

STATE-OF-THE-ART REVIEW

Preventive Stenting in Acute Myocardial Infarction



Ari Pollack, MD,* Bibhu D. Mohanty, MD,† Rishi Handa, MD,‡ Patrick M. Looser, MD,§ Valentin Fuster, MD, PhD,* Spencer B. King III, MD,|| Samin K. Sharma, MD*

ABSTRACT

Current practice guidelines advocate culprit vessel intervention alone in patients with ST-segment elevation myocardial infarction (STEMI) found to have multivessel coronary disease during primary percutaneous coronary intervention (PCI). The debate on the timing of noninfarct artery intervention has recently been reinvigorated by the PRAMI (Preventive Angioplasty in Acute Myocardial Infarction) trial, in which patients undergoing preventive PCI of significant nonculprit lesions at the time primary PCI for STEMI had reduced rates of cardiac death, nonfatal myocardial infarction, and refractory angina. Given that previous literature has cautioned against multivessel PCI during STEMI, this raises the question of whether technical and pharmacological advances in PCI may have opened the door to safely revisit this issue with additional clinical rigor. The impact of STEMI pathophysiology on nonculprit vessel plaque, how treatment of nonculprit lesions alters the natural history of coronary disease after STEMI, and whether this results in a clinical benefit remain unclear, and much of the existing data are retrospective. Additionally, the PRAMI trial did not include a staged PCI, leaving questions as to how this approach might fare compared with simultaneous preventive PCI. In this review, we discuss the pathophysiology of nonculprit vessel plaque in STEMI, provide a summary of the existing literature on the topic, and discuss the PRAMI trial in the face of previous data and possible future directions for further study. (J Am Coll Cardiol Intv 2015;8:131-8) © 2015 by the American College of Cardiology Foundation.

Timely treatment of the culprit lesion in acute ST-segment elevation myocardial infarction (STEMI) is essential to minimizing myocardial necrosis, curbing recurrent ischemia, and reducing mortality (1). Primary percutaneous coronary intervention (PCI) is the gold standard for restoration of blood flow in the infarct artery (2). STEMI patients with multivessel (MV) coronary artery disease (CAD) have higher mortality rates and a higher incidence of recurrent myocardial infarction (MI) than patients with single-vessel CAD, and the presence of triple-vessel CAD diagnosed during MI portends a worse prognosis (3,4). Although it can be

assumed that the extent of CAD has a direct impact on post-STEMI outcomes, practice guidelines unequivocally support culprit vessel intervention alone in the acute setting, despite many patients with STEMI possessing obstructive MV-CAD (5,6). The American College of Cardiology/American Heart Association practice guidelines state that “PCI should not be performed in a non-infarct artery at the time of primary PCI in patients with STEMI who are hemodynamically stable (Class III harm, Level of Evidence: B)” (7). The European Society of Cardiology guidelines are more liberal, giving a Class IIA recommendation of PCI in this setting (8). In clinical practice,

From the *Zena and Michael A. Wiener Cardiovascular Institute, Mount Sinai Heart, New York, New York; †Division of Cardiology, Johns Hopkins School of Medicine, Baltimore, Maryland; ‡Department of Medicine, Morristown Medical Center, Morristown, New Jersey; §Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York; and the ||St. Joseph’s Health System, Atlanta, Georgia. Dr. Sharma is on the Speakers Bureau of Abbott, Angioscore, Boston Scientific Corp., Lilly/DSI, and The Medicine Company. Dr. King is a consultant for Celonova Biosciences; and serves on the Data Safety Monitoring Board of Duke University, Harvard Clinical Research Institute, Merck & Co. Inc., Capricor Inc., and Wyeth Pharmaceuticals. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Anthony N. DeMaria, MD, served as Guest Editor for this paper.

