Coronary Artery Disease

Predictive Power of In-Hospital and Long-Term Mortality of the GRACE, TIMI, Revised CADILLAC and PAMI Score in NSTEMI Patients with Diabetes – Data from TSOC ACS-DM Registry

Chih-Wei Chen,[1,2] Yi-Chen Hsieh,[3,4,5] Ming-Hsiung Hsieh,[2,6] Yung-Kuo Lin,[2,6] Chun-Yao Huang[1,2] and Jong-Shiuan Yeh[2,6]

Background: Risk score is widely used in non-ST segment elevation myocardial infarction (NSTEMI) patients to predict the in-hospital outcome for immediate coronary angiography decision and care of unit selection.

Objectives: This study compared the performances of the thrombolysis in myocardial infarction (TIMI), Global Registry of Acute Coronary Events (GRACE), Primary Angioplasty in Myocardial Infarction (PAMI), and Revised Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (Revised CADILLAC) risk scores in predicting in-hospital and long-term outcomes in diabetic NSTEMI patients.

Methods: A total of 750 diabetic NSTEMI patients from 27 hospitals were enrolled between January 2013 and December 2015 in the nationwide registry initiated by the Taiwan Society of Cardiology. Four score systems were calculated with receiver operator characteristic analysis used to compare outcome discrimination performance.

Results: No studied risk scores reached acceptable discrimination per area under curve (AUC) in the prediction of in-hospital outcome except for the revised CADILLAC score which reached acceptable discrimination in new-onset cardiogenic shock (AUC = 0.7191) and acute renal failure (AUC = 0.7283). In long-term outcomes, only the revised CADILLAC score reached acceptable discrimination of mortality prediction at 6, 12 and 24 months (AUC = 0.7261 at 6 months, 0.7319 at 12 months, and 0.7256 at 24 months). Subgroup analysis based on the revised CADILLAC score risk class showed a significant difference in adjusted mortality rate between low-risk group/intermediate-risk group and high-risk group.

Conclusions: Only the revised CADILLAC score showed acceptable accuracy to predict the long-term mortality outcome among the scores studied.

Key Words: CADILLAC score • Diabetes mellitus • GRACE score • NSTEMI • PAMI score • TIMI score

[1]Division of Cardiology, Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University; Division of Cardiology, Department of Internal Medicine and Cardiovascular Research Center, Taipei Medical University Hospital; [2]Division of Cardiology, Department of Internal Medicine, School of Medicine, College of Medicine; [3]PhD Program of Neural Regenerative Medicine, College of Medical Science and Technology; [4]PhD Program in Biotechnology Research and Development, College of Pharmacy; [5]Master Program in Applied Molecular Epidemiology, College of Public Health, Taipei Medical University; [6]Division of Cardiovascular Medicine, Department of Internal Medicine, Taipei Municipal Wan-Fang Hospital, Taipei, Taiwan.

Corresponding author: Dr. Jong-Shiuan Yeh, Division of Cardiovascular Medicine, Department of Internal Medicine, Taipei Municipal Wan-Fang Hospital, No. 111, Sec. 3, Xinglong Rd., Wenshan District, Taipei 116, Taiwan. Tel: 886-2-2930-7930; E-mail yvesyeh@gmail.com

INTRODUCTION

Diabetes is one of the major risk factors for cardiovascular disease. Furthermore, diabetes is also an independent predictor of mortality in non-ST-segment elevation myocardial infarction (NSTEMI).[1] Patients with diabetes have demonstrated poorer cardiovascular outcomes after NSTEMI when compared to non-diabetic patients.[2]

Several risk scores have been developed to identify the high-risk patients who may benefit more from aggressive treatment and also predict short-term outcomes.[3-6] Among the developed risk scores, some were

suggested by practical guidelines for acute risk assessment.[7,8] The thrombolysis in myocardial infarction (TIMI) and primary angioplasty in myocardial infarction (PAMI) scores are the most commonly used in clinical practice. The GRACE score has shown reliable predictive power for short-term outcomes,[9] and the same also applies to diabetic patients.[10] However, the ability to predict long-term outcome in acute myocardial infarction (AMI) population remains controversial and only a limited number of studies have investigated the predictive value in ST-segment elevation myocardial infarction (STEMI) populations.[11,12] The controlled abciximab and device investigation to lower late angioplasty complications (CADILLAC)[5,13] and primary angioplasty in myocardial infarction (PAMI) scores[14] are mostly used for STEMI patients post primary percutaneous coronary intervention (PCI) prognosis prediction and few applications in NSTEMI population but little discussion has focused on NSTEMI in this regard. Furthermore, most of the developed risk scores were only validated in Western countries so there is limited data to support the effectiveness in predicting short-term and long-term outcomes in an Asian population. There is one retrospective, single center study conducted in Taiwan which validated the predictive value of the GRACE score in an AMI population and supported the predictive value in short-term and long-term outcomes.[15] However, there is still the need to conduct further investigation for the diabetes population.

