ORIGINAL RESEARCH

Guideline-Recommended Therapies and Clinical Outcomes According to the Risk for Recurrent Cardiovascular Events After an Acute Coronary Syndrome

Yoav Hammer, MD; Zaza Iakobishvili, MD, PhD; David Hasdai, MD; Ilan Goldenberg, MD; Nir Shlomo, MSc; Michal Einhorn, BSc; Tamir Bental, MD; Guy Witberg, MD; Ran Kornowski, MD; Alon Eisen, MD

***Background*—**Patients who have had an acute coronary syndrome (ACS) are at increased risk of recurrent cardiovascular events; however, paradoxically, high-risk patients who may derive the greatest benefit from guideline-recommended therapies are often undertreated. The aim of our study was to examine the management, clinical outcomes, and temporal trends of patients after ACS stratified by the Thrombolysis in Myocardial Infarction (TIMI) risk score for secondary prevention, a recently validated clinical tool that incorporates 9 clinical risk factors.

***Methods and Results*—**Included were patients with ACS enrolled in the biennial Acute Coronary Syndrome Israeli Surveys (ACSIS) between 2008 and 2016. Patients were stratified by the TIMI risk score for secondary prevention to *low* (score 0–1), *intermediate* (2), or *high* (≥3) risk. Clinical outcomes included 30-day major adverse cardiac events (death, myocardial infarction, stroke, unstable angina, stent thrombosis, urgent revascularization) and 1-year mortality. Of 6827 ACS patients enrolled, 35% were low risk, 27% were intermediate risk, and 38% were high risk. Compared with the other risk groups, high-risk patients were older, were more commonly female, and had more renal dysfunction and heart failure ($P<0.001$ for each). High-risk patients were treated less commonly with guideline-recommended therapies during hospitalization (percutaneous coronary intervention) and at discharge (statins, dual-antiplatelet therapy, cardiac rehabilitation). Overall, high-risk patients had higher rates of 30-day major adverse cardiac events (7.2% low, 8.2% intermediate, and 15.1% high risk; $P<0.001$) and 1-year mortality (1.9%, 4.6%, and 15.8%, respectively; $P<0.001$). Over the past decade, utilization of guideline-recommended therapies has increased among all risk groups; however, the rate of 30-day major adverse cardiac events has significantly decreased among patients at high risk but not among patients at low and intermediate risk. Similarly, the 1-year mortality rate has decreased numerically only among high-risk patients.

***Conclusions*—**Despite an improvement in the management of high-risk ACS patients, they are still undertreated with guideline-recommended therapies. Nevertheless, the outcome of high-risk patients after ACS has significantly improved in the past decade, thus they should not be denied these therapies. **(*J Am Heart Assoc*. 2018;7:e009885. DOI: 10.1161/JAHA.118.009885.)**

Key Words: acute coronary syndrome • cardiovascular outcomes • guideline-recommended therapies • risk score • secondary prevention

Acute coronary syndrome (ACS), the acute manifestation of ischemic heart disease, remains a major cause of morbidity and mortality worldwide. Although percutaneous coronary intervention (PCI) and pharmacological treatment have improved significantly in the past decade, patients admitted with an ACS still have significant residual risk for recurrent cardiovascular events.[1,2]

Optimal medical therapy with antiplatelet drugs, statins, and other guideline-recommended therapies[3–10] are of paramount importance in preventing recurrent

From the Department of Cardiology, Rabin Medical Center, Petah Tikva, Israel (Y.H., Z.I., D.H., T.B., G.W., R.K., A.E.); The Leviev Heart Center, Sheba Medical Center, Tel Hashomer, Israel (I.G.); Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel (Y.H., Z.I., D.H., I.G., T.B., G.W., R.K., A.E.); Israeli Association for Cardiovascular Trials, Sheba Medical Center, Tel Hashomer, Israel (I.G., N.S., M.E.).

An accompanying Table S1 is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.009885

Correspondence to: Alon Eisen, MD, Cardiology department, Rabin medical center, Derech Ze`ev Jabotinski 39, Petah Tikva, 4941492, Israel. E-mail: alon201273@gmail.com

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Clinical Perspective

What Is New?

- Despite advances in invasive and pharmacological treatment of patients with acute coronary syndrome (ACS), high-risk ACS patients (as determined by the TIMI risk score for secondary prevention) are still undertreated with guideline-recommended therapies.
- Nevertheless, clinical outcomes of high-risk ACS patients have improved significantly over the past decade, whereas outcomes of low- and intermediate-risk patients appear to be unchanged.

What Are the Clinical Implications?

