ORIGINAL RESEARCH

Varying Definitions for Periprocedural Myocardial Infarction Alter Event Rates and Prognostic Implications

Hanan Idris, MB ChB; Sidney Lo, MBBS; Ibrahim M. Shugman, MBBCh, PhD; Yousef Saad, MBBCh; Andrew P. Hopkins, MBBS; Christian Mussap, MBBS, PhD; Dominic Leung, MBBS, PhD; Liza Thomas, MBBS, PhD; Craig P. Juergens, MBBS, MD; John K. French, MB ChB, PhD

***Background*—**Periprocedural myocardial infarction (PMI) has had several definitions in the last decade, including the Society for Cardiovascular Angiography and Interventions (SCAI) definition, that requires marked biomarker elevations congruent with surgical PMI criteria.

***Methods and Results*—**The aim of this study was to examine the definition-based frequencies of PMI and whether they influenced the reported association between PMI and increased rates of late death/ myocardial infarction (MI). We studied 742 patients; 492 (66%) had normal troponin T (TnT) levels and 250 (34%) had elevated, but stable or falling, TnT levels. PMI, using the 2007 and the 2012 universal definition, occurred in 172 (23.2%) and in 99 (13.3%) patients, respectively, whereas 19 (2.6%) met the SCAI PMI definition ($P<0.0001$). Among patients with PMI using the 2012 definition, occlusion of a side branch ≤1 mm occurred in 48 patients (48.5%) and was the most common angiographic finding for PMI. The rates of death/MI at 2 years in patients with, compared to those without, PMI was 14.7% versus 10.1% ($P=0.087$) based on the 2007 definition, 16.9% versus 10.3% ($P=0.059$) based on the 2012 definition, and 29.4% versus 10.7% ($P=0.015$) based on the SCAI definition.

***Conclusion*—**In this study, PMI, according to the SCAI definition, was associated with more-frequent late death/MI, with ≈20% of all patients, who had PMI using the 2007 universal MI definition, not having SCAI-defined PMI. Categorizing these latter patients as SCAI-defined no PMI did not alter the rate of death/MI among no-PMI patients. **(*J Am Heart Assoc*. 2014;3:e001086 doi: 10.1161/JAHA.114.001086)**

Key Words: percutaneous coronary intervention • periprocedural myocardial infarction • reinfarction • troponin T

Periprocedural myocardial infarction (PMI) has had changing diagnostic criteria over the last decade. Elevation(s) in post–percutaneous coronary intervention (PCI) blood levels of markers of myocyte necrosis, preferably troponin T or I (TnT or TnI), were sufficient for the diagnosis of PMI using the 2000 and 2007 universal definitions of myocardial infarction (MI),[1–3] but the 2012 universal MI definition requires features additional to biomarker elevations for the diagnosis. These include ischemic chest pain ≥20 minutes, ischemic ECG changes, and/or abnormal findings on either invasive or noninvasive imaging.[4] Given that chest pain is very common post-PCI in the absence of cardiac biomarker elevations, it has usually been assumed to be nonischaemic in origin. Conversely, some patients have cardiac biomarker elevations, but do not have either chest pain or observed changes in invasive or noninvasive imaging that would otherwise meet the criteria for the 2012 PMI definition.[5–7]

Recently, the Society for Cardiovascular Angiography and Interventions (SCAI) has developed PMI criteria similar to post–coronary artery bypass graft (CABG) MI criteria with biomarkers elevation ≥10× upper reference limit (URL) for creatine kinase MB (CKMB) and/or ≥70×URL for troponin.[8] These PMI definition changes are likely to reduce the frequency of this event. The consequence of changing definitions may alter the prognostic significance of PMI.[9] Also MI, including PMI, is often a component of the primary endpoint of clinical trials, so if PMI is a less-frequent event, then trial costs may increase.

In order to evaluate the impact of using these different criteria to define PMI on event frequency, we examined post-PCI levels of TnT and CKMB and other additional PMI criteria in the 2012 universal MI definition. The influence of PMI definition on late outcomes after PCI was also studied.

From the Cardiology Department, Liverpool Hospital and South Western Sydney Clinical School, The University of New South Wales, Sydney, NSW, Australia.

Correspondence to: John K. French, MBChB, PhD, Cardiology Department, Liverpool Hospital, Elizabeth Street, Liverpool, New South Wales 2170, Australia. E-mail: j.french@unsw.edu.au

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Methods

Study Population

All patients undergoing PCI at the cardiac catheterization laboratories of Liverpool Hospital (Sydney, Australia) have clinical, angiographic, and procedural data recorded prospectively in cardiology and laboratory databases.[10] These data include procedural indications, patient demographics, medications, angiographic and lesion characteristics, and stent types (drug-eluting stent [DES] or bare-metal stent). The current study includes patients undergoing PCI for stable coronary heart disease (CHD), unstable angina, and non-ST-segment elevation MI (NSTEMI) from October 1, 2003 to September 2010, who had qualifying cardiac biomarkers measurements before and after PCI. These included normal preprocedural TnT levels, or when pre-PCI TnT levels were elevated, and 2 stable or falling levels 6 hours apart. Exclusion criteria included ST-segment elevation myocardial infarction (STEMI), missing pre- and/or post-PCI TnT results, post-PCI TnT and/or CKMB measurements >48 hours, or elevated pre-PCI TnT levels within 72 hours that were not stabilized or falling (Figure 1). Post-PCI outcomes are rou-

