (NIS) is the largest available database of the US hospitalizations developed for the Healthcare Cost and Utilization Project and sponsored by the Agency for Healthcare Research and Quality. The NIS contains anonymized data on diagnoses and procedures from over 7 million hospitalizations annually and represents a 20% stratified sample of all discharges from the US community hospitals, excluding rehabilitation and long-term acute care hospitals, with the sample representing 97% of the US population.[8]

Using the International Classification of Diseases 10th revision, adult hospitalizations (>18 years old) between October 2015 to December 2018 with a primary discharge diagnosis of AMI were identified and stratified according to their DANCAMI and rDANCAMI scores. (Supplementary

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Table 1).[3] Risk scores were computed using the predefined weights (Supplementary Table 2). Groups were constructed based on the cut-off values from the original research study into the following: no co-morbidity (score = 0), low burden (score = 1−3), moderate burden (score = 4−5), and severe co-morbidity burden (score ≥6).[3]

The International Classification of Diseases 10th revision codes were also used to extract data on patient characteristics, co-morbidities, management strategies, and hospital outcomes. Cases were excluded owing to missing data, elective admission, Type 2 myocardial infarction, and ages under 18 (Supplementary Figure 1). Analyses were weighted using discharge weights to estimate for national averages.

The primary clinical outcome of this study was the association of DANCAMI and rDANCAMI scores with all-cause mortality. Secondary outcomes included other adverse in-hospital outcomes (major adverse cardiovascular and cerebrovascular events [MACCE], major bleeding, and acute ischemic stroke) and receipt of invasive management (coronary angiography [CA] and percutaneous coronary intervention [PCI]). MACCE was a composite of all-cause mortality, acute ischemic stroke, and reinfarction. Major bleeding included subarachnoid hemorrhage, intracerebral hemorrhage, intracranial hemorrhage, gastrointestinal hemorrhage, epistaxis, and hemoptysis. Finally, the performance of DANCAMI and rDANCAMI risk scores for the prediction of all-cause mortality was studied.

Statistical Package for Social Sciences (SPSS) Statistics version 27 (IBM Corp, Armonk, New York) and Stata MP version 16.0 (StataCorp, College Station, Texas) were used for all statistical analyses.[9] Continuous variables such as age, length of stay, and total charges were summarized using median and interquartile range. Categorical variables were compared using the Chi-square test and summarized as percentages (%). Binomial multivariate logistic regression was performed to determine the adjusted odds ratio (aOR) for invasive management and adverse outcomes. The regression model was adjusted for the following variables: bed size of the hospital, region of the hospital, location/teaching status of the hospital, age, gender, primary expected payer, median household income, smoking status, previous myocardial infarction, previous PCI, previous coronary artery bypass graft, previous cerebrovascular accident, PCI, ST-elevation myocardial infarction, dyslipidemia, atrial fibrillation, and thrombocytopenia. Results were presented as aOR with 95% confidence intervals (CIs). The performance of DANCAMI and rDANCAMI scores in predicting all-cause mortality was tested using the receiver operating characteristic (ROC) curves, with a calculation of the area under the curve (AUC). Both continuous and categorical scores were used to test their performance in predicting mortality. To compare the AUC values with previous co-morbidity scores, ROC analysis of the CCI score was also produced. Finally, optimal cut-off points for DANCAMI and rDANCAMI risk scores were calculated using the Liu method (cutpt function) in the Stata software (StataCorp, College Station, Texas). Statistical significance was determined at the level of $p < 0.05$.

Results

A total of 2,587,614 patients with AMI were diagnosed between October 2015 and December 2018 (Supplementary Figure 1). Of these, 134,280 (5.2%) patients had a DANCAMI score of 0, whereas 495,060 (19.1%), 332,845 (12.9%), and 1,625,340 (62.8%) patients had a DANCAMI score of 1 to 3, 4 to 5, and ≥6, respectively ($p < 0.001$) (Table 1). Patients with a DANCAMI score of ≥6 were on average older, more likely to be women, and had the highest prevalence of cardiovascular co-morbidities such as atrial fibrillation (22.6%), previous AMI (16.6%), previous coronary artery bypass grafting (25.4%), previous cerebrovascular accident (CVA) (10.4%), and anemias (32.0%) compared with patients with a lower DANCAMI score ($p < 0.001$) (Table 1).

Patients with a DANCAMI score of ≥6 had the highest all-cause mortality (10.0%). This group also had the highest rate of major bleeding (5.4%) and lowest requirement of CA (41.8%), and PCI (25.5%) compared with their lower-risk counterparts ($p < 0.001$) (Figure 1, Supplementary Table 3). Results of multivariable adjusted analysis show that patients with a DANCAMI risk score of ≥4 were more likely to experience all-cause mortality, with the odds of mortality for the patients with a DANCAMI score of 1 to 3 showing no significant change when compared with patients with a DANCAMI score of 0. Similarly, the odds of major bleeding incrementally increased with a DANCAMI score of ≥1 compared with patients with a DANCAMI score of 0 (Figure 2, Table 1). Moreover, patients with a DANCAMI risk score of ≥1 were less likely to receive invasive management in the form of CA and PCI compared with patients with an rDANCAMI score of 0 (Figure 2, Table 2).

Similar results were observed when DANCAMI was modeled as a continuous variable whereby per 1-unit increase in DANCAMI score led to an increased odds of mortality (aOR 1.08, 95% CI 1.08 to 1.08), major bleeding (aOR 1.09, 95% CI 1.09 to 1.09), and decreased odds of invasive management in the form of CA (aOR 0.91, 95% CI 0.91 to 0.91) and PCI (aOR 0.90, 95% CI 0.90 to 0.90) (Supplementary Table 4).