The aim of the research was to compare the prognostic predictive value of the GRACE, TIMI, revised CADILLAC, and PAMI scores in NSTEMI with diabetes by using the Acute Coronary Syndrome-Diabetes Mellitus Registry of the Taiwan Society of Cardiology (TSOC ACS-DM Registry) database. Comparison of the risk scores and its components are shown in Table 1.

METHODS

Study population

This prospective, nationwide, multi-center, non-interventional, observational study, the TSOC ACS-DM Registry, was launched by the Scientific Committee of the TSOC.[16] Patients diagnosed of acute coronary syndrome (ACS) with type 2 diabetes were enrolled. Type 2 diabetes could be newly or previously diagnosed and the

diagnosis of type 2 diabetes is defined by the criteria of the World Health Organization and American Diabetes Association. Informed consent was provided to the potential patients to be included in this study. ACS accompanied or precipitated by significant co-morbidities were excluded by this registry such as trauma, motor vehicle accidents, severe gastrointestinal bleeding, peri-operative or peri-procedural related myocardial infarction, or participating in an investigational drug study. All patients could only be enrolled one time in the registry and any further ACS events were recorded as adverse events.

Data collection

The demographic data, clinical characteristics, biochemistry data, inpatient therapy, and in-hospital outcomes including mortality, recurrent non-fatal myocardial infarction (MI), and nonfatal stroke were collected by the study coordinators at the study sites. Medications at admission, during the in-hospital stay, and at discharge were also collected, retrospectively and pro-

Table 1. Risk scoring models and their components

Model components	GRACE	TIMI for NSTEMI	Revised CADILLAC	PAMI
Age	X	X	X	X
Low blood pressure	X	X		
Heart rate	X	X		X
Killip Class	X	X	X	X
Diabetes mellitus		X		X
Hypertension		X		
Angina pectoris		X		
Anterior MI or LBBB		X		X
Weight		X		
Ischemia time		X		
TIMI flow				
Ejection fraction			X	
Anemia			X	
Three-vessel disease			X	
ST-segment deviation	X			
Creatinine/renal insufficiency	X		X	
Cardiac arrest	X			
Increased cardiac markers	X			

CADILLAC, Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications; GRACE, Global Registry of Acute Coronary Events; LBBB, left bundle branch block; MI, myocardial infarction; NSTEMI, non ST-segment elevation myocardial infarction; PAMI, primary angioplasty in myocardial infarction; TIMI, thrombolysis in myocardial infarction.

spectively. The revised CARDILLAC score was used in the current study to exclude final TIMI flow because post-procedural TIMI flow was not included in the registry data collection. Missing TIMI flow data is also possible in NSTEMI patients as PCI treatment might not be performed. All data was then submitted electronically to a central laboratory for verification.

Endpoints

The primary endpoint of interest was all-cause mortality at 6 months, 12 months, and 24 months. The secondary endpoints included recurrent non-fatal MI, bleeding, new-onset cardiogenic shock, and acute renal failure. All records were collected from medical records by well-trained study nurses.

Statistical analysis

Continuous variables were expressed as the mean with standard deviation and categorical variables were shown as the frequency with percentage. Receiver operator characteristic curve analysis was used to determine the performance of each score to discriminate outcomes in NSTEMI patients. All statistical analyses were performed using SAS (version 9.4, SAS, Inc). A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 750 NSTEMI patients with diabetes were enrolled from 27 hospitals between January 2013 and December 2015.