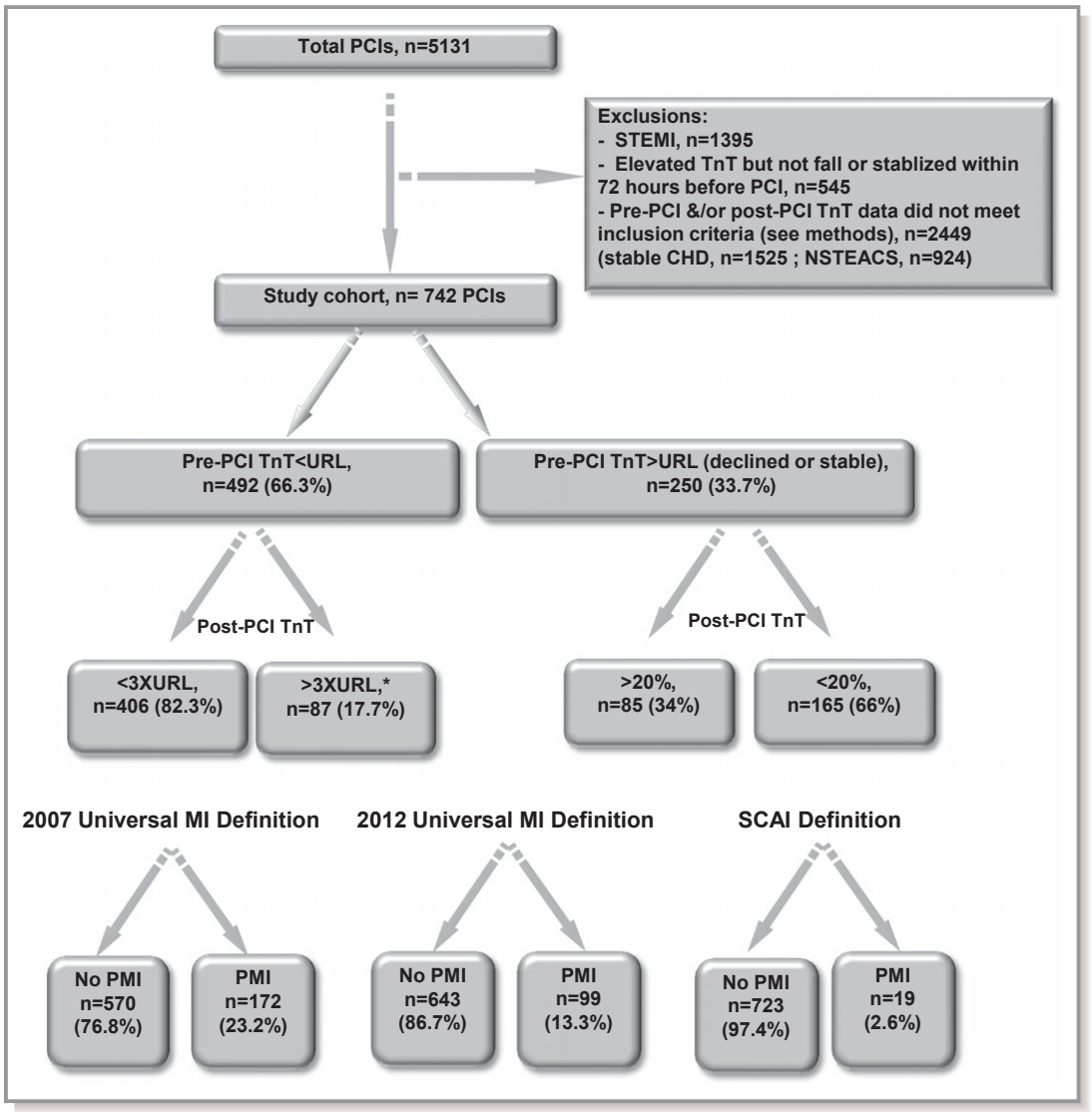

Figure 1. Study population. The diagram shows the patients from the total angioplasty cohort. Also, the reasons for exclusion from the current study for those who underwent PCI in the study period are shown. *Fifty-two patients had post-PCI TnT >5×URL. CHD indicates coronary heart disease; MI, myocardial infarction; NSTEACS, non-ST-segment elevation acute coronary syndrome; PCI, percutaneous coronary intervention; PMI, periprocedural myocardial infarction; SCAI, Society for Cardiovascular Angiography and Interventions; STEMI, ST-segment elevation myocardial infarction; TnT, troponin T; URL, upper reference limit.

tinely assessed for quality assurance (project QA2008/034, approved by the Liverpool Hospital Ethics Committee).

PCI Procedures

Procedural details were as previously described.[10] Stent deployment was performed according to our institutions' DES selective use criteria,[11,12] and angiographic successful procedures were defined as final post-PCI minimum stenosis diameter reduction to <20% in cases after stenting or to <50% after balloon angioplasty in the presence of grade 3 Thrombolysis In Myocardial Infarction (TIMI) flow.[13]

Definition of PMI

The 2007 universal MI definition of PMI merely required elevation of cardiac biomarkers, preferably TnT or TnI, post-PCI (an ischemic setting),[2] whereas the 2012 universal MI definition of PMI required ischemic chest pain ≥20 minutes, ischemic ECG change, and/or abnormal changes on either invasive or noninvasive imaging, in addition to elevations in cardiac biomarkers. The SCAI definition requires elevation of cardiac biomarkers, preferably CKMB (Table 1).[4,8] Among patients who met the TnT or CKMB criteria for diagnosis of PMI, as required for the 2012 universal MI definition and the SCAI definition, the data on ischemic chest pain and ischemic ECG changes were collected from the recorded cardiology databases. The angiographic and noninvasive imaging criteria for diagnosis of PMI, as required for the 2012 universal MI definition, included identifiable side-branch occlusion (defined as ≤1 mm, >1 to <2 mm, and ≥2 mm), persistent or transient slow or no-reflow, distal embolization, or dissection. These were reviewed by 5 experienced interventional cardiologists, and noninvasive imaging and disagreements were reviewed by a consensus panel of 3 (H.I., S.L., and J.F.), if necessary.

Laboratory Assays

Venous blood samples for TnT measurements were made using the third- and fourth-generation TnT assay (Roche, Mannheim, Germany). Only patients with TnT and/or CKMB measured within 48 hours post-PCI were included, and the highest value was included for the analysis. The URL for TnT using the third- and fourth-generation assays (used before and after January 15, 2006, respectively) was 0.03 μg/L, defined as the level at <10% coefficient of variation, complying with the European Society of Cardiology (ECS)/American College of Cardiology (ACC) consensus requirements.[1]

Clinical Follow-up

Late clinical outcomes included death, MI, stent thrombosis (ST), and target vessels revascularization (TVR), defined as ischemia-driven repeat revascularization of the culprit lesion,

Table 1. ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction and SCAI Definition With PCI

	2007 Universal MI Definition	2012 Universal MI Definition	SCAI Definition
Biomarkers criteria			
Normal baseline values	Elevation of TnT values >3×URL	Elevation of TnT values >5×URL	Elevation of CKMB values ≥10×URL or TnT values ≥70×URL Elevation of CKMB values ≥5×URL or TnT values ≥35×URL*
Elevated baseline values, but stable or falling	Elevation of TnT values >20%	Elevation of TnT values >20%	Increment rise of CKMB ≥10×URL or TnT values ≥70×URL
Elevated baseline, but not stable or falling			Increment rise of CKMB≥10×URL or TnT values ≥70×URL*
Additional criteria	Not required	Ischemic chest pain ≥20 minutes or ischemic ECG changes or angiographic evidence: side-branch occlusion Slow flow or no-reflow embolization. . .. or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality	New pathological Q-waves in 2 contiguous leads or new persistent LBB in ECG