Patients with an rDANCAMI score of ≥6 were on average younger and had a higher prevalence of thrombocytopenia (14.4%), smoking (1.6%), and anemias (61.1%) than lower-risk patients ($p < 0.001$) (Table 3). Patients with an rDANCAMI score of ≥6 had the highest all-cause mortality (13.8%, $p < 0.001$), MACCE (19.4%, $p < 0.001$), major bleeding (7.2%, $p < 0.001$), and stroke (6.4%, $p < 0.001$) (Figure 1, Supplementary Table 5). Patients with an rDANCAMI score of ≥6 had lower rates of CA (33.2%, $p < 0.001$), coronary artery bypass grafting (6.0%, $p < 0.001$), and PCI (18.7%, $p < 0.001$) (Figure 1, Supplementary Table 5). With multivariable adjustment, patients with an increasing rDANCAMI score (≥1) were more likely to suffer all-cause mortality, MACCE, major bleeding, and ischemic stroke compared with patients with an rDANCAMI score of 0 (Figure 2, Table 4). Patients with an increasing rDANCAMI score (≥1) were less likely to receive CA and PCI compared with patients with an rDANCAMI score of 0 (Figure 2, Table 4).

Table 1
Patient characteristics according to the groups of DANCAMI risk score

Characteristics	DANCAMI score 0 (5.2%)	DANCAMI score 1-3 (19.1%)	DANCAMI score 4-5 (12.9%)	DANCAMI score ≥6 (62.8%)	Overall p-value	Trend p-value
Number of hospitalizations	134,280	495,060	332,845	1,625,430		
Age (years), median (interquartile range)	59 (50, 68)	64 (55, 74)	67 (57, 79)	72 (62, 81)	<0.001	<0.001
Women	30.5%	36.9%	41.0%	43.5%	<0.001	<0.001
White	79.9%	78.7%	75.5%	72.4%	<0.001	<0.001
Black	6.6%	9.4%	11.6%	13.9%	<0.001	<0.001
Hispanic	7.2%	6.6%	7.4%	7.9%	<0.001	<0.001
Other	6.3%	5.3%	3.3%	5.8%	<0.001	<0.001
ST-elevation myocardial infarction	42.5%	31.6%	25.5%	15.7%	<0.001	<0.001
Weekend admission	27.3%	27.0%	26.7%	26.3%	<0.001	<0.001
Primary expected payer					<0.001	<0.001
Medicare	30.8%	47.5%	56.4%	71.1%		
Medicaid	10.1%	9.1%	10.2%	9.1%		
Private Insurance	47.2%	34.0%	24.9%	14.6%		
Self-pay	7.7%	5.9%	5.3%	2.7%		
No charge	0.7%	0.6%	0.6%	0.3%		
Other	3.5%	3.0%	2.7%	2.2%		
Median household income (percentile)					<0.001	<0.001
0-25th	24.3%	28.0%	30.4%	34.4%		
26th-50th	27.2%	27.5%	27.6%	27.5%		
51st-75th	25.5%	24.3%	23.4%	22.4%		
76th-100th	23.0%	18.6%	18.6%	16.6%		
Cardiogenic shock	3.6%	3.4%	4.8%	6.9%	<0.001	<0.001
Cardiac arrest	3.1%	2.9%	3.3%	4.3%	<0.001	<0.001
Ventricular tachycardia	7.4%	6.0%	6.1%	6.6%	<0.001	<0.001
Ventricular fibrillation	4.0%	3.1%	3.0%	2.5%	<0.001	<0.001
Atrial fibrillation	7.1%	12.1%	17.1%	22.6%	<0.001	<0.001
Dyslipidaemia	43.9%	61.9%	61.2%	61.6%	<0.001	<0.001
Thrombocytopenia	<0.1%	2.9%	5.8%	8.3%	<0.001	<0.001
Smoker	2.8%	2.4%	1.9%	1.4%	<0.001	<0.001
Previous acute myocardial infarction	5.9%	11.7%	13.7%	16.6%	<0.001	<0.001
History of ischemic heart disease	67.5%	72.3%	69.5%	69.5%	<0.001	<0.001
Previous percutaneous coronary intervention	7.4%	14.3%	15.7%	17.6%	<0.001	<0.001
Previous coronary artery bypass grafting	8.4%	17.2%	20.4%	25.4%	<0.001	<0.001
Previous cerebrovascular accident	1.9%	4.9%	7.3%	10.4%	<0.001	<0.001
Anemia	2.4%	9.3%	17.1%	32.0%	<0.001	<0.001
Heart failure	<0.1%	4.0%	27.1%	57.1%	<0.001	<0.001
Valvular disease	<0.1%	4.9%	4.7%	14.0%	<0.001	<0.001
Hypertension	<0.1%	74.4%	57.0%	32.2%	<0.001	<0.001
Peripheral vascular disorders	0.9%	3.8%	5.5%	12.5%	<0.001	<0.001
Chronic pulmonary disease	3.1%	14.3%	13.9%	32.4%	<0.001	<0.001
Coagulopathy	0.2%	4.0%	7.7%	11.1%	<0.001	<0.001
Dementia	<0.1%	0.9%	5.3%	7.9%	<0.001	<0.001
Liver disease	0.4%	0.7%	1.8%	4.4%	<0.001	<0.001
Chronic renal failure	<0.1%	<0.1%	9.1%	42.5%	<0.001	<0.001
Metastatic cancer	<0.1%	<0.1%	<0.1%	2.7%	<0.001	<0.001
Bed size of hospital					<0.001	<0.001
Small	16.9%	17.0%	17.2%	17.4%		
Medium	30.0%	30.3%	30.0%	29.9%		
Large	53.2%	52.6%	52.8%	52.8%		
Hospital Region					<0.001	<0.001
Northeast	22.8%	21.6%	21.2%	21.2%		
Midwest	23.8%	23.2%	23.1%	23.7%		
South	38.6%	41.4%	41.6%	40.8%		
West	14.8%	13.8%	14.2%	14.3%		
Location/teaching status of hospital					<0.001	<0.001
Rural	7.4%	8.0%	8.2%	8.5%		
Urban non-teaching	26.4%	25.8%	24.7%	24.0%		
Urban teaching	66.2%	66.2%	67.1%	67.5%		