Demographics and baseline characteristics

The average age of the enrolled patients was 66.8 ± 12 years with a male preponderance (66.5%). 92.7% of the patients had a history of type 2 diabetes, and 7.3% of them had newly diagnosed diabetes during this ACS episode. 39.1% had known coronary artery disease (CAD), 18.1% had a history of myocardial infarction and 27.6% of patients already had received PCI. Nearly half of the patients had Killip class I at presentation. Nearly 50% of the patients had Killip class II and III at presentation. 59.1% of them had renal insufficiency in admission. Around one fourth (28%) of patients were under insulin treatment and the average glycated hemoglobin (HbA1C)

level was 8.1%. During the hospitalization, guideline-directed medical therapy (GDMT), dual anti-platelet (DAPT) was used in 82.7% of patients, renin-angiotensin blockers, beta-blocker and statin prescription rate were all higher than 60%. Most of the patients (81.3%) received reperfusion therapy, and 74% of them received PCI. 18.3% of the patients did not receive coronary artery angiography and this resulted in missing data for the number of diseased vessels. Other baseline characteristics, laboratory tests and invasive procedure characteristics are shown in Table 2 and Table 3.

Accuracy of predictive in-hospital outcome

In-hospital outcome includes recurrent myocardial infarction (Re-MI), bleeding episode, new onset cardiogenetic shock and acute renal failure. Among the 4 risk scores studied, the prediction of the majority of the in-hospital outcome did not reach acceptable discrimination per area under curve (AUC) except for the revised CADILLAC score which reached acceptable discrimination in new onset cardiogenic shock (AUC = 0.7191) and acute renal failure (AUC = 0.7283). Details of the results are in Table 4.

Accuracy of predictive mortality

Among the 4 risk scores studied, the prediction of mortality did not reach acceptable discrimination per AUC except for the revised CADILLAC score which reached acceptable discrimination at 6, 12 and 24 months (AUC = 0.7261 at 6 months, 0.7319 at 12 months, and 0.7256 at 24 months). Details of the results are listed in Table 4. Further subgroup analysis based on the revised CADILLAC score risk class showed a significant difference in adjusted mortality rate at 6 months, 1 year and 2 years between the low-risk group (0-2 points)/intermediate-risk group (3-5 points) and high-risk group (≥ 6 points). Details of the results are shown in Table 5. The basic characteristics of the CADILLAC low/intermediate-risk group and high-risk group are listed in Supplemental Table 1.

DISCUSSION

It is observed in the current study that the revised CADILLAC score is the only scoring system that showed acceptable accuracy to predict the long-term mortality

Table 2. Baseline characteristics of patients and medical therapy upon hospital admission

	Non-ST elevation MI (N = 750) Mean (SD) or N (%)
Age (years)	66.8 (12.0)
Gender (female)	251 (33.5%)
Height (cm)	162.2 (8.1)
Weight (kg)	68.4 (13.8)
Body mass index (kg/m^2)	26.0 (4.4)
Systolic blood pressure (mmHg)	147.1 (31.7)
Diastolic blood pressure (mmHg)	82.2 (18.9)
Heart rate (min^{-1})	90.3 (22.2)
Smoker	201 (27.8%)
History of dyslipidemia	359 (47.9%)
History of hypertension	609 (81.2%)
History of diabetes	695 (92.7%)
Known CAD	293 (39.1%)
Previous myocardial infarction	136 (18.1%)
Previous PCI	207 (27.6%)
Previous CABG	50 (6.7%)
History of atrial fibrillation	38 (5.1%)
Previous heart failure	89 (11.9%)
COPD	24 (3.2%)
Obstructive sleep apnea	15 (2.0%)
Peripheral arterial disease	39 (5.2%)
Cerebrovascular disease	89 (11.9%)
Killip Class 1	333 (46.6%)
Killip Class 2	243 (34.0%)
Killip Class 3	107 (15.0%)
Killip Class 4	31 (4.3%)
Reperfusion therapy	610 (81.3%)
PCI	556 (74.1%)
Thrombolysis	2 (0.3%)
CABG	52 (8.5%)
Ejection fraction < 40%	231 (30.8%)
In-hospital medication	
Acetylsalicylic acid	664 (88.5%)
P2Y12	686 (91.5%)
Clopidogrel	491 (65.5%)
Licodin	3 (0.4%)
Ticargrelor	216 (28.8%)
DAPT	620 (82.7%)
Renin-angiotensin blockers	469 (62.5%)
Beta blocker	478 (63.7%)
Statin	561 (74.8%)
Insulin	230 (30.7%)
Sulfonylurea agent	250 (33.3%)
Mitiglinde	58 (7.8%)
Metformin	302 (40.3%)
DPP4-inhibitor	267 (35.6%)
TZD	14 (1.9%)

CABG, coronary artery bypass surgery; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; DAPT, dual antiplatelet therapy; DDP4, dipeptidyl peptidase-4; EF, ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation; TZD, thiazolidinedione.