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**ABBREVIATIONS
AND ACRONYMS****ACS** = acute coronary syndrome(s)**CAD** = coronary artery disease**CI** = confidence interval**MACE** = major adverse cardiac event(s)**MI** = myocardial infarction**MV** = multivessel**NNT** = number needed to treat**OR** = odds ratio**PCI** = percutaneous intervention**STEMI** = ST-segment elevation myocardial infarction

however, several strategies are widely used for STEMI patients with additional obstructive plaques after successful culprit lesion PCI: immediate coronary stenting, staged PCI, and medical therapy only. Advances in interventional technologies, increased operator experience, and improved pharmacotherapies have made PCI safer and effective in high-risk circumstances. Coupled with emerging literature that questions current guidelines, these factors have opened the door to revisit this clinical dilemma and suggest that this contentious area may not be immune to change (9).

The debate regarding the appropriate strategy has recently intensified in light of the PRAMI (Preventive Angioplasty in Myocardial Infarction) trial, in which Wald et al. (9) studied PCI in nonculprit coronary lesions at the time of primary PCI for STEMI, a practice they termed “preventive stenting.” In contrast to current guidelines and the studies that informed them (10-13), the PRAMI investigators demonstrated that in patients undergoing primary PCI for STEMI, the combined rate of cardiac death, nonfatal MI, and refractory angina (defined as angina despite medical therapy supported by objective evidence of ischemia including electrocardiographic changes during a spontaneous episode of pain, a positive stress test result, or pressure-wire assessment) was reduced by 65% in the preventive PCI group, with an absolute risk reduction of 14%, compared with the group that did not undergo additional stenting (9). However, only 2 strategies were tested: simultaneous, preventive PCI of nonculprit vessel obstructive disease versus culprit vessel revascularization only. There was no arm for nonculprit vessel staged PCI.

Naturally, this investigation has raised a variety of intriguing questions. Does more complete revascularization overcome any adverse effects of treating nonculprit lesions in the acute setting? What are the pathophysiological principles at play during STEMI, and how are nonculprit vessel plaques affected? Does targeting such mechanisms via PCI offer a clinical benefit, and how might this change the natural history of nonculprit obstructive disease in the immediate aftermath of acute coronary syndromes (ACS)? Why are the findings in the PRAMI trial so contrary to what we already know? If MV-CAD is present during STEMI and an aggressive strategy is preferred, does the timing of the subsequent PCI make a difference?

Cautioning against treating multiple vessels during STEMI, especially in patients without hemodynamic compromise, the guidelines, in part, originate from

safety concerns related to increased complications of an MV intervention. Potential drawbacks of a preventive strategy include operating in an inflammatory and prothrombotic milieu, which may lead to overestimation of nonculprit lesion severity, increased procedural risk, and increased incidence of stent thrombosis (10). MV-PCI also leads to more contrast use and may place several myocardial territories at risk should unforeseen complications occur (9,10). However, it may be that the pathophysiological milieu of acute STEMI alters the behavior of noninfarct lesions, rendering intervention beneficial. The contemporary literature relating to this clinical context is largely indirect in its investigation, retrospective in its analysis, and contradictory in its findings (10-18). The PRAMI trial questions the current practice guidelines and obliges us to re-examine the existing evidence.

PATHOPHYSIOLOGY

The higher morbidity and mortality seen in STEMI patients with MV-CAD are likely multifactorial and include the presence of diffuse atherosclerosis as a harbinger of plaque instability, total ischemic burden, and impaired contractility of non-infarct zones in the presence of multiple obstructive stenosis (5). When examining the role of preventive PCI and more complete revision in the context of STEMI, one must consider the impact of these factors to determine how an aggressive strategy may offer clinical benefit.

Autopsy and natural history studies demonstrate that most ACS result from the loss of integrity of a thin fibrous cap overlying atherosclerotic plaque, either from rupture or erosion (5,19-22). Factors such as the inflammatory cascade, which instigates weakening of the fibrous cap, catecholamine-mediated intraluminal mechanical forces, and heightened sympathetic tone, operate beyond the culprit lesion, effecting nonculprit plaque and the hemodynamics of nonculprit coronary arteries (19,23,24). Patients with acute myocardial infarction are also more likely to harbor multiple complex coronary plaques that are associated with adverse clinical outcomes, and the majority of patients who die of MI have more than 1 culprit lesion (5,25). Taken together, these findings suggest that acute myocardial infarction reflects more generalized pathophysiological derangements of endothelial dysfunction, coagulation, and inflammation, with the potential to impair coronary perfusion beyond the culprit lesion distribution and destabilize plaque throughout the coronary vasculature (5,26,27). Perhaps the benefit seen in the PRAMI trial reflects the impact of stabilizing such vulnerable plaques with PCI.