DANCAMI = Danish Co-morbidity Index for Acute Myocardial Infarction; rDANCAMI = Restricted Danish co-morbidity index for Acute Myocardial Infarction.

DANCAMI risk score = Score to identify prognosis of patients with AMI, composed of the cardiovascular (heart failure, intermittent arterial claudication, aortic disease, valvular heart disease, stroke, hypertension, diabetes uncomplicated, diabetes with end-organ damage, chronic kidney disease) and non-cardiovascular co-morbidities (high-risk cancer, low-risk cancer, coagulopathy, dementia, alcohol and drug abuse, schizophrenia, affective disorder, epilepsy, neurodegenerative disorder, hemiplegia, chronic pulmonary disease, ulcer disease, mild liver disease, moderate to severe liver disease, chronic pancreatitis).

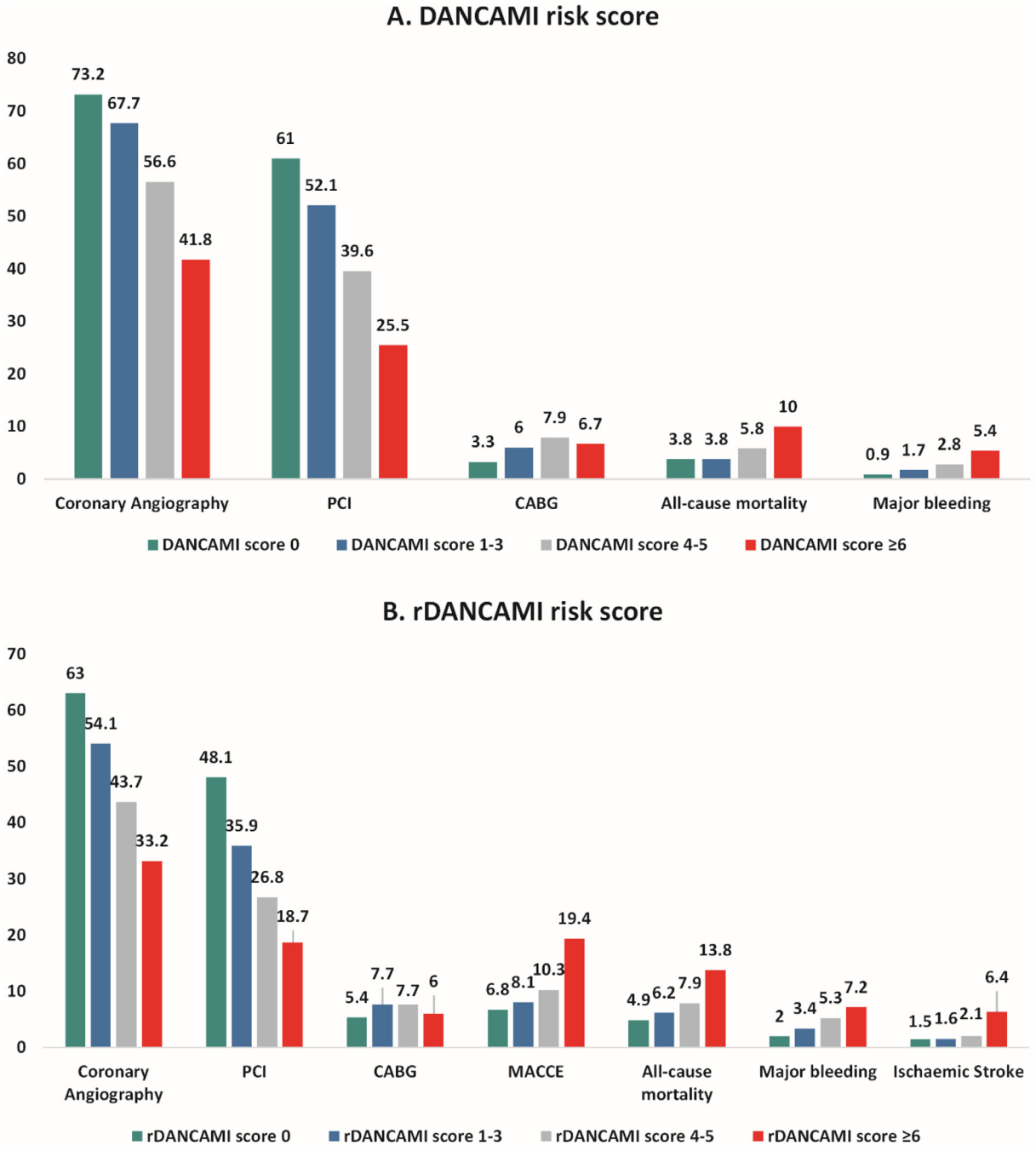

Figure 1. Unadjusted rates of invasive management and clinical outcomes in different groups: (*A*) DANCAMI risk score; (*B*)**.** rDANCAMI risk score. **Note:** 'MACCE' and 'ischemic stroke' were not calculated due to 'stroke' being a part of the DANCAMI risk score. **DANCAMI risk score** – score to identify prognosis of patients with AMI, composed of the cardiovascular (heart failure, intermittent arterial claudication, aortic disease, valvular heart disease, Stroke, hypertension, diabetes uncomplicated, diabetes with end-organ damage, chronic kidney disease) and non-cardiovascular co-morbidities (high-risk cancer, low-risk cancer, coagulopathy, dementia, alcohol and drug abuse, schizophrenia, affective disorder, epilepsy, neurodegenerative disorder, hemiplegia, chronic pulmonary disease, ulcer disease, mild liver disease, moderate to severe liver disease, chronic pancreatitis). **rDANCAMI risk score** – score to identify prognosis of patients with AMI, composed of non-cardiovascular co-morbidities only (high-risk cancer, low-risk cancer, coagulopathy, obesity, dementia, alcohol and drug abuse, schizophrenia, affective disorder, epilepsy, neurodegenerative disorder, hemiplegia, chronic pulmonary disease, ulcer disease, mild liver disease, moderate to severe liver disease, chronic pancreatitis, connective tissue disease).

Similar results were observed when rDANCAMI was modeled as a continuous variable whereby per 1-unit increase in rDANCAMI score led to an increased odds of mortality (aOR 1.10, 95% CI 1.10 to 1.10). There were also increased odds of major bleeding (aOR 1.10, 95% CI 1.10 to 1.10), MACCE (aOR 1.11, 95% CI 1.11 to 1.11) and stroke (aOR 1.14, 95% CI 1.14 to 1.14), and decreased odds of invasive management in the form of CA (aOR 0.88, 95% CI 0.88 to 0.89) and PCI (aOR 0.88, 95% CI 0.87 to 0.88) (Supplementary Table 4).