- High-risk ACS patients (eg, elderly patients and those with renal dysfunction, diabetes mellitus, heart failure, or peripheral arterial disease) should not be denied guideline-recommended therapies.
- Patient stratification after ACS will help identify patients who may benefit the most from guideline-recommended therapies.

cardiovascular events in patients after an ACS.[11] In addition, other strategies for risk-factor modification and lifestyle changes such as diet, cardiac rehabilitation, exercise, and smoking cessation reduce the rate of recurrent cardiovascular events.[12–14] Despite these treatment strategies, not all ACS patients receive optimal treatment. Paradoxically, patients who are at increased risk (eg, elderly, female, those with renal dysfunction and other comorbidities) are often undertreated.[15]

The Thrombolysis in Myocardial Infarction (TIMI) risk score for secondary prevention (TRS 2°P) is a validated tool to stratify patients after an ACS, based on their clinical characteristics and according to their risk for recurrent cardiovascular events.[16] We aimed to examine the management, clinical outcomes, and temporal trends over the past decade of patients with ACS stratified by the TRS 2°P, and to identify risk groups that might particularly benefit from optimal therapy.

Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

The ACSIS (Acute Coronary Syndrome Israel Survey) is a biennial prospective national registry of all patients with ACS hospitalized in 25 coronary care units and cardiology departments in all general hospitals in Israel over a 2-month period (March to April).[17,18] Clinical, historical, and demographic data were recorded on prespecified forms for all admitted patients diagnosed with ACS. Admission and discharge diagnoses were recorded by the attending physicians based on electrocardiographic, clinical, and biochemical criteria. Patient management was at the discretion of the attending physicians. All patients signed an informed consent form for participating in the ACSIS registry at each medical center, and each institution received the approval of its institutional review board.

All patients enrolled in the ACSIS registry between 2008 and 2016 were included in the present study. Although the ACSIS registry has been available since 2000, the time period was chosen to describe a contemporary cohort of patients with ACS in the past decade, during which PCI has become the mainstay of treatment, and to examine relevant temporal trends.

Patients were stratified according to the TRS 2°P for recurrent cardiovascular events after an ACS.[16] This score incorporates 9 simple clinical characteristics: age ≥75 years, diabetes mellitus, hypertension, current smoking, peripheral arterial disease, prior stroke, prior coronary artery bypass grafting surgery, chronic heart failure, and estimated glomerular filtration rate <60 mL/min. Patients were stratified as *low risk* (0–1 characteristics), *intermediate risk* (2 characteristics), or *high risk* (≥3 characteristics).

Clinical outcomes included 30-day major adverse cardiac events (MACE; death, myocardial infarction [MI], stroke, unstable angina, stent thrombosis, and urgent revascularization) and 1-year mortality. Data of 30-day MACE were ascertained by hospital chart review, telephone contact, and clinical follow-up data. Mortality data at 30 days were determined for all patients from hospital charts and by matching identification numbers of patients with the Israeli National Population Register. One-year mortality data were ascertained through the use of the Israeli National Population Registry.

Statistical Analysis

Baseline characteristics, management, and treatment were stratified by the 3 TRS 2°P groups (Tables 1–3). Differences in continuous parameters were tested using 1-way ANOVA for normally distributed values or the Kruskal–Wallis test for nonnormally distributed values. Categorical parameters were compared using the χ^2 test. Temporal trends in treatment and outcomes stratified by the 3 TRS 2°P groups (Tables 4 and 5) were calculated using the χ^2 test for trend. Clinical outcomes were examined using Cox regression analysis (1-year mortality) or logistic regression models (30-day MACE).

A sensitivity analysis with the same statistical methods as for the main results included only patients who were discharged alive from their index ACS hospitalization.

Table 1. Baseline Characteristics

	TIMI Risk Score for Secondary Prevention		
	Low Risk (n=2421)	Intermediate Risk (n=1788)	High Risk (n=2618)
Age, y, mean±SD	56.9±10.6	62.9±11.5	70.9±12.1
Sex (male)	2082 (86.0)	1390 (77.7)	1881 (71.8)
Dyslipidemia	1495 (62.0)	1365 (76.6)	2230 (85.3)
Hypertension	582 (24.0)	1339 (74.9)	2436 (93.0)
Current smoking	931 (38.5)	799 (44.7)	936 (35.8)
Diabetes mellitus	149 (6.2)	680 (38.0)	1821 (69.6)
Family history of CAD	848 (37.5)	459 (28.9)	512 (23.3)
BMI (kg/m^2), mean (SD)	27.78 (11.0)	29.17 (15.4)	28.98 (16.0)
Prior MI	402 (16.6)	564 (31.6)	1271 (48.8)
Prior CABG	9 (0.4)	66 (3.7)	565 (21.6)
Prior PCI	466 (19.3)	588 (33.0)	1243 (47.6)
CKD*	22 (0.9)	74 (4.1)	729 (27.9)
PVD	5 (0.2)	39 (2.2)	463 (17.7)
Status post CVA/TIA	6 (0.2)	55 (3.1)	473 (18.1)
Prior heart failure	7 (0.3)	32 (1.8)	492 (18.8)
eGFR mL/min, median (IQR)	84 (74–97)	80 (65–95)	56 (40–77)
EF <30%	49 (2.6)	63 (4.7)	221 (11.3)