ACCF indicates American College of Cardiology Foundation; AHA, American Heart Association; CKMB, creatine kinase MB; ESC, European Society of Cardiology; MI, myocardial infarction; PCI, percutaneous coronary intervention; SCAI, Society for Cardiovascular Angiography and Interventions; TnT, troponin T; URL, upper reference limit, WHF, World Heart Federation.
*Additional criteria required.

by PCI or CABG (as defined by the Academic Research Consortium).[14] The composite of major adverse cardiac events (MACEs) include death/MI/TVR/ST, as previously reported.[11] In brief, trained research staff (nurses or doctors) contacted patients, their relatives, or local physicians by phone and were asked about recurrent cardiac symptoms requiring hospitalization, particularly coronary revascularization, or MI. Data regarding death were obtained from family members, physicians, medical records, and death registry. Other clinical outcomes, such as repeated procedures for stent thrombosis and restenosis, were also evaluated and documented in our database.

Statistical Analysis

Statistical analysis was performed using SPSS (version 21; SPSS, Inc., Chicago, IL). Categorical variables were expressed as numbers and percentages per group, continuous variables as mean±SD for normally distributed variables, and medians and (25th and 75th percentiles) for skewed variables. For group comparisons, Pearson's chi-square (χ^2) test or Fisher's exact test were used, as appropriate, for unpaired categorical variables. McNemar's test was used for comparison of 2 related categorical variables and Cochran's Q test for comparisons of 3 related categorical variables. The Student *t* tests or the Mann-Whitney's U tests (for skewed variables) were used for continuous variables.

Multivariable analysis was performed with the logistic regression analysis method to determine independent predictors of PMI. Variables with *P* values <0.2 on univariable analysis were included in multivariable analysis models. These included age, sex, body mass index (BMI), hypertension (HTN), smoking, clinical indication for PCI, elevated pre-PCI TnT level, an estimated pre-PCI glomerular filtration rate (eGFR) >30 to <60 mL/min per 1.73 m^2, using the MDRD formula ($eGFR=186.3\times SerumCr^{-1.154}\times age^{-0.203}\times 0.742$ [if female]),[15] ACC/American Heart Association (AHA) class B2 and C lesions, calcified lesion, dissection, rotablation, pre-PCI stenosis, culprit lesion length ≥20 mm, deployment of more than 1 stent, maximum deployment pressure duration, and TIMI 3 flow grade post-PCI applied. Odds ratio (OR) and 95% confidence interval (CI) were reported.

Hazard ratios (HRs) with 95% CI were performed with Cox's regression analysis of the following events—death, MI, TVR, and ST—which represented MACEs and combined death or MI and at 30 days, 1 year, and 2 years in patients with, and without, PMI according to 2007 and 2012 universal MI definitions and the SCAI definition, respectively. Also, HRs for death and/or MI at 2 years were adjusted for age, pre-PCI TnT level, and eGFR >30 to <60 mL/min per 1.73 m^2. Five patients whose PCIs were unsuccessful as a result of failure to open chronic total occlusions, and 47 patients who were lost to follow-up, were excluded from Cox's regression analysis of late clinical outcomes. Kaplan-Meier's curves for late outcomes were compared using log-rank testing. *P* values <0.05 were considered statistically significant.

Results

Patients Clinical and Procedural Characteristics

This study included 742 patients who underwent PCI, 132 for stable CHD and 610 patients for acute coronary syndrome (315 NSTEMI and 295 unstable angina; Table 2). The mean age was 64±11 years, 74% were males, 28% had diabetes, and 60% had ACC/AHA class B2 and C lesions. Periprocedural GPIIb/IIIa inhibitors were used in 20% of PCIs, and in 97% of PCIs, at least 1 stent was deployed (32% had ≥1 DES); 4 patients had rotational atherectomy.

Patients with PMI, compared to those without, were more likely to have HTN, had more renal dysfunction (eGFR 30 to <60 mL/min per 1.73 m^2), had longer procedural time, and had ACC/AHA class B2 and C lesions. Demographic and angiographic characteristics of patients with, and without PMI, according to the 2007 and the 2012 universal definitions of MI and the SCAI definition, are shown in Tables 2 and 3.

Pre-PCI TnT levels were <URL in 492 (66%) and were elevated in 250 (34%) patients. PMI using the 2007 universal MI definition occurred in 172 (23%) patients (87 had post-PCI TnT levels elevations >3×URL, and 85 had >20% elevation post-PCI TnT levels), whereas PMI, based on the 2012 universal MI definition, occurred only in 99 (13%) patients (44 had post-PCI TnT-level elevations >5×URL and 55 with elevated pre-PCI TnT had >20% increase post-PCI levels). The most common additional criteria for the 2012 universal PMI definition was side-branch occlusion in 53 patients (54%); side-branch diameters were ≤1 mm in 48 patients, >1 to <2 mm in 3, and ≥2 mm in 2. Other reasons included persistent or transient slow or no-reflow in 33% and 21% had distal embolization, whereas only 11% patients had ischemic chest pain and 12% had ischemic ECG changes; some had >1 criteria (Figure 2). An additional 38 patients met the TnT elevation criteria for the 2012 universal MI definition of PMI without an additional feature (8 patients with normal pre-PCI TnT levels and 30 with elevated pre-PCI TnT levels). According to the SCAI definition, PMI occurred in 19 (2.6%) patients (11 with normal pre-PCI TnT and 8 with elevated pre-PCI TnT levels; 3-way frequency comparison, *P*<0.001). All 19 patients who fulfilled the SCAI definition of PMI fulfilled the 2007 universal definition of MI, but 2 of these did not fulfil the 2012 universal MI definition.