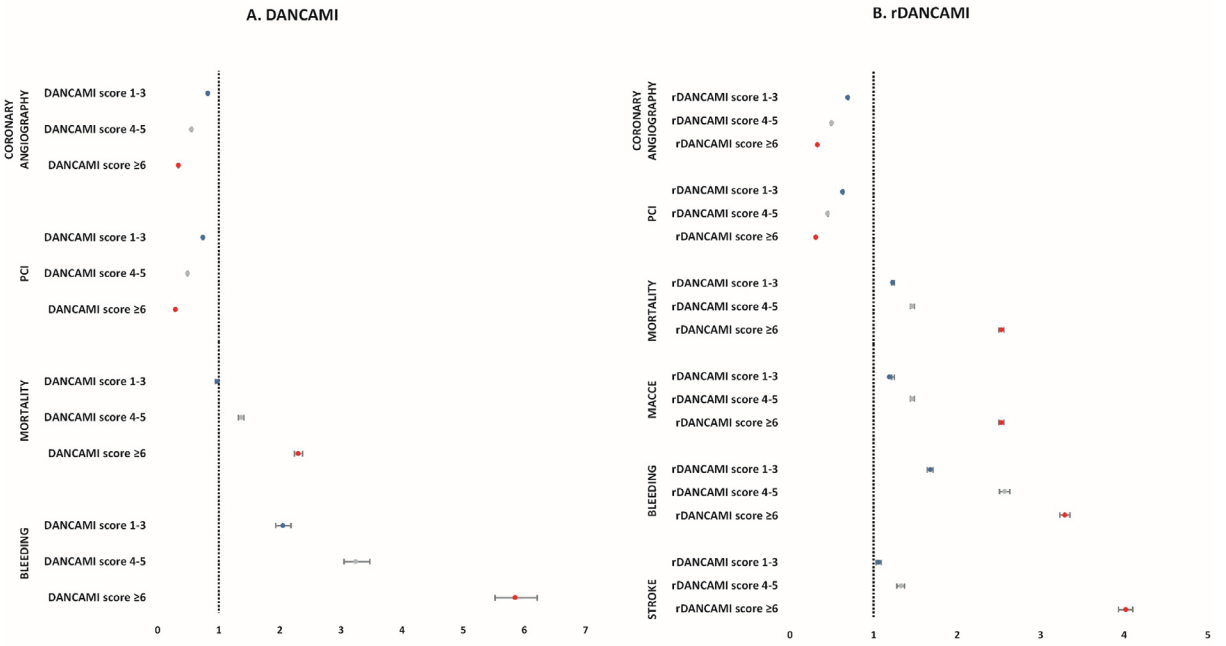

Figure 2. aOR of invasive management and clinical outcomes in different groups: (*A*) DANCAMI risk score; (*B*) rDANCAMI risk score. Reference group is group with a DANCAMI risk score of 0. Reference group is the group with an rDANCAMI risk score of 0. **Note:** 'MACCE' and 'ischemic stroke' were not calculated due to 'stroke' being a part of the DANCAMI risk score. **Multivariable logistic regression model** adjusted for bed size of the hospital, region of the hospital, location/teaching status of the hospital, age, gender , primary expected payer, median household income, smoking status, previous myocardial infarction, previous percutaneous coronary intervention, previous coronary artery bypass graft, previous cerebrovascular accident, dyslipidemia, atrial fibrillation, and thrombocytopenia. **DANCAMI risk score** – score to identify prognosis of patients with AMI, composed of the cardiovascular (heart failure, intermittent arterial claudication, aortic disease, valvular heart disease, stroke, hypertension, diabetes uncomplicated, diabetes with end-organ damage, chronic kidney disease) and non-cardiovascular co-morbidities (high-risk cancer, low-risk cancer, coagulopathy, dementia, alcohol and drug abuse, schizophrenia, affective disorder, epilepsy, neurodegenerative disorder, hemiplegia, chronic pulmonary disease, ulcer disease, mild liver disease, moderate to severe liver disease, chronic pancreatitis). **rDANCAMI risk score** – score to identify prognosis of patients with AMI, composed of non-cardiovascular co-morbidities only (high-risk cancer, low-risk cancer, coagulopathy, obesity, dementia, alcohol and drug abuse, schizophrenia, affective disorder, epilepsy, neurodegenerative disorder, hemiplegia, chronic pulmonary disease, ulcer disease, mild liver disease, moderate to severe liver disease, chronic pancreatitis, connective tissue disease).

Table 2
aOR of in-hospital invasive management and clinical outcomes in the groups of the DANCAMI risk score*

Variables	DANCAMI score 1-3 (19.1%)		DANCAMI score 4-5 (12.9%)		DANCAMI score ≥6 (62.8%)	
	aOR [95% CI]	p-value	aOR [95% CI]	p-value	aOR [95% CI]	p-value
Invasive management:						
Coronary angiography	0.84 [0.83-0.85]	<0.001	0.55 [0.55-0.56]	<0.001	0.34 [0.33-0.34]	<0.001
Percutaneous coronary intervention	0.78 [0.77-0.79]	<0.001	0.54 [0.53-0.55]	<0.001	0.34 [0.33-0.34]	<0.001
Clinical outcomes:						
All-cause mortality	0.99 [0.96-1.02]	0.077	1.32 [1.29-1.37]	<0.001	2.25 [2.18-2.32]	<0.001
Major adverse cardiac and coronary events	/	/	/	/	/	/
Major bleeding	1.94 [1.82-2.06]	<0.001	2.86 [2.69-3.04]	<0.001	4.79 [4.52-5.08]	<0.001
Ischemic stroke	/	/	/	/	/	/

aOR = adjusted Odds Ratios; CI = Confidence Interval; DANCAMI = DANish co-morbidity index for Acute Myocardial Infarction; rDANCAMI = Restricted Danish co-morbidity index for Acute Myocardial Infarction.

Note – 'MACCE' and 'ischemic stroke' were not calculated due to 'stroke' being a part of the DANCAMI risk score.

Multivariable logistic regression model adjusted for: bed size of the hospital, region of the hospital, location/teaching status of the hospital, age, gender , primary expected payer, median household income, smoking status, previous myocardial infarction, previous percutaneous coronary intervention, previous coronary artery bypass graft, previous cerebrovascular accident, STEMI, PCI (for outcomes only)., Dyslipidemia, atrial fibrillation, and thrombocytopenia.

DANCAMI risk score = Score to identify prognosis of patients with AMI, composed of the cardiovascular (heart failure, intermittent arterial claudication, aortic disease, valvular heart disease, stroke, hypertension, diabetes uncomplicated, diabetes with end-organ damage, chronic kidney disease) and non-cardiovascular co-morbidities (high-risk cancer, low-risk cancer, coagulopathy, dementia, alcohol and drug abuse, schizophrenia, affective disorder, epilepsy, neurodegenerative disorder, hemiplegia, chronic pulmonary disease, ulcer disease, mild liver disease, moderate to severe liver disease, chronic pancreatitis).

Reference group is the group with a DANCAMI risk score of 0.