Values are presented as n (%) unless otherwise specified. $P<0.05$ for each variable. BMI indicates body mass index; CAD, coronary artery disease; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; CVA, cerebrovascular event; EF, ejection fraction; eGFR, estimated glomerular filtration rate; IQR, interquartile range; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; TIA, transient ischemic attack; TIMI, Thrombolysis in Myocardial Infarction.
*CKD was defined as creatinine ≥1.5 mg/dL or creatinine clearance <50 mL/min or on dialysis.

Table 2. Characteristics of Index ACS

	TIMI Risk Score for Secondary Prevention			
	Low Risk (n=2421)	Intermediate Risk (n=1788)	High Risk (n=2618)	*P* Value
STEMI on presentation	1241 (51.3)	773 (43.2)	840 (32.1)	<0.001
Coronary angiogram (during index hospitalization)	2342 (96.9)	1676 (93.6)	2161 (82.6)	<0.001
Any PCI (during index hospitalization)	1913 (79.0)	1340 (74.9)	1594 (60.9)	<0.001
PCI in non–STE-ACS (during index hospitalization)	783 (67.0)	655 (64.7)	925 (52.3)	<0.001
CABG (during index hospitalization)	127 (5.2)	99 (5.5)	144 (5.5)	0.8
GRACE score >140	52 (2.7)	131 (9.1)	851 (40.0)	<0.001
Killip class III/IV on admission	42 (1.7)	243 (9.4)	243 (9.4)	<0.001
Radial vascular access (STEMI patients)	445 (60.6)	256 (56.5)	213 (49.9)	0.009
3-vessel disease on angiogram	484 (20.7)	491 (29.5)	970 (44.7)	<0.001
TIMI grade flow after PCI	2.83±0.61	2.82±0.63	2.68±0.81	<0.001
Peak CK values, U/L	340.5 (134–1032)	285.0 (112–831)	232.0 (100–646)	<0.001
Peak troponin T values, ng/L	939 (76.8)	686 (75.3)	1021 (78.1)	0.300
LDL-C on admission, mg/dL	114.00 (90–141)	102.50 (79–130)	88.00 (68–113)	<0.001
Triglycerides on admission, mg/dL	129.00 (90–181)	132.00 (93–193)	129.00 (93–184)	0.051
HDL-C on admission, mg/dL	38.00 (32–46)	38.00 (31–45)	38.00 (31–45)	0.04

Values are presented as n (%), mean±SD, or median (IQR). ACS indicates acute coronary syndrome; CABG indicates coronary artery bypass grafting; CK, creatine phosphokinase; GRACE, Global Registry of Acute Coronary Events; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; non–STE-ACS, non–ST-segment–elevation acute coronary syndrome; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction.

Statistical significance was defined as $P<0.05$. All analyses were performed using R (R Foundation for Statistical Computing).

Results

During 2008–2016, 6827 ACS patients were enrolled in the ACSIS registry. Of those, 2421 (35%) were categorized as low risk, 1788 (27%) as intermediate risk, and 2618 (38%) as high risk, according to the TRS 2°P (Figure 1). Patient characteristics are presented in Table 1. Compared with low- and intermediate-risk patients, those at high risk were more likely to be older, to be female, and to have more comorbidities such as renal dysfunction, prior PCI, and peripheral arterial disease ($P<0.001$ for each). In addition, high-risk patients presented more frequently with non–ST-segment–elevation ACS than with ST-segment–elevation MI and were more likely to have 3-vessel coronary disease compared with patients at low and intermediate risk ($P<0.001$ for each).

Patients at high risk underwent coronary angiography and stent implantation less often compared with low- and intermediate-risk patients ($P<0.001$ for each), with no significant difference in referral for coronary artery bypass grafting (Table 2). At discharge, compared with low- and intermediate-risk patients, high-risk patients received less guideline-recommended medical therapy, such as antiplatelet therapy and statins, and were referred less often to cardiac rehabilitation (Table 3). Among patients who underwent PCI (n=4846), high-risk patients were treated less frequently with