Table 3. Characteristics of laboratory tests and invasive procedures

	Non-ST elevation MI (N = 750) Mean (SD) or N (%)
Initial CK (U/L)	321.5 (461.9)
Initial CKMB (μg/L)	26.4 (38.1)
Initial troponin (μg/L)	32.0 (217.5)
Peak CK (U/L)	634.2 (924.0)
Peak CKMB (μg/L)	48.8 (69.6)
Peak troponin (μg/L)	132.2 (651.7)
Creatinine (mg/dl)	2.3 (2.6)
Hemoglobin (mg/dl)	12.6 (2.6)
HbA1c (%)	8.1 (1.9)
Total cholesterol (mg/dl)	168.4 (48.9)
HDL (mg/dl)	40.9 (12.3)
LDL (mg/dl)	101.3 (43.7)
Triglyceride (mg/dl)	172.3 (228.3)
Culprit lesion (%)	88.3 (14.1)
Number of diseased vessels	
0	13 (1.7)
1	185 (24.7)
2	167 (22.3)
≥ 3	248 (33.1)
Missing	137 (18.3)

CK, creatine kinase; CKMB, creatine kinase-MB; HbA1C, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein, MI, myocardial infarction; SD, standard deviation; TIMI, thrombolysis in myocardial infarction.

outcome compared with the other scores. The components of the revised CADILLAC score and the niche of the diabetic population of the current study may be a possible explanation. As shown in several prior studies, multiple vessel disease had the worst long-term prognosis in coronary artery disease patients,[17] and some of the studies showed that the GRACE score was not a good predictor in identifying triple-vessel disease (TVD) and left main disease (LM).[18] On the other hand, the diabetes population had a higher prevalence to TVD/LM in ACS[19] and 33% of our patients have triple-vessel disease. Among the 4 prediction scores evaluated, the revised CADILLAC score is the only scoring systemic with parameters to evaluate TVD and it may explain why it is the only scoring system noted with acceptable statistical discrimination.

The other ACS risk scores (including TIMI, PAMI, GRACE) in this study showed little prediction in either the short-term (in-hospital outcome) or long-term out-

Table 4. AUC of the risk scores at different time points in patient with NSTEMI

	TIMI	PAMI	Revised CADILLAC	GRACE
In hospital outcomes				
Re MI	0.6405 (0.3616-0.9193)	0.5722 (0.3088-0.8356)	0.6357 (0.4718-0.7996)	0.6756 (0.4530-0.8981)
Bleed	0.5496 (0.4674-0.6319)	0.6307 (0.5491-0.7122)	0.6606 (0.5880-0.7332)	0.6728 (0.5956-0.7500)
New onset cardiogenic shock	0.5258 (0.4264-0.6251)	0.6348 (0.5245-0.7451)	0.7191 (0.6182-0.8199)*	0.6628 (0.5193-0.8062)
Acute renal failure	0.4997 (0.4003-0.5992)	0.6719 (0.5684-0.7755)	0.7283 (0.6399-0.8167)*	0.6935 (0.5949-0.7921)
Death				
6 months	0.5171 (0.4336-0.6005)	0.6444 (0.5644-0.7244)	0.7261 (0.6598-0.7923)*	0.6675 (0.5829-0.7521)
1 years	0.4994 (0.4298-0.5691)	0.6484 (0.5849-0.7118)	0.7319 (0.6827-0.7811)*	0.6851 (0.6230-0.7472)
2 years	0.5172 (0.4570-0.5774)	0.6754 (0.6215-0.7292)	0.7256 (0.6801-0.7711)*	0.6952 (0.6416-0.7488)

AUC, area under curve; CADILLAC, Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications; GRACE, Global Registry of Acute Coronary Events; MI, myocardial infarction; NSTEMI, non ST-segment elevation myocardial infarction; PAMI, primary angioplasty in myocardial infarction; TIMI, thrombolysis in myocardial infarction.
* Reach acceptable discrimination.