Table 3
Patient characteristics according to the groups of rDANCAMI risk score

Characteristics	rDANCAMI score 0 (31.9%)	rDANCAMI score 1-3 (30.8%)	rDANCAMI score 4-5 (10.8%)	rDANCAMI score ≥6 (26.4%)	Overall p-value	Trend p-value
Number of hospitalizations	824,925	798,170	280,415	684,105		
Age (years), median (interquartile range)	67 (57, 78)	68 (58, 78)	71 (60, 82)	71 (61, 81)	<0.001	<0.001
Women	35.6%	40.5%	48.8%	45.8%	<0.001	<0.001
White	74.5%	73.9%	74.6%	74.7%	<0.001	0.600
Black	10.7%	12.7%	13.4%	13.6%	<0.001	0.600
Hispanic	8.0%	7.9%	7.2%	6.9%	<0.001	0.600
Other	6.8%	5.5%	4.8%	4.9%	<0.001	0.600
ST-elevation myocardial infarction	29.2%	20.6%	16.2%	15.0%	<0.001	<0.001
Weekend admission	26.6%	26.5%	26.6%	26.6%	<0.001	<0.001
Primary expected payer					<0.001	<0.001
Medicare	55.1%	60.5%	68.9%	71.6%		
Medicaid	8.1%	9.5%	8.4%	10.8%		
Private Insurance	28.7%	22.6%	17.5%	12.6%		
Self-pay	5.0%	4.4%	2.7%	2.5%		
No charge	0.4%	0.4%	0.3%	0.3%		
Other	2.7%	2.6%	2.3%	2.3%		
Median Household Income (percentile)					<0.001	<0.001
0-25th	28.7%	31.9%	31.9%	34.4%		
26th-50th	27.4%	27.7%	27.5%	27.5%		
51st-75th	24.0%	23.2%	27.5%	21.9%		
76th-100th	19.9%	17.3%	22.9%	16.2%		
Cardiogenic shock	4.4%	5.3%	5.0%	8.3%	<0.001	0.039
Cardiac arrest	2.8%	3.5%	3.4%	5.8%	<0.001	<0.001
Ventricular tachycardia	6.4%	6.3%	5.8%	6.8%	<0.001	<0.001
Ventricular fibrillation	2.8%	2.7%	2.2%	3.1%	<0.001	<0.001
Atrial fibrillation	15.1	19.0%	21.7%	23.0%	<0.001	<0.001
Dyslipidaemia	63.2%	63.1%	62.9%	53.9%	<0.001	<0.001
Thrombocytopenia	<0.1%	6.4%	6.5%	14.4%	<0.001	<0.001
Smoker	1.9%	1.9%	1.2%	1.6%	<0.001	<0.001
Previous acute myocardial Infarction	13.8%	15.6%	15.1%	14.6%	<0.001	<0.001
History of ischemic heart disease	74.9%	72.9%	67.6%	61.3%	<0.001	<0.001
Previous percutaneous coronary intervention	16.8%	17.5%	16.2%	14.0%	<0.001	<0.001
Previous coronary artery bypass grafting	22.4%	23.9%	22.5%	20.3%	<0.001	<0.001
Previous cerebrovascular accident	6.8%	8.0%	10.0%	10.4%	<0.001	<0.001
Anemia	4.8%	26.1%	26.3%	44.8%	<0.001	<0.001
Heart failure	28.1%	41.1%	45.5%	51.2%	<0.001	<0.001
Valvular disease	8.8%	10.6%	11.6%	11.4%	<0.001	<0.001
Hypertension	49.7%	42.1%	39.9%	33.8%	<0.001	<0.001
Peripheral vascular disorders	6.7%	9.9%	9.2%	11.7%	<0.001	<0.001
Chronic pulmonary disease	3.0%	26.2%	24.8%	50.4%	<0.001	<0.001
Coagulopathy	0.1%	8.4%	8.8%	19.4%	<0.001	<0.001