Table 3. Medication at Discharge and Clinical Outcomes

	TIMI Risk Score for Secondary Prevention			
	Low Risk (n=2421)	Intermediate Risk (n=1788)	High Risk (n=2618)	*P* Value
Medication at discharge				
Aspirin	2349 (97.7)	1708 (96.1)	2367 (92.7)	<0.001
$P2Y_{12}$ inhibitor	2116 (88.0)	1518 (85.7)	2048 (80.3)	<0.001
Statin	2271 (95.0)	1693 (96.1)	2324 (92.1)	<0.001
ACEI/ARB	1712 (70.8)	1450 (81.0)	1980 (75.7)	<0.001
β-Blockers	1861 (78.8)	1433 (81.8)	2040 (81.0)	0.041
Anticoagulants	68 (2.8)	79 (4.5)	236 (9.2)	<0.001
Outcomes				
30-d rehospitalization	369 (17.1)	307 (19.3)	430 (19.5)	0.077
30-d recurrent MI	32 (1.3)	24 (1.3)	53 (2.0)	0.084
30-d MACE	173 (7.2)	147 (8.2)	395 (15.1)	<0.001
30-d mortality	26 (1.1)	35 (2.0)	191 (7.3)	<0.001
30-d MI or UAP	96 (4.0)	76 (4.2)	176 (6.7)	<0.001
30-d CVA	3 (0.1)	8 (0.4)	16 (0.8)	0.52
30-d stent thrombosis	17 (0.7)	14 (0.8)	23 (0.9)	0.77
30-d urgent revascularization	90 (3.7)	63 (3.5)	107 (4.1)	0.60
1-y mortality*	45 (1.9)	81 (4.6)	409 (15.8)	<0.001

Values are presented as n (%). Anticoagulants include warfarin, enoxaparin, dabigatran, apixaban, rivaroxaban, and fondaparinux. MACE includes death, UAP, MI, CVA, stent thrombosis, and urgent revascularization. $P2Y_{12}$ inhibitors include clopidogrel, ticagrelor, and prasugrel. ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CVA, cerebrovascular accident; MI, myocardial infarction; MACE, major adverse cardiac events; TIMI, Thrombolysis in Myocardial Infarction; UAP, unstable angina pectoris.
*Percentages are Kaplan–Meier rates.

Table 4. Temporal Trends in Guideline-Recommended Therapies

	2008	2010	2013	2016	*P* Trend
Entire cohort					
n	1716	1720	1665	1724	
PCI during hospitalization	1192 (69.5)	1241 (72.2)	1164 (69.9)	1249 (72.4)	0.1
Statins at discharge	1548 (91.9)	1618 (95.0)	1535 (92.3)	1587 (97.8)	<0.001
DAPT at discharge	1298 (75.6)	1421 (82.6)	1368 (82.2)	1446 (83.9)	<0.001
Cardiac rehabilitation referral	749 (45.8)	864 (53.0)	623 (50.9)	896 (60.5)	<0.001
Low risk					
n	641	599	569	609	
PCI during hospitalization	503 (78.5)	489 (81.6)	443 (77.9)	475 (78.0)	0.5
Statins at discharge	598 (93.6)	573 (95.8)	524 (92.1)	576 (98.5)	0.006
DAPT at discharge	527 (82.2)	535 (89.3)	487 (85.6)	542 (89.0)	0.006
Cardiac rehabilitation referral	325 (52.9)	358 (61.8)	261 (61.3)	364 (67.3)	<0.001
Intermediate risk					
n	433	462	437	458	
PCI during hospitalization	312 (72.1)	355 (76.8)	325 (74.4)	350 (76.4)	0.2
Statins at discharge	407 (94.9)	441 (96.3)	411 (94.3)	434 (98.9)	0.01
DAPT at discharge	332 (76.7)	390 (84.4)	369 (84.4)	392 (85.6)	<0.001
Cardiac rehabilitation referral	201 (47.3)	242 (54.8)	174 (51.9)	259 (66.4)	<0.001
High risk					
n	642	659	659	657	
PCI during hospitalization	377 (58.7)	397 (60.2)	396 (60.1)	424 (64.5)	0.04
Statins at discharge	543 (88.0)	604 (93.2)	600 (91.2)	577 (96.3)	<0.001
DAPT at discharge	439 (68.4)	496 (75.3)	512 (77.7)	512 (77.9)	<0.001
Cardiac rehabilitation referral	223 (37.4)	264 (43.4)	188 (40.7)	273 (49.6)	<0.001

Values are presented as n (%). DAPT indicates dual-antiplatelet therapy; PCI, percutaneous coronary intervention.

dual-antiplatelet therapy (95.9%, 94.3%, and 90.7% in the low-, intermediate-, and high-risk groups, respectively; $P<0.001$). Among patients who did not undergo PCI (n=1978), there was no difference among the groups (51.0%, 48.3%, and 50.2%, in the low-, intermediate-, and high-risk groups, respectively; $P=0.6$).

The rate of 30-day MACE was 7.2% in patients at low risk, 8.2% in patients at intermediate risk, and 15.1% in patients at high risk ($P<0.001$; Table 3). Similarly, there was a graded 1-year mortality rate by risk group (1.9% for low risk, 4.6% for intermediate risk, and 15.8% for high-risk; $P<0.001$; Figure 2).