Based on our previously reported correlation between CKMB and TnT using the equation: TnT (μg/L)=$e^{[(1.202[lnCKMB}$

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Table 2. Baseline Demographic and Clinical Features of Patients With and Without PMI Using the 2007 and the 2012 Universal MI Definition and SCAI Definition

Variable	All (n=742)	2007 Universal MI Definition			2012 Universal MI Definition			SCAI Definition		
		No PMI (n=570)	PMI (n=172)	*P* Value	No PMI (n=643)	PMI (n=99)	*P* Value	No PMI (n=723)	PMI (n=19)	*P* Value
Age, y*	64±11	63±12	68±11	<0.0001	64±12	68±10	0.001	64±11	69±8	0.087
Male sex	552 (74)	431 (76)	121 (70)	0.166	484 (75)	68 (69)	0.162	539 (75)	13 (68)	0.595
BMI, kg/m^2†	28 [25 to 31]	28 [25 to 32]	27 [24 to 30]	0.037	28 [25 to 32]	27 [24 to 30]	0.104	27 [25 to 31]	28 [26 to 31]	0.960
Diabetes mellitus	209 (28)	160 (28)	49 (28)	0.915	176 (27)	33 (33)	0.220	202 (28)	7 (37)	0.394
Cigarette smoker	166 (22)	134 (24)	32 (19)	0.176	147 (23)	19 (19)	0.415	164 (23)	2 (10)	0.273
Hypertension	494 (67)	369 (65)	126 (73)	0.038	420 (65)	75 (76)	0.040	478 (66)	17 (89)	0.033
Hyperlipidemia‡	533 (72)	410 (72)	123 (71)	0.915	463 (72)	70 (71)	0.789	517 (71)	16 (84)	0.224
Family history of CHD	136 (18)	109 (19)	27 (16)	0.309	121 (19)	15 (15)	0.380	130 (18)	6 (32)	0.136
Previous PCI	98 (13)	75 (13)	23 (13)	0.942	82 (13)	16 (16)	0.351	95 (13)	3 (16)	0.729
Previous CABG	75 (10)	55 (10)	20 (12)	0.450	64 (10)	11 (12)	0.722	72 (10)	3 (16)	0.428
Clinical presentation										
Stable CHD	132 (18)	106 (19)	26 (15)	0.296	120 (19)	12 (12)	0.113	128 (18)	4 (21)	0.760
Unstable angina	295 (40)	250 (44)	45 (26)	<0.0001	274 (43)	21 (21)	<0.0001	288 (40)	7 (37)	0.793
NSTEMI	315 (42)	214 (37)	101 (59)		249 (39)	66 (67)		307 (42)	8 (42)	0.975
Pre-PCI TnT										
<URL	492 (66)	405 (71)	87 (51)	<0.0001	448 (70)	44 (44)	<0.0001	481 (66)	11 (58)	0.432
>URL	250 (34)	165 (29)	85 (49)		195 (30)	55 (56)		242 (33)	8 (42)	
eGFR										
30 to <60	196 (27)	141 (25)	58 (35)	0.010	160 (25)	36 (42)	0.001	186 (26)	10 (56)	0.012
<30	21 (3)	13 (2)	8 (5)	0.026	18 (3)	3 (3)	0.731	20 (3)	1 (6)	0.416

Values are expressed as n (%), unless otherwise indicated. Five patients with NSTEMI had shock, of whom 2 had PMI using either the 2007 or the 2012 universal definition and neither met the SCAI definition. BMI indicates body mass index; CABG, coronary artery bypass graft; CHD, coronary heart disease; eGFR, estimated glomerular filtration rate (mL/min per 1.73 m^2); MI, myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; PMI, periprocedural myocardial infarction; SCAI, Society for Cardiovascular Angiography and Interventions; TnT, troponin T; URL, upper reference limit.

*Mean±SD.

†Median [25th percentile to 75th percentile].

‡Hyperlipidemia defined as previous diagnosis of hypercholesterolemia, including treatment with lipid-lowering agents or fasting low-density lipoprotein cholesterol of ≥130 mg/dL or total cholesterol of ≥200 mg/dL.

Table 3. Angiographic and Procedural Characteristics of Patients With and Without PMI Using the 2007 and the 2012 Universal MI Definition and SCAI Definition

Variable	All (n=742)	2007 Universal MI Definition			2012 Universal MI Definition			SCAI Definition		
		No PMI (n=570)	PMI (n=172)	*P* Value	No PMI (n=643)	PMI (n=99)	*P* Value	No PMI (n=723)	PMI (n=19)	*P* Value
Culprit coronary artery										
Left main	8 (1.1)	5 (0.9)	3 (1.7)	0.396	7 (1.1)	1 (1.0)	0.999	7 (1)	1 (5)	0.188
LAD	293 (39)	222 (39)	71 (41.3)	0.583	257 (40.0)	36 (36.4)	0.495	287 (40)	6 (32)	0.475
LCX*	188 (2 5)	145 (25)	43 (25)	0.908	162 (25)	26 (26)	0.520	185 (26)	3 (16)	0.430
RCA	219 (29)	173 (30)	46 (27)	0.363	190 (29)	29 (29)	0.959	213 (29)	6 (32)	0.842
Bypass graft	33 (4)	24 (4)	9 (5)	0.569	26 (4)	7 (7)	0.187	30 (4)	3 (16)	0.048
B2/C Lesion (ACC/AHA)	441 (60)	329 (58)	112 (65)	0.097	366 (57)	75 (78)	0.0001	425 (59)	16 (84)	0.027
Proximal LAD lesion	175 (24)	136 (24)	39 (23)	0.748	15 (24)	23 (23)	0.929	171 (24)	4 (21)	0.999
Lesions at bifurcation	153 (21)	113 (20)	40 (23)	0.330	134 (21)	19 (19)	0.706	148 (20)	5 (26)	0.565
Lesions calcifications	106 (14)	72 (13)	34 (20)	0.019	89 (14)	17 (17)	0.378	101 (14)	5 (26)	0.172
Pre-PCI coronary artery stenosis (%)†	86±11	86±11	88±10	0.003	86±11	89±10	0.003	86±11	89±10	0.281
Lesion length ≥20 mm	311 (42)	226 (40)	85 (50)	0.025	254 (40)	57 (58)	0.001	303 (42)	8 (42)	0.985
≥1 drug-eluting stent	299 (32)	179 (32)	50 (30)	0.647	199 (32)	30 (32)	0.967	224 (32)	5 (29)	0.833
>1 stent	182 (24)	124 (22)	58 (34)	0.001	141 (22)	41 (41)	<0.0001	175 (24)	7 (37)	0.276
PCI duration (minutes)‡	65 [50 to 84]	65 [5 to 0]	70 [55 to 95]	0.0001	65 [50 to 82]	78 [57 to 98]	0.0001	64 [50 to 82]	90 [77 to 100]	0.0001
Maximal deployment pressure (atm)‡	18 [16 to 20]	18 [16 to 20]	18 [16 to 20]	0.441	18 [16 to 20]	18 [16 to 20]	0.846	18 [16 to 20]	18 [16 to 20]	0.956
Maximal deployment pressure duration (s)‡	25 [20 to 30]	25 [20 to 30]	26 [20 to 30]	0.070	25 [20 to 30]	25 [20 to 30]	0.403	25 [20 to 30]	30 [20 to 30]	0.191
Glycoprotein IIb/IIIa inhibitor	149 (20)	105 (18)	44 (26)	0.040	122 (19)	27 (27)	0.055	142 (20)	7 (37)	0.080
Rotablation	4 (0.5)	1 (0.2)	3 (2)	0.014	2 (0.3)	2 (2)	0.088	4 (0.6)	0 (0)	
Dissection	28 (4)	6 (1)	22 (12.8)	<0.0001	13 (2)	15 (15)	<0.0001	23 (3)	5 (26)	<0.0001
TIMI 3 flow grade after PCI	730 (99)	564 (99)	166 (99)	0.035	636 (96)	94 (94)	0.022	731 (99)	17 (94)	0.200
Angiographic success	723 (98)	556 (98)	167 (98)	0.746	627 (98)	96 (97)	0.439	705 (98)	18 (95)	0.326