Dementia	<0.1%	<0.1%	23.8%	20.2%	<0.001	<0.001
Liver disease	0.5%	1.0%	3.0%	8.8%	<0.001	<0.001
Chronic renal failure	18.0%	29.5%	32.9%	35.8%	<0.001	0.03
Metastatic cancer	<0.1%	<0.1%	0.1%	6.3%	<0.001	0.01
Bed size of hospital					<0.001	<0.001
Small	17.0%	17.1%	17.8%	17.5%		
Medium	30.3%	29.9%	29.9%	29.7%		
Large	52.7%	53.0%	52.3%	52.8%		
Hospital region					<0.001	<0.001
Northeast	23.0%	20.9%	21.2%	20.0%		
Midwest	22.0%	23.5%	25.0%	24.8%		
South	41.1%	41.5%	39.9%	40.4%		
West	13.9%	14.1%	13.9%	14.8%		
Location/teaching status of hospital					<0.001	<0.001
Rural	8.0%	8.3%	8.9%	8.4%		
Urban non-teaching	25.2%	24.5%	24.4%	23.9%		
Urban teaching	66.8%	67.2%	66.7%	67.7%		

DANCAMI – Danish co-morbidity index for Acute Myocardial Infarction; rDANCAMI – Restricted Danish co-morbidity index for Acute Myocardial Infarction.

rDANCAMI risk score = Score to identify prognosis of patients with AMI, composed of non-cardiovascular co-morbidities only (high-risk cancer, low-risk cancer, coagulopathy, obesity, dementia, alcohol and drug abuse, schizophrenia, affective disorder, epilepsy, neurodegenerative disorder, hemiplegia, chronic pulmonary disease, ulcer disease, mild liver disease, moderate to severe liver disease, chronic pancreatitis, connective tissue disease).

Table 4
aOR of in-hospital invasive management and clinical outcomes in the groups of the rDANCAMI risk score

Variables	rDANCAMI score 1-3 (30.8%)		rDANCAMI score 4-5 (10.8%)		rDANCAMI score ≥6 (26.4%)	
	aOR [95% CI]	p-value	aOR [95% CI]	p-value	aOR [95% CI]	p-value
Invasive management:						
Coronary angiography	0.72 [0.71-0.72]	<0.001	0.54 [0.53-0.55]	<0.001	0.34 [0.34-0.35]	<0.001
Percutaneous Coronary Intervention	0.68 [0.67-0.68]	<0.001	0.51 [0.51-0.52]	<0.001	0.33 [0.33-0.33]	<0.001
Clinical outcomes:						
All-cause mortality	1.21 [1.20-1.23]	<0.001	1.38 [1.36-1.41]	<0.001	2.34 [2.31-2.37]	<0.001
Major adverse cardiac and cerebrovascular events	1.16 [1.14-1.17]	<0.001	1.33 [1.31-1.35]	<0.001	2.58 [2.51-2.61]	<0.001
Major bleeding	1.55 [1.52-1.58]	<0.001	2.31 [2.26-2.36]	<0.001	2.80 [2.75-2.86]	<0.001
Ischemic stroke	0.98 [0.95-1.00]	<0.001	1.18 [1.14-1.21]	<0.001	3.38 [3.31-3.46]	<0.001

AOR = adjusted Odds Ratios; CI = Confidence Interval; DANCAMI = Danish co-morbidity index for Acute Myocardial Infarction; rDANCAMI = Restricted Danish co-morbidity index for Acute Myocardial Infarction.