During the past decade, there was no change in TRS 2°P (2008: median: 2.0 [interquartile range: 1.0–3.0]; mean±SD: 2.19±1.44; 2016: median: 2.0 [interquartile range: 1.0–3.0]; mean±SD: 2.22±1.44; $P=0.4$). Similarly, when examining only the high-risk patients (score >2), there was no change in the TRS 2°P during that time (2008: median: 3 [interquartile range: 3.0–4.0]; mean±SD: 3.73±0.97; 2016: median: 3 [interquartile range: 3.0–4.0]; mean±SD: 3.76±0.95; $P=0.4$). Utilization of guideline-recommended therapies, such as dual-antiplatelet therapy, statins, and cardiac rehabilitation, has increased among all risk groups but remained the lowest among the high-risk group (Table 4).

The rate of 30-day MACE has significantly decreased among patients at high risk (from 21.0% in 2008 to 9.7% in 2016; $P<0.001$) but not among patients at low and intermediate risk (Figure 3A). Compared with the early period (2008–2010) and with low- and intermediate-risk patients, patients at high risk had a significant decrease in 30-day MACE in the

Table 5. Temporal Trends in Clinical Outcomes

	2008	2010	2013	2016	*P* Trend
Entire cohort					
n	1716	1720	1665	1724	
30-d MACE	215 (12.5)	173 (10.1)	176 (10.6)	151 (8.8)	0.001
30-d mortality	72 (4.2)	68 (4.0)	61 (3.7)	51 (3.0)	0.05
1-y mortality	135 (8.0)	133 (7.8)	136 (8.3)	131 (7.7)	0.9
Low risk					
n	641	599	569	609	
30-d MACE	41 (6.4)	36 (6.0)	46 (8.1)	50 (8.2)	0.11
30-d mortality	7 (1.1)	4 (0.7)	6 (1.1)	9 (1.5)	0.4
1-y mortality	8 (1.3)	9 (1.5)	14 (2.5)	14 (2.3)	0.1
Intermediate risk					
n	433	462	437	458	
30-d MACE	39 (9.0)	36 (7.8)	40 (9.2)	32 (7.0)	0.4
30-d mortality	8 (1.9)	8 (1.7)	10 (2.3)	9 (2.0)	0.7
1-y mortality	17 (4.0)	20 (4.4)	24 (5.6)	20 (4.5)	0.5
High risk					
n	642	659	659	657	
30-d MACE	135 (21.0)	101 (15.3)	90 (13.7)	69 (10.5)	<0.001
30-d mortality	57 (8.9)	56 (8.5)	45 (6.9)	33 (5.0)	0.004
1-y mortality	110 (17.2)	104 (15.8)	98 (15.1)	97 (15.0)	0.2

Values are presented as n (%). MACE includes death, unstable angina pectoris, myocardial infarction, cerebrovascular accident, stent thrombosis, and urgent revascularization. MACE indicates major adverse cardiac events.

late period (2013–2016; odds ratio: 0.54; 95% confidence interval, 0.39–0.74; $P<0.001$).

The rate of 1-year mortality has numerically decreased among high-risk patients (from 17.2% in 2008 to 15.0% in 2016) but not among low- and intermediate-risk patients ($P=0.1$; Figure 3A). In a Cox regression analysis, compared with the early period (2008–2010) and with low- and intermediate-risk patients, patients at high risk had a significant decrease in 1-year mortality in the late period (2013–2016; hazard ratio: 0.64; 95% confidence interval, 0.43–0.97; $P=0.04$), but this was not statistically significant after adjusting for age as a continuous variable (hazard ratio: 0.70; 95% confidence interval, 0.47–1.05; $P=0.09$).

Consistent qualitative results were demonstrated among patients with ST-segment–elevation MI and non–ST-segment–elevation ACS (Figure 3B and 3C).

In a sensitivity analysis that included only patients who were discharged alive from the index hospitalization with ACS (n=6686), consistent results were demonstrated. The rate of 30-day MACE was 6.7% in patients at low risk, 7.3% in patients at intermediate risk, and 11.4% in patients at high risk ($P<0.001$). During the past decade, the rate of 30-day MACE decreased significantly among patients at high risk (from 16.2% in 2008 to 7.7% in 2016; $P<0.001$) but not among patients at low and intermediate risk (Table S1). There was no significant change in the rate of 1-year mortality among each risk group.

Discussion

In this study from a prospective biennial national registry of patients with ACS, patients at high risk for recurrent cardiovascular events based on their clinical characteristics had increased rates of 30-day MACE and 1-year mortality. Despite improvement in treatment strategies among all patients during the past decade, high-risk patients were still undertreated with guideline-recommended therapies. Most important, although the clinical outcomes of low- and intermediate-risk patients admitted with an ACS have not changed over the past decade, the prognosis of high-risk patients has significantly improved.