Values are expressed as n (%), unless otherwise indicated. ACC/AHA indicates American College of Cardiology/American Heart Association; atm, atmospheres; LAD, left anterior descending coronary artery; LCX, left circumflex artery; MI, myocardial infarction; PCI, percutaneous coronary intervention; PMI, periprocedural myocardial infarction; RCA, right coronary artery; SCAI, Society for Cardiovascular Angiography and Interventions; TIMI, Thrombolysis in Myocardial Infarction.

*Ten patients with ramus intermediate PCIs were included in the LCX group.

†Mean±SD.

‡Median [25th percentile to 75th percentile].

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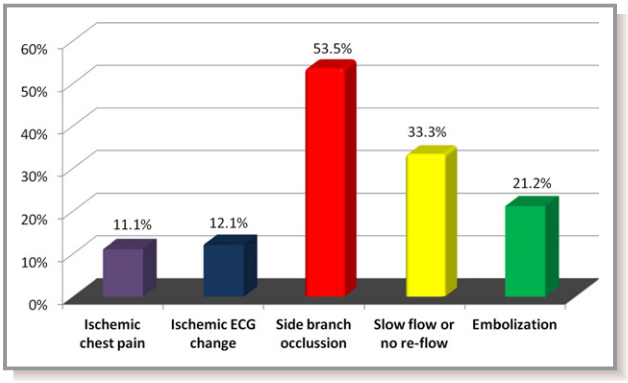

Figure 2. Additional criteria for periprocedural myocardial infarction according to the 2012 universal MI definition. MI indicates myocardial infarction.

μg/L))−4.693+0.264(if eGFR<30)], when the pre-PCI TnT level was <URL, and the equation: additional TnT elevation (μg/L) $=e^{[(1.103[\ln CKMB\ \mu g/L])-4.824+0.406(\text{if eGFR}<30)]}$, when pre-PCI TnT level >URL,[10] we found the PMI frequency based on biomarker levels of ≥10×URL for CKMB, which equates to TnT levels of ≥17×URL in females and ≥33×URL in males, occurred in 32 (4.3%) patients.

Independent predictors for PMI, based on the 2007 universal MI definition, on the multivariable logistic regression analysis model were coronary dissection, pre-PCI (TnT) >URL, age, and coronary artery stenosis (%) pre-PCI. Applying the 2012 universal MI definition and using the same model identified ACC/AHA class B2 and C lesions and deployment of ≥1 stent as additional independent predictive factors. However, using the same model for the SCAI definition of PMI, the independent predictors were only coronary dissection and renal dysfunction (eGFR, >30 to <60 mL/min per 1.73 m^2; Table 4).

Clinical Outcomes

Late outcomes of death—recurrent MI, TVR, and MACE—were assessed at a median of 37 (interquartile range, 20 to 55) months post-PCI and were not significantly different in patients with and without PMI, based on the 2007 universal MI definition (Figure 3 and Table 5). Though according to the 2012 universal definition of MI, there was a trend toward worse outcomes in patients with PMI, compared to patients without PMI (death/MI at 2 years; *P*=0.059). However, the SCAI definition showed an increased frequency of death/MI at 2 years in patients with PMI, compared to those without (*P*=0.015; Figure 3). Kaplan-Meier's analysis for death, MI, and the combination in patients with or without PMI, according to the 2007 and the 2012 universal MI definitions and the SCAI definition, are shown in Figure 4. The late events of death and/or nonfatal MI were more frequent in patients with normal pre-PCI TnT, but not in patients with elevated pre-PCI TnT levels, according to the 3 definitions of PMI (Table 6).

Table 4. Independent Predictors of Periprocedural Myocardial Infarction

Variables	OR (95% CI)	*P* Value
2007 MI definition		
Dissection	10.72 (3.95 to 29.11)	<0.0001
Pre-PCI troponin (TnT) >URL	2.76 (1.81 to 4.19)	<0.0001
Age, y	1.03 (1.01 to 1.05))	0.001
Coronary artery stenosis Pre-PCI (%)	1.02 (1.00 to 1.04)	0.041
2012 MI definition		
Dissection	5.04 (1.93 to 13.15)	0.001
Pre-PCI troponin (TnT) >URL	3.24 (1.93 to 5.44)	<0.0001
Age, y	1.03 (1.01 to 1.05)	0.0
Coronary artery stenosis Pre-PCI, %	1.03 (1.01 to 1.06)	0.020
Lesion B2/C type (ACC/AHA)	1.95 (1.07 to 3.57)	0.030
>1 stent	1.84 (1.06 to 3.19)	0.031
SCAI definition		
Dissection	10.12 (2.88 to 35.55)	<0.0001
eGFR (mL/min per 1.73 m^2) 30 to <60	4.13 (1.51 to 11.25)	0.006

ACC/AHA indicates American College of Cardiology/American Heart Association; CI, confidence interval; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; OR, odds ratio; PCI, percutaneous coronary intervention; SCAI, Society for Cardiovascular Angiography and Interventions; TnT, troponin T; URL, upper reference limit.