As the PROSPECT (Predictors of Response to CRT) study demonstrated, however, high-risk plaque need not be obstructive. Of the 106 nonculprit lesions determined to be responsible for major adverse cardiovascular events (MACE) in the follow-up of patients with previous ACS, the mean angiographic percentage of stenosis was $32.3 \pm 20.6\%$ (21). Many of these lesions were angiographically inconspicuous. These findings suggest that nonculprit lesions causing recurrent events in PROSPECT study were unlikely to have been targeted for preventive PCI by PRAMI criteria (>50% angiographic stenosis). If not plaque vulnerability, what other mechanisms may account for the clinical benefit seen in the PRAMI trial? Possibilities include reduction of residual and border zone ischemia, improved pump function of noninfarct areas, and more favorable ventricular remodeling. In the TAMI (Thrombolysis and Angioplasty in Myocardial Infarction) study (4), patients with MV disease had lower ejection fractions compared with patients with single-vessel disease. This was attributed to noninfarct zone function, hyperkinetic in the group with single-vessel disease, but in some cases, hypocontractile or dyskinetic in those with MV-CAD. However, we do not know whether these mechanisms were operating in the PRAMI trial patients.

THE LITERATURE

Our review of the existing literature was similar to the method used more formally in the meta-analysis

recently published by Zhang et al. (28). In general, we reviewed studies that included the following: 1) a population of STEMI patients with MV disease; 2) PCIs encompassing both the culprit vessel PCI and MV-PCI; 3) MV-PCI performed during the index procedure or within a specific time period for a staged intervention; and 4) pertinent endpoint data.

RETROSPECTIVE. PCI of a noninfarct artery with Thrombolysis In Myocardial Infarction flow grade 3 at the time of primary PCI in hemodynamically stable patients has been associated with worse clinical outcomes in several studies (10-13), although others suggest that it may be performed safely (Table 1) (14-18). The approach advocated by the guidelines stems largely from registry data. In the HORIZONS-AMI (Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction) trial, MV-PCI performed at the time of the primary PCI for STEMI was associated with higher 1-year mortality (9.2% vs. 2.3%, $p < 0.0001$), cardiac mortality (6.2% vs. 2.0%, $p = 0.005$), stent thrombosis rate (5.7% vs. 2.3%, $p = 0.02$), and a trend toward greater MACE (18.1% vs. 13.4%, $p = 0.08$) than staged PCI. A staged strategy was independently associated with lower all-cause mortality at 30 days and 1 year (13).

Hannan et al. (10) reviewed the New York State experience in this context. STEMI patients with MV disease undergoing PCIs in New York State over a 3-year period were subdivided into the following 4 therapeutic categories: 1) culprit vessel PCI alone; 2) MV-PCI during the index procedure; 3) PCI during

TABLE 1 Data From Prospective Trials

	Di Mario et al. (31)	Politi et al. (30)	Wald et al. (9) (PRAMI)	Ochala et al. (33)
Study design	Multicenter RCT	Single-center RCT	Multicenter RCT	Single-center RCT
No. of subjects	69	214	465	92
Comparator groups	COR MV-PCI	COR Staged PCI MV-PCI	Preventive PCI (MV-PCI) No preventive PCI (COR)	Culprit vessel PCI MV-PCI
In-hospital mortality	COR, 0% vs. MV-PCI, 1.9% ($p = 0.754$)	COR, 8.3% vs. staged PCI, 0% vs. MV-PCI, 3.1% ($p = 0.037$)	Not reported	Culprit vessel PCI, 0% vs. MV-PCI, 0%
Long-term mortality	At 1 yr: COR, 0% vs. MV-PCI, 1.9% ($p = 0.754$)	At 2.5 yrs: COR, 15.5% vs. staged PCI, 6.2% vs. MV-PCI, 9.2% ($p = 0.17$)	At 23 months: MV-PCI, 1.7% vs. COR, 4.3% ($p = 0.07$)	At 6 months: culprit vessel PCI, 0% vs. MV-PCI, 0%
Other outcomes	MACE at 1 yr: COR, 35.3% vs. MV-PCI, 21.1% ($p = 0.33$) Repeat revascularization or CABG: COR, 35.3% vs. MV-PCI, 17.3% ($p = 0.174$)	MACE at 2.5 yrs: COR, 50.0% vs. staged PCI, 20.0% vs. MV-PCI, 23.1% ($p < 0.001$) Repeat revascularization: COR, 33.3% vs. staged PCI, 12.3% vs. MV-PCI 9.2% ($p < 0.001$)	Noncardiac mortality at 3 yrs: MV-PCI, 3.4% vs. COR, 2.6% ($p = 0.86$) Repeat revascularization: MV-PCI, 16% vs. COR, 19.9% (HR: 0.30, 95% CI: 0.17-0.56; $p < 0.001$)	The study was not powered to assess the MACE Results supported the following hypothesis that multivessel, complete 1-stage PCI in patients with STEMI and MVD leads to quicker and more substantial improvement of LVEF compared with standard 2-stage PCI