The term *ACS* encompasses several cardiac conditions that require prompt identification and appropriate treatment to reduce the risk of in-hospital complications and future cardiovascular events. Numerous studies have demonstrated that several ACS patient populations, such as those that are elderly, are female, or have coexisting comorbidities, are still undertreated both pharmacologically and with invasive treatments, mainly because of the complexity involved in treating these patients.[15] Indeed, in this study, high-risk patients (who represented 38% of all ACS patients) were treated less frequently with guideline-recommended therapies; paradoxically, although treatment has improved during the past decade, these patients remained undertreated. We can speculate that high-risk patients were less likely to undergo coronary angiography, given a higher risk of contrast-induced nephropathy, and PCI, given coronary features that increase the risk of procedural complications. In addition, high-risk patients were treated less often with dual-antiplatelet therapy, perhaps because of their bleeding risk and the higher use of anticoagulation. Differences in the use of other medications across the TRS 2°P groups may also be related to between-group differences such as the left ventricular ejection fraction. Although high-risk patients in our study were undertreated with guideline-recommended therapies and had worse outcomes, an analysis of temporal trends during the past decade revealed that the overall improvement in outcomes of patients with ACS derived mainly from the improvement in the outcomes of these high-risk patients. Consequently, high-risk patients might benefit the most from the advancement of medical and interventional treatment in comparison to patients at low and intermediate risk, for whom outcomes have not changed during the past decade.

In this study we aimed to examine risk groups that are often undertreated during and after ACS. Although there are several risk scores for cardiovascular risk estimation in

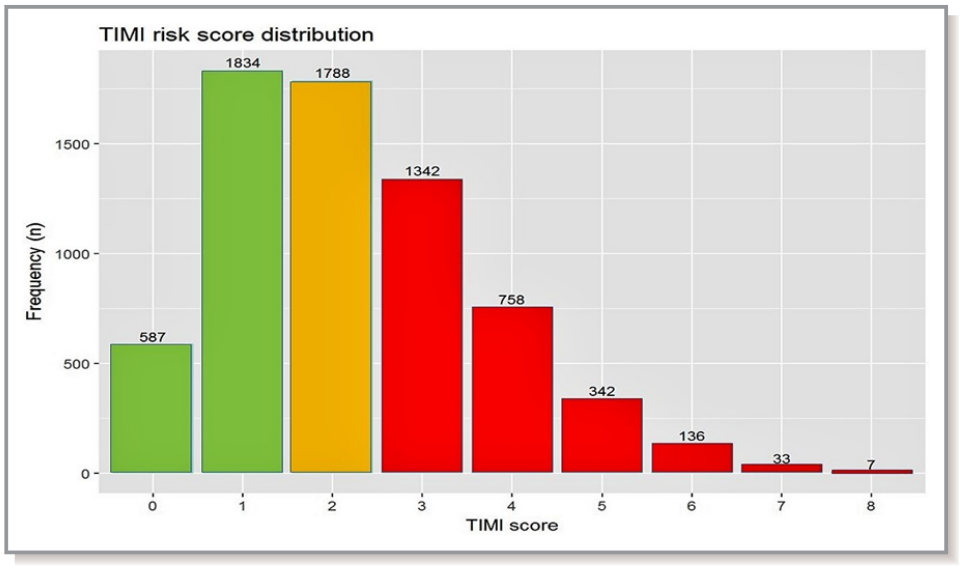

Figure 1. Distribution of the Thrombolysis in Myocardial Infarction (TIMI) risk score for secondary prevention in the study patients. Risk factors: age ≥75 years, diabetes mellitus, hypertension, current smoking, peripheral arterial disease, prior stroke, prior coronary artery bypass graft surgery, chronic heart failure, and estimated glomerular filtration rate <60 mL/min. Low risk: 0 to 1 risk factor; intermediate risk: 2 risk factors; high risk: ≥3 risk factors.

patients with ACS,[19,20] we have utilized the TRS 2°P, a simple risk score based solely on the patient's clinical characteristics and not on the type of ACS, physical examination, ECG findings, or biomarkers. This score was validated in patients with prior myocardial infarction and in patients stabilized after an ACS.[16] When applying this score in the IMPROVE-IT (Improved Reduction of Outcomes: Vytorin Efficacy International Trial) study, high-risk patients derived the greatest benefit from the addition of ezetimibe to statin therapy.[21] This finding is consistent with our findings and emphasize that high-risk patients may derive the most benefit from guideline-recommended treatment.