Multivariable logistic regression model adjusted for: bed size of the hospital, region of the hospital, location/teaching status of the hospital, age., gender primary expected payer, median household income, smoking status, previous myocardial infarction, previous percutaneous coronary intervention, previous coronary artery bypass graft, previous cerebrovascular accident, AMI, PCI (for outcomes only) dyslipidemia, atrial fibrillation, and thrombocytopenia.

* Reference group is the group with an rDANCAMI risk score of 0.

rDANCAMI risk score – Score to identify prognosis of patients with AMI, composed of non-cardiovascular co-morbidities only (high-risk cancer, low-risk cancer, coagulopathy, obesity, dementia, alcohol and drug abuse, schizophrenia, affective disorder, epilepsy, neurodegenerative disorder, hemiplegia, chronic pulmonary disease, ulcer disease, mild liver disease, moderate to severe liver disease, chronic pancreatitis, connective tissue disease).

ROC analysis suggested that the AUC of DANCAMI for mortality (AUC 0.646, 95% CI 0.643 to 0.648, p <0.001 as a continuous variable; and AUC 0.593, 95% CI 0.590 to 0.595, p <0.001 as a categorical variable) was relatively modest (Figure 3). Similarly, rDANCAMI had an AUC of 0.638 for mortality (95% CI 0.635 to 0.641, p <0.001) when treated as a continuous variable, and AUC of 0.625 (95% CI 0.622 to 0.628, p <0.001) when treated as a categorical variable (Figure 3). These AUC values were poorer than those of CCI score (AUC 0.697, 95% CI 0.695 to 0.700, p <0.001). The optimal cut-off values for DANCAMI and rDANCAMI risk scores were ≥8 (sensitivity of 61.0% and specificity of 60.0%) and ≥3 (sensitivity of 57.0% and specificity of 64.0%), respectively (Supplementary Table 6).Calibration plots of DANCAMI and rDANCAMI scores for mortality are presented in Supplementary Figure 2.

When stratifying patients by their DANCAMI/rDANCAMI score and whether they experienced an ST-elevated myocardial infarction (STEMI) or Non-STEMI (NSTEMI), the results were consistent with the findings in the total cohort, irrespective of the AMI type (Supplementary Tables 7 and 8). When investigating the interaction between mortality and PCI and STEMI and previous AMI, the odds with PCI (aOR 0.30, 95% CI 0.30 to 0.30) and previous AMI (aOR 0.82, 95% CI 0.80 to 0.83) were lower but higher with STEMI (aOR 3.39 95% CI 3.36 to 3.43).

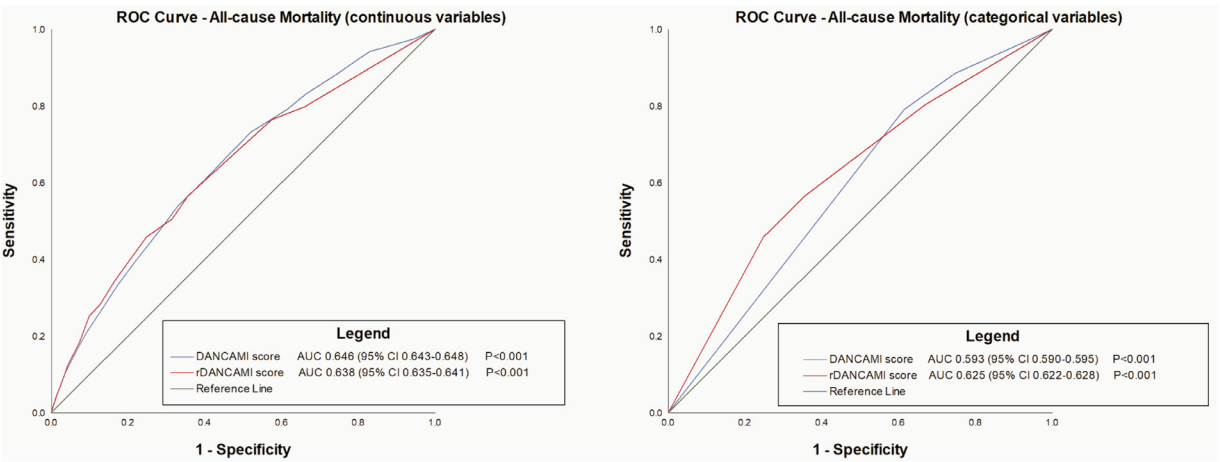

Figure 3. ROC curves for DANCAMI and rDANCAMI. **DANCAMI risk score** – score to identify prognosis of patients with AMI, composed of the cardiovascular (heart failure, intermittent arterial claudication, aortic disease, valvular heart disease, stroke, hypertension, diabetes uncomplicated, diabetes with end-organ damage, chronic kidney disease) and non-cardiovascular co-morbidities (high-risk cancer, low-risk cancer, coagulopathy, dementia, alcohol and drug abuse, schizophrenia, affective disorder, epilepsy, neurodegenerative disorder, hemiplegia, chronic pulmonary disease, ulcer disease, mild liver disease, moderate to severe liver disease, chronic pancreatitis). **rDANCAMI risk score** – score to identify prognosis of patients with AMI, composed of non-cardiovascular co-morbidities only (high-risk cancer, low-risk cancer, coagulopathy, obesity, dementia, alcohol and drug abuse, schizophrenia, affective disorder, epilepsy, neurodegenerative disorder, hemiplegia, chronic pulmonary disease, ulcer disease, mild liver disease, moderate to severe liver disease, chronic pancreatitis, connective tissue disease.