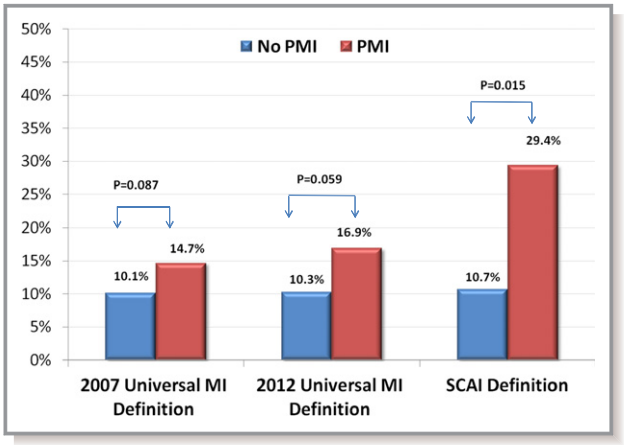

Figure 3. Death/MI rate at 2 years based on the 2007 and 2012 universal MI definitions and SCAI definition. Kaplan-Meier's analysis *P* values are reported for comparisons PMI versus no PMI. MI indicates myocardial infarction; PMI, periprocedural myocardial infarction; SCAI, Society for Cardiovascular Angiography and Interventions.

Table 5. Different Definitions of PMI and Late Outcomes

		Patients Without PMI	Patients With PMI	HR and 95% CI	*P* Value
2007 MI definition, n (%)		n=534 (77.4)	n=156 (22.6)		
30 days	Death, n (%)	3 (0.6)	3 (1.9)	3.43 (0.69 to 17.00)	0.131
	MI, n (%)	7 (1.3)	3 (1.9)	1.48 (0.38 to 5.70)	0.573
	Death/MI, n (%)	9 (1.7)	5 (3.2)	1.91 (0.64 to 5.71)	0.245
	TVR, n (%)	6 (1.1)	2 (1.3)	1.15 (0.23 to 5.96)	0.865
	MACE, n (%)	11 (2.1)	6 (3.8)	1.88 (0.70 to 5.09)	0.213
1 year	Death, n (%)	21 (3.9)	6 (3.8)	1.06 (0.43 to 2.64)	0.903
	MI, n (%)	26 (4.9)	13 (8.3)	1.77 (0.91 to 3.44)	0.093
	Death/MI, n (%)	45 (8.4)	18 (11.5)	1.422 (0.82 to 2.45)	0.270
	TVR, n (%)	32 (6.0)	16 (10.3)	1.80 (0.99 to 3.27)	0.056
	MACE, n (%)	63 (11.8)	24 (15.4)	1.36 (0.85 to 2.18)	0.198
2 years	Death, n (%)	25 (4.7)	8 (5.1)	1.14 (0.51 to 2.52)	0.754
	MI, n (%)	32 (6.0)	17 (10.9)	1.90 (1.05 to 3.42)	0.033
	Death/MI, n (%)*	54 (10.1)	23 (14.7)	1.53 (0.93 to 2.49)	0.090
	TVR, n (%)	43 (8.1)	18 (11.5)	1.51 (0.87 to 2.62)	0.142
	MACE, n (%)	79 (14.8)	29 (18.6)	1.32 (0.86 to 2.02)	0.202
2012 MI definition, n (%)		n=601 (87.1)	n=89 (12.9)		
30 days	Death, n (%)	4 (0.7)	2 (2.2)	3.40 (0.62 to 18.56)	0.158
	MI, n (%)	7 (1.2)	3 (3.4)	2.94 (0.76 to 11.39)	0.118
	Death/MI, n (%)	10 (1.7)	4 (4.5)	2.75 (0.86 to 8.76)	0.088
	TVR, n (%)	7 (1.2)	1 (1.1)	0.98 (0.12 to 7.95)	0.984
	MACE, n (%)	13 (2.2)	4 (4.5)	2.12 (0.69 to 6.49)	0.190
1 year	Death, n (%)	24 (4.0)	3 (3.4)	0.90 (0.27 to 3.00)	0.867
	MI, n (%)	30 (5.0)	9 (10.1)	2.09 (0.99 to 4.40)	0.052
	Death/MI, n (%)	52 (8.7)	11 (12.4)	1.48 (0.77 to 2.84)	0.236
	TVR, n (%)	39 (6.5)	9 (10.1)	1.63 (0.79 to 3.36)	0.187
	MACE, n (%)	74 (12.3)	13 (14.6)	1.24 (0.69 to 2.23)	0.480
2 years	Death, n (%)	29 (4.8)	4 (4.5)	0.96 (0.34 to 2.72)	0.933
	MI, n (%)	37 (6.2)	12 (13.5)	2.28 (1.19 to 4.39)	0.013
	Death/MI, n (%)†	62 (10.3)	15 (16.9)	1.71 (0.97 to 3.01)	0.062
	TVR, n (%)	51 (8.5)	10 (11.2)	1.39 (0.71 to 2.75)	0.337
	MACE, n (%)	91 (15.1)	17 (19.1)	1.33 (0.79 to 2.22)	0.287
SCAI definition, n (%)		n=673 (97.5)	n=17 (2.5)		
30 days	Death, n (%)	6 (0.9)	0 (0.0)	0.05 (0.00 to 4583)	0.796
	MI, n (%)	8 (1.2)	2 (11.8)	10.24 (2.18 to 48.25)	0.003
	Death/MI, n (%)	12 (1.8)	2 (11.8)	6.84 (1.53 to 30.55)	0.012
	TVR, n (%)	7 (1.0)	1 (5.9)	5.82 (0.71 to 47.33)	0.099
	MACE, n (%)	15 (2.2)	2 (11.8)	5.51 (1.26 to 24.12)	0.023
1 year	Death, n (%)	26 (3.9)	1 (5.9)	1.52 (0.21 to 11.18)	0.684
	MI, n (%)	36 (5.3)	3 (17.6)	3.47 (1.07 to 11.26)	0.039
	Death/MI, n (%)	59 (8.8)	4 (23.5)	2.82 (1.03 to 7.77)	0.045
	TVR, n (%)	45 (6.7)	3 (17.6)	2.86 (0.89 to 9.19)	0.078
	MACE, n (%)	82 (12.2)	5 (29.4)	2.72 (1.10 to 6.72)	0.030
2 years	Death, n (%)	31 (4.6)	2 (11.8)	2.44 (0.58 to 10.19)	0.222
	MI, n (%)	46 (6.8)	3 (17.6)	2.75 (0.86 to 8.84)	0.090
	Death/MI, n (%)‡	72 (10.7)	5 (29.4)	2.92 (1.18 to 7.24)	0.020
	TVR, n (%)	58 (8.6)	3 (17.6)	2.23 (0.70 to 7.12)	0.175
	MACE, n (%)	102 (15.2)	6 (35.3)	2.65 (1.63 to 6.04)	0.020

CI indicates confidence interval; HR, hazard ratio; MACE, major adverse cardiac events; MI, myocardial infarction; PMI, periprocedural myocardial infarction; SCAI, Society for Cardiovascular Angiography and Interventions; TVR, target vessel revascularization.