Table 5. Adjusted rate and HRs of mortality by revised CADILLAC risk class

	Alive	Death	HR (95% CI)	p-value	HR* (95% CI)	p-value
6 months						
Low risk (0-2)/intermediate risk (3-5)	285 (40.20)	4 (9.8)	1.0		1.0	
High risk (≥ 6)	424 (59.8)	37 (90.2)	6.1 (2.2-17.0)	0.0006	5.5 (2.0-15.5)	0.0012
1 year						
Low risk (0-2)/intermediate risk (3-5)	284 (41.5)	5 (7.6)	1.0		1.0	
High risk (≥ 6)	400 (58.5)	61 (92.4)	8.3 (3.3-20.6)	< 0.0001	7.5 (3.0-18.8)	< 0.0001
2 year						
Low risk (0-2)/intermediate risk (3-5)	281 (42.5)	8 (9.0)	1.0		1.0	
High risk (≥ 6)	380 (57.5)	81 (91.0)	7.4 (3.6-15.2)	< 0.0001	6.7 (3.2-14.0)	< 0.0001

CADILLAC, Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications; CI, confidence intervals; HR, Hazard ratios.
* Adjustment for gender, hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation.

comes (6 months to 24 months mortality) in the studied NSTEMI patients with diabetes. There are several possible reasons which may explain the distinctive finding from prior studies. For instance, there is the difference in the researched niche of the current study compared to previous GRACE and CADILLAC score studies. All of our patients were diabetic with 92.7% of patients diagnosed before the NSTEMI episode and 7.3% of the patients diagnosed during this NSTEMI episode. More than one fourth of diabetes patients were treated with insulin which suggested a long history of diabetes. In addition, the average creatinine level was 2.2 mg/dl and nearly 60% of patients had renal insufficiency in admission, which presented a population with diabetes nephropathy. And that is distinct to the original GRACE score study which consisted of only 23.3% of diabetic and 7.2% of renal dysfunction among the enrolled pa-

tient pool.[4,5] Since renal insufficiency is one of the known factors of the GRACE score, the percentage of chronic kidney disease (CKD) may decrease the statistical discrimination ability to predict an outcome. When using Killip classification, it was noted that 50% of enrolled patients were classified as Killip class II/III at presentation while only 16% and 10.9% of patients were classified the same in prior GRACE and CADILLAC score studies at presentation.[4,5] This should indicate that the condition of our patients was worse than those of other prior studies due to the comorbidity resulting from diabetic nature. The remaining comparison of baseline characteristic in our study, the GRACE and CADILLAC study patients, are shown in Table 6.

It was unexpected that the GRACE score failed to show predicted value for in-hospital outcome which it was initially designed for and is widely used in clinical

Table 6. Comparison of TSOC-ACS DM (NSTEMI), GRACE and CADILLAC study patient baseline characteristic

Variable	TSOC-ACS DM (NSTEMI) (N = 750)	GRACE 2003[4] (N = 11389)	CADILLAC 2005[5] (N = 2082)
Age (years)	66.8	66.3	59.0
Female	33.5%	33.5%	27.0%
Risk factor			
DM	92.7%	23.3%	16.6%
Dyslipidemia	52.2%	52.2%	37.9%
HTN	81.2%	57.8%	48.1%
Smoking	27.8%	56.7%	43.1%
Renal dysfunction	59.1%	7.2%	-
Dialysis dependent	11.2%	-	-
CAD known	39.1%	22.0%	-
MI history	18.1%	32.0%	13.7%
Killip			
I	46.6%	82.7%	-
II	34.0%	13.2%	10.9% (II and III)
III	15.0%	3.1%	
IV	4.3%	1.0%	-
TVD	37.0%	-	15.6%
Reperfusion strategy			
PCI	74.1%	-	-
Thrombolysis	0.3%	-	-
CABG	8.5%	-	-
Outcome			
In hospital death	1.5%	3.5%	1.6%
6 month	5.5%	-	-
1 year	8.8%	-	4.3%
2 year	11.9%	-	-

ACS, acute coronary syndrome; CABG, coronary artery bypass surgery; CAD, coronary artery disease; CADILLAC, Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications; DM, diabetes mellitus; GRACE, Global Registry of Acute Coronary Events; HTN, hypertension; MI, myocardial infarction; NSTEMI, non ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; TSOC, Taiwan Society of Cardiology; TVD, triple vessel diseas.