CABG = coronary artery bypass graft; CI = confidence interval; COR = culprit artery only revascularization; HR = hazard ratio; MACE = major adverse cardiac events; MVD = multivessel disease; MV-PCI = multivessel percutaneous coronary intervention (index procedure); RCT = randomized, controlled trial; STEMI = ST-segment elevation myocardial infarction.

the index admission; or 4) staged MV-PCI within 60 days of the index admission. Patients with cardiogenic shock were excluded. For patients without hemodynamic compromise, left ventricular ejection fraction <20% or malignant ventricular arrhythmia, culprit vessel PCI was associated with lower in-hospital mortality than MV-PCI during the index procedure (0.9% vs. 2.4%, $p = 0.04$), results that trended toward significance at 24 and 42 months. Patients undergoing staged MV-PCI during the index admission experienced lower mortality rates at 12, 24, and 42 months compared with culprit vessel PCI alone, but none of the differences reached statistical significance. However, patients undergoing staged MV-PCI within 60 days after the index procedure had a significantly lower 12-month mortality rate than patients undergoing culprit vessel PCI only (1.3% vs. 3.3%, $p = 0.04$). No statistical analysis comparing patients undergoing staged MV-PCI during the index admission versus within 60 days after the index procedure was performed. This study suggests that a complete revision strategy, addressed in a staged manner, may be associated with improved clinical outcomes (29).

Registry data, however, remain inconclusive. Qarawani et al. (14) reported that complete revision during the primary PCI is associated with a reduced incidence of MACE (recurrent ischemia, reinfarction, heart failure, and in-hospital mortality) during the index hospitalization (16.7% vs. 52%, $p = 0.0001$), although transient renal dysfunction was observed more frequently (8.4% vs. 4%, $p = 0.01$). Other studies have suggested that MV-PCI in STEMI patients may help to limit infarct size (15). In a large meta-analysis comparing MV revascularization with culprit vessel revascularization in 61,764 STEMI patients with MV-CAD, Bangalore et al. (18) reported that for early outcomes (<30 days), there was no significant difference in mortality, MI, stroke, and target vessel revascularization, although there was a 44% decrease in risk of repeat PCI in patients undergoing MV revascularization. Likewise, for long-term outcomes (follow-up of 2.0 ± 1.1 years), there was no difference in MI, target vessel revascularization, or stent thrombosis. However, the risk of mortality, repeat PCI, and coronary artery bypass graft decreased by 33%, 43%, and 53%, respectively with MV revascularization. Although some studies have supported these results (17), others have drawn contradictory conclusions, as shown by a contemporary meta-analysis that reported that MV-PCI was associated with a 60% higher risk of long-term mortality than culprit vessel PCI (odds ratio [OR]: 1.6, 95% confidence interval [CI]: 1.3 to 2.0) (12). MV-PCI was

also associated with higher long-term mortality than staged PCI (OR: 2.88, 95% CI: 1.73 to 4.89, $p = 0.001$).