Adjusted HRs for death/MI at 2 years according to different PMI definitions were: *2007 PMI definition, HR=1.3 (95% CI, 0.78 to 2.21; *P*=0.302); †2012 PMI definition, HR=1.49 (95% CI, 0.80 to 2.76; *P*=0.208); ‡SCAI PMI definition, HR=2.70 (95% CI: 1.08 to 6.78, *P*=0.034).

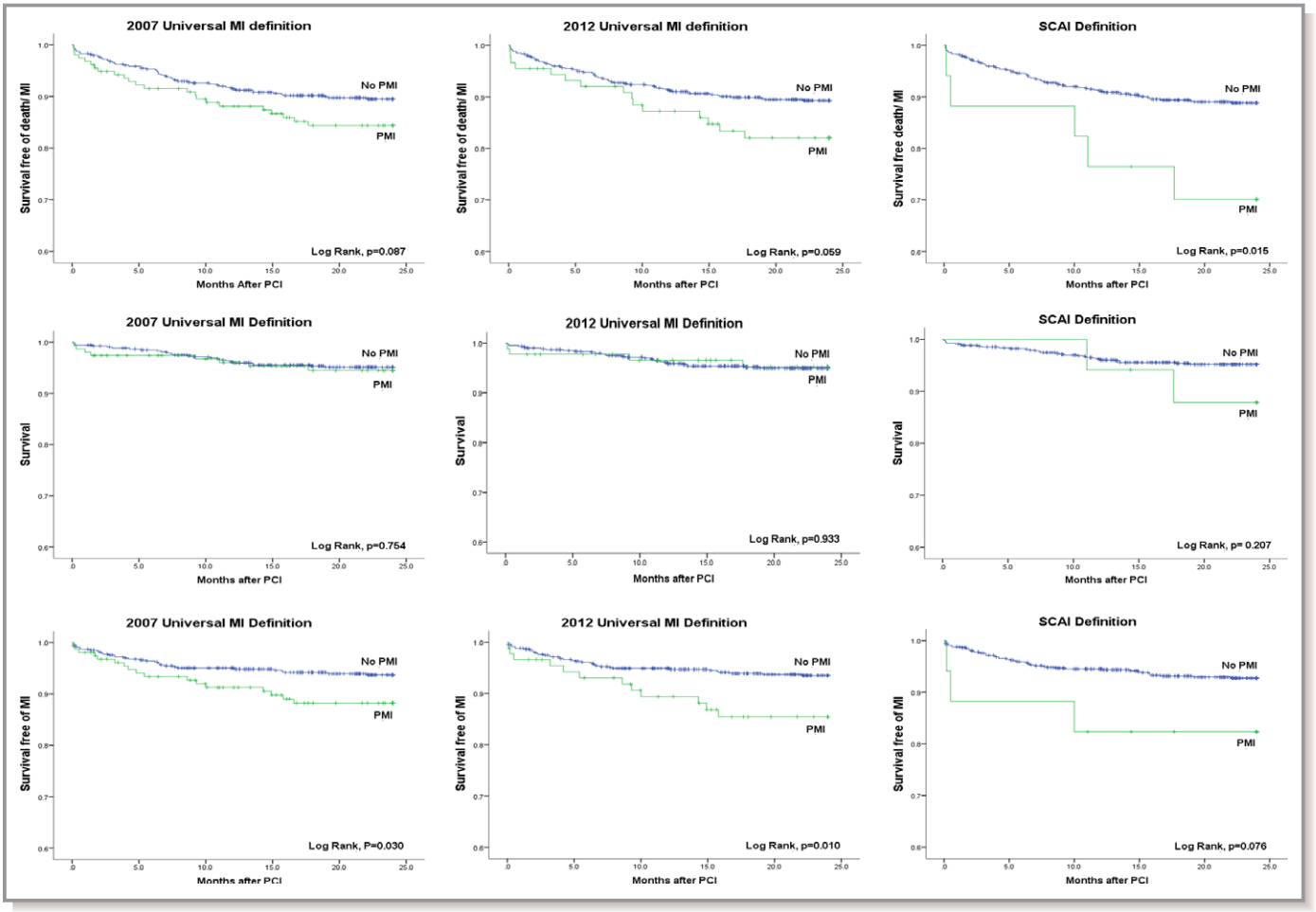

Figure 4. Kaplan-Meier's curve for death, MI, and combined death and MI. Actuarial outcomes for 690 patients are shown. Five patients who had unsuccessful PCI as a result of failure to recanalize chronic total occlusion and 47 (6.3%) had <30 days follow-up; those patients were not included in late Kaplan-Meier's analysis. MI indicates myocardial infarction; PCI, percutaneous coronary intervention; PMI, periprocedural myocardial infarction; SCAI, Society for Cardiovascular Angiography and Interventions.

Discussion

In this study, we report that the frequency of PMI was ≈60% lower using the 2012, compared to the 2007, universal MI definition and even lower using the SCAI definition. Based on the late outcome data, it appears that PMIs, which were identified using the 2007 universal definition of MI but did not qualify using the 2012 definition or SCAI definition, did not influence the rates of late death or MI. Whereas the universal definitions of PMI are not focused on prognosis, the SCAI definition has been based on post-CABG prognosis.