Discussion

This is the first study to externally validate the DANCAMI and rDANCAMI scores in a national cohort of over 2.5 million patients with AMI. We report several important findings. First, only minority of patients had no co-morbid conditions, highlighting the significant prevalence of co-morbid conditions in patients presenting with AMI. Second, patients with increasing DANCAMI and rDANCAMI scores (≥1) were less likely to receive invasive management and experienced more adverse outcomes. Finally, the use of only non-cardiovascular co-morbidities in the rDANCAMI score yielded a similar performance as DANCAMI in predicting mortality.

The DANCAMI and rDANCAMI risk scores were initially derived and validated in Danish (36,685 patients) and New Zealand (75,069 patients) AMI cohorts.[3] These scores marginally outperformed the CCI and ECI in predicting 1-year mortality.[3] Novel scores had similar c-statistics to CCI and ECI (AUC 0.77 and 0.76 for DANCAMI and rDANCAMI, respectively, vs AUC 0.77 for CCI and AUC 0.76 for ECI) and similar integrated discrimination improvement, but CCI had a lower Net Reclassification Index.[3] However, in this study, AUC values of DANCAMI and rDANCAMI were poorer than those of CCI, suggesting the need for further comparisons in different populations.

Our findings support those reported in the initial study. Increased DANCAMI and rDANCAMI scores were associated with an increased risk of adverse outcomes.[3] Our work adds novelty by externally validating risk scores in a 7-fold larger cohort and investigating score performance to several additional outcome measures. The differences between the original and this study include follow-up duration, as the original study reported 1-year outcomes, whereas this study investigated in-hospital outcomes. Therefore, it may be possible that these risk scores are useful in predicting long-term mortality, but their value is less certain for in-hospital mortality. This may be because other factors contributing to the patient presentation (e.g., size of infarction, hemodynamic stability, time from presentation to intervention) could be more important than co-morbidities when predicting short-term outcomes.[10–12]

Several studies have demonstrated an association between co-morbidity burden and AMI prognosis. A large UK study concluded that co-morbid illness significantly impacts 180-day mortality among 330,367 patients with AMI.[13] Another Swiss study demonstrated a strong association of co-morbidity burden with in-hospital adverse outcomes.[14] Few studies have investigated the impact of non-cardiovascular co-morbidities only on AMI prognosis. Canivell et al[15] demonstrated that both cardiovascular and non-cardiovascular co-morbidities increased the risk of future cardiovascular events. Other studies showed that patients with AMI with multiple co-morbidities have lower survival and increased length of stay.[15–19]

There are several possible reasons for why co-morbidities lead to poorer outcomes. First, increased co-morbidity burden could be associated with lower utilization of guideline-directed medical treatment ("risk-treatment paradox") and reduced effectiveness of clinical management.[15,20] Cardiovascular co-morbidities have direct effects on cardiovascular prognosis, either by potentiating a positive feedback loop, or by multiple perturbations in cardiovascular homeostasis (multiple parallel hits hypothesis), or simply by labeling patients with a higher-risk profile.[21–23] Similarly, the mechanisms by which non-cardiovascular co-morbidities contribute to poorer outcomes are numerous and could be related to a pro-inflammatory environment, accelerated atherosclerosis, drug toxicity impaired pharmacokinetics, and later diagnosis/diagnosis mimicking.[15,16,24–26]

DANCAMI and rDANCAMI included contemporary co-morbidities such as psychiatric disorders and excluded non-contemporary co-morbidities from previous indices, such as AIDS.[3] Although ECI and CCI include psychiatric conditions, their weighting was low, whereas in DANCAMI and rDANCAMI, weighting was relatively high.[3] This is supported by previous studies that have highlighted the association between mental health diagnoses and cardiovascular risk, the mechanism of which is poorly understood.[27–29] Several studies have investigated the use of other well-known co-morbidity indices in hospitalized patients. The ECI has repeatedly been demonstrated to significantly outperform the CCI in predicting prognosis of patients with AMI in five different European countries as well as the United States and Taiwan.[30–32] However, these studies included co-morbidities as separate variables instead of weighing and scoring each variable.[3,6,30–32]

The European Society of Cardiology guidelines advise that clinicians should consider co-morbidity burden in conjunction with the clinical presentation of the patient to tailor the use of invasive management and estimate prognosis.[33] However, no specific co-morbidity indices have been recommended, and this study re-affirms the potential for co-morbidity indices to be used in clinical practice, utilizing both cardiovascular and non-cardiovascular co-morbidities.[34] For example, the rDANCAMI score could be used to risk-stratify different subpopulations with AMI with less common co-morbidities in everyday practice.[35,36] Finally, it encourages cardiovascular clinicians to consider cross-specialty input to optimize non-cardiovascular risk factors as a potential means to improve AMI outcomes.

The limitations of this study include several inherent to the use of the NIS database. Data coding is potentially subject to errors due to inaccuracies with coding and missing data.[37] In addition , detailed clinical information such as cardiac markers and medications that could have an impact on mortality are not available in the NIS database. Only the in-hospital data are available in the NIS, and the use of DANCAMI and rDANCAMI for long-term outcomes is not studied. Finally, this is an observational study and hence, confounders not included in this study could contribute to adverse outcomes despite the broad scope of diseases covered by the NIS.

In conclusion, increased DANCAMI and rDANCAMI scores were associated with lower utilization of invasive management and more adverse in-hospital outcomes in patients admitted for AMI. Despite the omission of cardiovascular risk factors, rDANCAMI showed good performance emphasizing the importance of non-cardiovascular co-morbidities. These findings reassure that DANCAMI and rDANCAMI could be useful for risk stratification of patients with AMI in addition to other conventional risk scores.

Disclosures

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2022.06.008.

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