practice. It may be that the progress in patient care over time by using troponin testing has aided early detection of NSTEMI and further contributes to the improvement of short-term outcome. In the current used registry, NSTEMI patients in-hospital mortality rate was only 1.5%, which is relatively low compared to studies conducted 20 years ago.[4,5,20] The difference in mortality rate could be the result of increasing use of GDMT in the early stages, including DAPT and beta-blockers, which may also help to lower the in-hospital outcome and long-term mortality.[21,22] Increased early reperfusion strategy may also play an important role in lowering the outcomes as 74.1% of NSTEMI patients received PCI for reperfusion in the current registry which is much different from scoring systems in the developed era.[20] Comparisons of patient basic characteristics, management and outcome with the prior GRACE and CADILLAC scores are shown in Table 4. To sum up, as patient care strategies evolve over time, the GRACE score was developed in a time when troponin, early reperfusion and ACS-GDMT had not been widely applied and it may not continue to be superior in predictive value in in-hospital outcome and long-term outcome in current clinical settings and in diabetes patients with NSTEMI.

There are several limitations to this study. First, selection bias may exist as this study was a post-hoc data analysis based on the TSOC ACS-DM Registry. Second, several parameters were not including in this study, such as how long the patients had diabetes, and the scoring system, like syntax score which applies angiography findings. Third, some patients may have transit hyperglycemia during acute coronary syndrome which could be an over-diagnosis of a diabetes patient. Fourth, there were few studies regarding the application of the CADILLAC score in NSTEMI patients as the original study design of the CADILLAC score was for prognosis evaluation post

primary PCI for AMI patients and it only enrolled few NSTEMI patients and excluded NSTEMI patients who required multivessel PCI.[5] Furthermore, the original registry data used in the current study did not include final TIMI flow data so the revised CADILLAC score which excluded TIMI flow from the calculation was used for prognosis evaluation. This might be different from the original population and design of the CADILLAC score but the current study result has demonstrated that the revised CARDILLAC score is reliable in prognostic evaluation. Last, the calculated CADILLAC score may be underestimated in some patients in the current study since only 81.3% of the patients from the current registry study received reperfusion therapy.

CONCLUSIONS

The revised CADILLAC score is the only scoring system that showed acceptable accuracy to predict long-term mortality outcome compared with other scores. The GRACE score and other scoring systems cannot show good predictive value either in in-hospital outcome or long-term survival outcome. Based on our findings, we may consider that in the era of high prevalence of troponin use and early reperfusion strategy, a new scoring system, especially in NSTEMI and diabetes patients, may be needed.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTEREST

All the authors declare no conflict of interest.

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SUPPLEMENT

Supplement Table 1. Basic characteristic of low/intermediate and high-risk group by CADILLAC risk class

	Low risk (0-2)/Intermediate risk (3-5)	High risk (6+)	p-value
AGE (years)	60.2 (10.9)	69.8 (11.3)	< 0.0001
Gender (female)	58 (24.9)	193 (37.3)	0.0008
Height (cm)	163.9 (8.6)	161.5 (7.7)	0.0003
Weight (kg)	72.2 (14.1)	66.5 (13.3)	< 0.0001
Body mass index (kg/m^2)	26.9 (4.5)	25.5 (4.3)	0.0003
Systolic blood pressure (mmHg)	147.3 (28.8)	146.9 (32.9)	0.8708
Diastolic blood pressure (mmHg)	85.8 (17.5)	80.6 (19.3)	0.0003
Heart rate (min^{-1})	86.8 (21.3)	91.9 (22.4)	0.0038
Smoker	83 (36.9)	118 (23.7)	0.0002
History of dyslipidemia	106 (45.5)	253 (48.9)	0.3825
History of hypertension	173 (74.3)	436 (84.3)	0.0011
History of diabetes	205 (88.0)	490 (94.8)	0.0010
Known CAD	65 (27.9)	228 (44.1)	< 0.0001
Previous myocardial infarction	33 (14.2)	103 (19.9)	0.0582
Previous PCI	44 (18.9)	163 (31.5)	0.0003
Previous CABG	6 (2.6)	44 (8.5)	0.0025
History of atrial fibrillation	9 (3.9)	29 (5.6)	0.3128
Previous heart failure	10 (4.3)	79 (15.3)	< 0.0001
COPD	5 (2.2)	19 (3.7)	0.2709
Obstructive sleep apnea	3 (1.3)	12 (2.3)	0.3495
Peripheral arterial disease	6 (2.6)	33 (6.4)	0.0297
Cerebrovascular disease	20 (8.6)	69 (13.4)	0.0620
EF < 40%	1 (0.4)	109 (21.1)	< 0.0001

CABG, coronary artery bypass surgery; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; PCI, percutaneous coronary intervention.