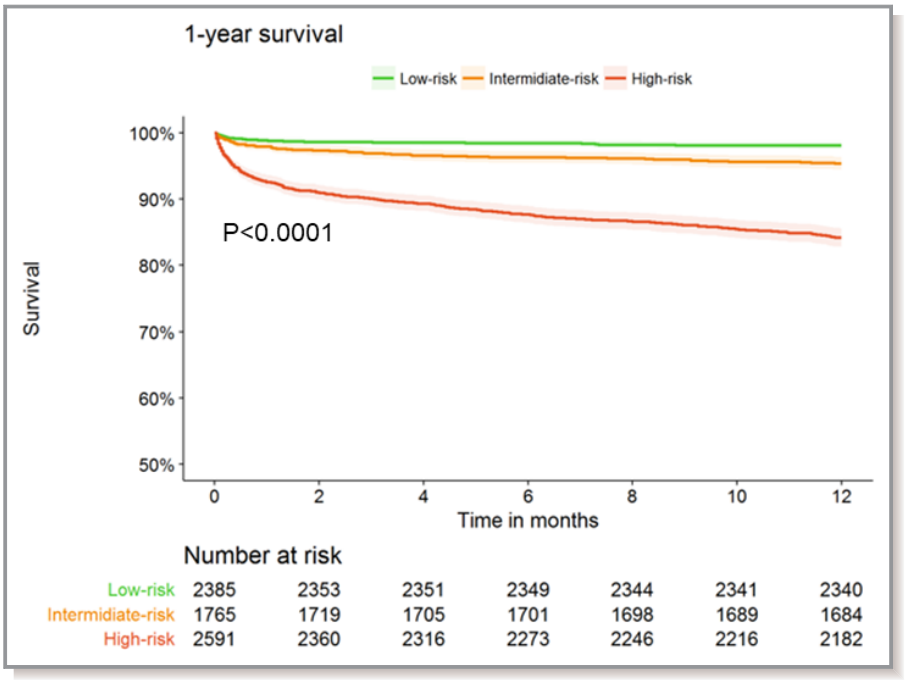

Figure 2. Kaplan–Meier curves for 1-year mortality in acute coronary syndrome patients according to the Thrombolysis in Myocardial Infarction (TIMI) risk score for secondary prevention.