The diagnosis of PMI using the 2012 universal MI definition requires post-PCI TnT-level elevation to >5×URL, which corresponds to ≈3×URL for CKMB (mass). Using cardiac magnetic resonance (CMR) imaging, the threshold for detection is ≥3×URL for CKMB (mass), which has previously been reported to be prognostic.[16,17] However, the SCAI definition requires post-PCI TnT-level elevation to ≥70×URL or CKMB ≥10×URL.[8]

Defining PMI, with respect of the amount of myonecrosis, has been traditionally based on CKMB (mass) levels. The equivalent extent of myonecrosis, in terms elevations in troponin levels, requires definition of which troponin assay T or I is used and, in particular, if a "conventional" or high sensitivity assay was performed. Additionally, in the case of TnI, detail of the assay manufacturer are also required. A recent study showed that post-PCI troponin (various site assays) elevations to >60×URL predicts similar risk of death to >3×URL for CKMB,[18] whereas we report here a less-marked ratio between CKMB and TnT, perhaps reflecting use of the TnT assay. The relationship between TnT levels using the fourth-generation Roche assay and the new "high-sensitivity" TnT assay is not linear at levels <5×URL, though these assays tend to correlate very highly at TnT levels >10×URL, that is, ≈>140 ng/mL (0.14 μg/L) using high-sensitivity TnT. The SCAI definition sets similar biomarker criteria for PMI, whether post-PCI or post-CABG, whereas the mortality and the morbidity associated with these 2 proce-

Table 6. PMI and Late Outcomes According to Pre-PCI TnT Levels

	Normal Pre-PCI TnT			Elevated Pre-PCI TnT		
	Patients Without PMI	Patients With PMI	*P* Value	Patients Without PMI	Patients With PMI	*P* Value
2007 MI definition, n (%)	n=382 (82.5)	n=81 (17.5)		n=152 (67.0)	n=75 (33.0)	
Death, n (%)	16 (4.2)	4 (4.9)	0.764	9 (5.9)	4 (5.3)	0.999
MI, n (%)	23 (6.0)	10 (12.3)	0.044	9 (5.9)	7 (9.3)	0.345
Death/MI, n (%)	37 (9.7)	14 (17.3)	0.047	17 (11.2)	9 (12.0)	0.856
TVR, n (%)	37 (9.7)	10 (12.3)	0.472	6 (3.9)	8 (10.7)	0.075
MACE, n (%)	59 (15.4)	16 (19.8)	0.339	20 (13.2)	13 (17.3)	0.401
2012 MI definition, n (%)	n=425 (91.8)	n=38 (8.2)		n=176 (77.5)	n=51 (22.5)	
Death, n (%)	18 (4.2)	2 (5.3)	0.675	11 (6.3)	2 (3.9)	0.738
MI, n (%)	26 (6.1)	7 (18.4)	0.012	11 (6.3)	5 (9.8)	0.364
Death/MI, n (%)	42 (9.9)	9 (23.7)	0.025	20 (11.4)	6 (11.8)	0.937
TVR, n (%)	40 (9.4)	7 (18.4)	0.091	11 (6.3)	3 (5.9)	0.999
MACE, n (%)	65 (15.3)	10 (26.3)	0.077	26 (14.8)	7 (13.7)	0.852
SCAI definition, n (%)	n=453 (97.8)	n=10 (2.2)		n=220 (96.9)	n=7 (3.1)	
Death, n (%)	18 (4.0)	2 (20.0)	0.065	13 (5.9)	0 (0)	0.999
MI, n (%)	31 (6.8)	2 (20.0)	0.155	15 (6.8)	1 (14.3)	0.405
Death/MI, n (%)	47 (10.4)	4 (40.0)	0.017	25 (11.4)	1 (14.3)	0.578
TVR, n (%)	45 (9.9)	2 (20.0)	0.269	13 (5.9)	1 (14.3)	0.364
MACE, n (%)	71 (15.7)	4 (40.0)	0.062	31 (14.1)	2 (28.6)	0.270

MACE indicates major adverse cardiac events cardiovascular; MI, myocardial infarction; PCI, percutaneous coronary intervention; PMI, periprocedural myocardial infarction; TnT, troponin T; TVR, target vessel revascularization.

dures are different. Recently, the group from the Mayo Clinic have reported an adverse prognostic association with post-PCI TnT elevations to >0.25ng/L (25× URL), when the pre-PCI TnT levels are normal.[19] We have also shown that marked TnT elevations post-PCI, when the baseline levels were normal, are associated with increased late death/MI occurrences, though number of events were small. Our findings are similar to those of others,[18] in not finding such an association when pre-PCI TnT levels were elevated. Further it seems plausible, though as yet unproven, that the prognostic importance of TnT elevations may vary with the degree of left ventricular dysfunction and/or haemodynamic instability. It is uncertain as to whether prognostic, rather than diagnostic, criteria for PMI will prevail.[20]

We found that the majority of the PMIs using the 2012 definition, which required imaging, were the result of small side-branch occlusions, as previously reported.[21] These were apparently unappreciated by the interventionalist performing the PCI. In routine clinical practice, these are not routinely reported given that the vessels were generally ≤1 mm in diameter and were only identified by careful review comparing the pre- and post-PCI angiography. Nevertheless, the ensuing MIs are of a similar size in term of biomarker elevation to those previously reported on CMR and reported to be prognostic in an earlier era.[22,23] Whereas PMI has an attributable risk for late mortality,[9,10,24–26] almost all the side-branch occlusions identified were in vessels ≤1 mm, which were too small for side-branch protection and/or intervention techniques. Further study is required to determine whether any strategies were feasible to reduce the frequency of these events, which has been previously reported to be an independent risk for late outcomes.[27]

Our study has some limitations. First, it is a single-center study of PCI data collection, which limited study power, especially with respect to mortality. Second, these data were analyzed retrospectively and represent a subgroup of patients —those who had qualifying cardiac biomarkers measured. Operator-requested biomarker assays may be more frequent in instances with clinical symptoms and complicated procedures that may have resulted in a degree of selection bias, leading to our relatively high reported incidence of PMI. Also, high-sensitivity TnT assays only became available in June 2011. The duration of chest pain and slow flow/no-reflow were not recorded, so we cannot specify how transient/persistent the reduced flow was. Pre-PCI, in this CHD population, there was incomplete database recording of left ventricular (LV) function, and the failure to include an LV function parameter in multivariable analysis is a limitation—

though, in this population, this factor is likely to be less important prognostically over 2-year follow-up than in a post-STEMI cohort.

In conclusion, the 2012 universal definition of MI has reduced the frequency of PMI by ≈60%, compared with the 2007 universal MI definition. However, this reduction in PMI rate seems to be mainly the result of exclusions of events that were not prognostically significant. Furthermore, the main additional factor in the 2012 universal MI definition accounting for these PMI events was small side-branch occlusion. The SCAI definition of PMI resulted in much fewer events, which were associated with a significantly increased rate of late adverse outcomes. Whether this PMI definition or the SCAI definition will achieve widespread acceptance awaits large, prospective studies.

Disclosures

None.

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