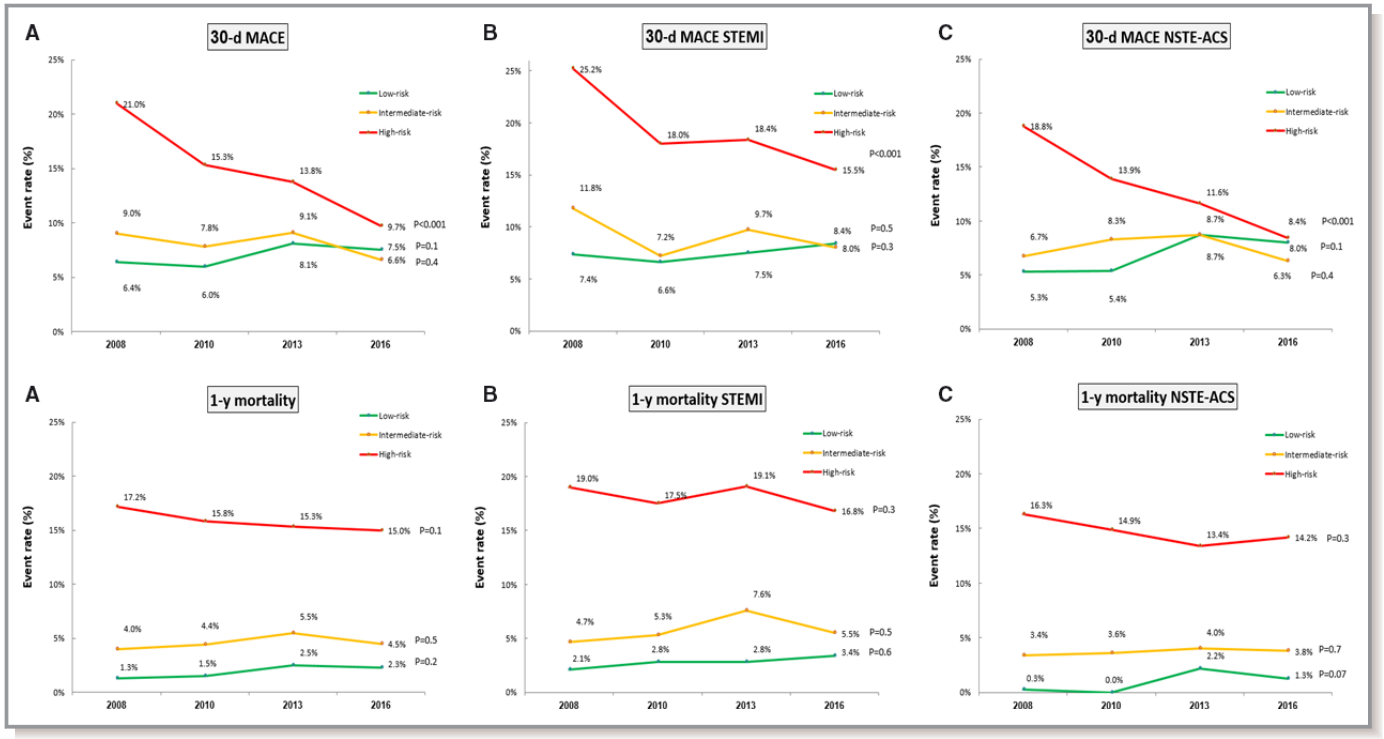

Figure 3. Temporal trends of 30-day major adverse cardiovascular events (MACE) and 1-year mortality according to the Thrombolysis in Myocardial Infarction (TIMI) risk score for secondary prevention among all patients (A), patients with ST-segment–elevation myocardial infarction (STEMI) (B), and patients with non-STEMI acute coronary syndrome (NSTE-ACS) (C).

Contemporary ST-segment–elevation MI and non–ST-segment–elevation ACS guidelines recommend treating patients similarly, regardless of their age, sex, renal status, and other clinical characteristics.[22,23] Nevertheless, our data demonstrate that clinically high-risk patients are often undertreated in current practice. Although one may assume that patients at increased age and with additional comorbidities should be managed with a more conservative approach, our study sheds light on these patients and demonstrates they might benefit the most and should probably not be denied these therapies (medical and interventional). Nevertheless, because our study did not aim to demonstrate the causal association between treatment and outcome, future efforts should focus on further reducing the rate of recurrent cardiovascular events among high-risk patients.

Our study has several limitations. Results are derived from the ACSIS registry, which is composed of a population admitted to cardiology wards and intensive cardiac care units nationwide with the diagnosis of ACS. Patients with less typical chest pain, although ultimately diagnosed as ACS, may have been managed in the internal medicine wards and thus are not represented in the current study. In addition, the ACSIS registry has limited follow-up data beyond the index hospitalization with respect to long-term medical treatment, adherence to treatment, and additional interventions. Consequently, the long-term outcomes may be significantly influenced by these and other postdischarge intervening factors. Data regarding complete revascularization were not available. Our study utilized the TRS 2°P even though this score was developed among patients stabilized after MI and was demonstrated to predict MI, stroke, or cardiovascular death. We have extrapolated this score in the current study because it incorporates clinical characteristics and thus is very useful and readily available in clinical practice. In addition, it includes the wide spectrum of ACS patients, both non–ST-segment–elevation ACS and ST-segment–elevation MI. Moreover, the sensitivity analysis, which included only patients who were stabilized after ACS and were discharged alive, demonstrated consistent results.

Conclusion

Despite an improvement in the management of high-risk ACS patients during the past decade, they are still undertreated with guideline-recommended therapies. Nevertheless, the outcome of high-risk ACS patients has improved significantly in the past decade; therefore, these patients should not be denied these therapies.

Disclosures

None.

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SUPPLEMENTAL MATERIAL

Table S1. Temporal trends in clinical outcomes in patients who survived the index ACS hospitalization.

	2008	2010	2013	2016	P trend
Entire cohort					
N	1673	1686	1632	1695	
30 day MACE	172 (10.3)	139 (8.2)	144 (8.8)	123 (7.3)	0.006
30 day mortality	29 (1.7)	34 (2.0)	29 (1.8)	23 (1.4)	0.334
1 year mortality	92 (5.6)	99 (5.9)	103 (6.4)	103 (6.2)	0.387
Low-risk					
N	639	597	566	605	
30 day MACE	39 (6.1)	34 (5.7)	43 (7.6)	46 (7.6)	0.1
30 day mortality	5 (0.8)	2 (0.3)	3 (0.5)	5 (0.8)	0.8
1 year mortality	6 (1.0)	7 (1.2)	11 (2.0)	10 (1.7)	0.1
Intermediate-risk					
N	429	457	433	453	
30 day MACE	35 (8.2)	31 (6.8)	36 (8.3)	28 (6.2)	0.4
30 day mortality	4 (0.9)	3 (0.7)	6 (1.4)	5 (1.1)	0.5
1 year mortality	13 (3.1)	15 (3.3)	20 (4.7)	16 (3.6)	0.4
High-risk					
N	605	632	633	637	
30 day MACE	98 (16.2)	74 (11.7)	65 (10.3)	49 (7.7)	<0.001
30 day mortality	20 (3.3)	29 (4.6)	20 (3.2)	13 (2.1)	0.1
1 year mortality	73 (12.1)	77 (12.2)	72 (11.6)	77 (12.3)	0.9

Values are presented as n (%).

DAPT: Dual antiplatelet therapy; MACE: Death/Unstable angina pectoris/MI/CVA/Stent thrombosis/Urgent revascularization.