PROSPECTIVE, RANDOMIZED TRIALS. The results of prospective studies before the PRAMI trial are underpowered to show a mortality difference. Although combined results of 9 cohort studies involving 5,128 patients suggested higher long-term mortality after MV-PCI compared with culprit vessel PCI (OR: 1.8, 95% CI: 1.4 to 2.2), the collective results of the 288 patients analyzed in a randomized fashion did not show a difference in long-term mortality (OR: 0.7, 95% CI: 0.3 to 1.6) (12). A review of the prospective, randomized trial literature, however, reveals only a small number of existing trials, each with a small number of patients (Table 2) (30,31). The largest of these prospective trials and first to test 3 treatment strategies (compared with 2 in the PRAMI trial) randomized 214 patients with STEMI and MV-CAD to the following: 1) culprit vessel PCI alone; 2) staged PCI; or 3) simultaneous PCI of all significant stenoses (defined as >70% of visually estimated diameter stenosis of ≥ 2 epicardial coronary arteries or their major branches) (30). Exclusion criteria were similar to those of the PRAMI trial. After a mean follow-up of 2.5 years, in patients with multiple coronary lesions treated with primary PCI, MV revascularization had a better outcome than culprit lesion PCI only, both with a simultaneous and staged treatment strategy. Event rates, however, were driven by repeat revascularization as there was no significant difference in reinfarction rate or mortality. The mortality rates after staged PCI versus simultaneous MV-PCI versus culprit vessel-only PCI were 6.2%, 9.2%, and 15.5%, respectively ($p < 0.17$).

The PRAMI trial was a multicenter randomized trial that enrolled 465 patients with STEMI who underwent infarct-artery PCI and were then randomized to preventive PCI ($n = 234$) of any additional angiographically significant lesions (>50% diameter stenosis) or no additional intervention ($n = 231$). There was no staged arm, and patients and physicians were not blinded to the enrollment arm. Both groups received appropriate medical therapy. Patients with cardiogenic shock, previous coronary artery bypass graft, surgical MV disease, and noninfarct chronic total occlusion were excluded. Interestingly, the majority of AMIs involved the inferior wall. Over the 23-month follow-up period, the combined incidence of cardiac death, nonfatal MI, and refractory angina occurred in 21 preventive PCI patients compared with 53 culprit vessel intervention-only patients. In other words, the primary outcome was reduced by 65%,

TABLE 2 Data From Retrospective Trials or Post-Hoc Analyses

	Hannan et al. (10)	Toma et al. (11)	Vlaar et al. (12)	Qarawani et al. (14)	Kornowski et al. (13)	Navarese et al. (17)	Bangalore et al. (18)	Cavender et al. (38)
Study design	Retrospective New York State database review	Post-hoc analysis of RCT (APEX-AMI)	Pairwise and network meta-analysis	Retrospective cohort, single center	Post-hoc analysis of RCT (HORIZONS-AMI)	Meta-analysis	Meta-analysis	Retrospective NCDR database, multicenter
No. of subjects	3,521	2,201	40,280	120	668	27,047	61,764	28,936
Comparator groups	COR MV-PCI Staged PCI	COR MV-PCI	COR MV-PCI Staged PCI	COR MV-PCI	COR Staged PCI	COR MV-PCI	COR MV-PCI	COR MV-PCI
Short-term mortality	COR, 0.9% vs. MV-PCI, 2.4% (p = 0.04)	COR, 5.6% vs. MV-PCI, 12.5% (p < 0.001)	COR vs. MV-PCI (OR: 0.66, 95% CI: 0.48-0.89, p = 0.007)	COR, 4% vs. MV-PCI, 4.2% (p > 0.05)	Not reported	MV-PCI vs. COR (OR: 1.30, 95% CI: 0.79-2.12, p = 0.31)	MV-PCI vs. COR (OR: 0.79, 95% CI: 0.46-1.35, p = 0.024, I ² = 47.7%)	MV-PCI vs. COR Excluding patients with CS (OR: 1.23, 95% CI: 0.94-1.61, p = 1.23) Including patients with CS (OR: 1.54, 95% CI: 1.22-1.95, p < 0.01)
Long-term mortality	COR, 1.3% vs. staged PCI, 3.3% (p = 0.04)	Not reported	COR vs. MV-PCI (OR: 0.63, 95% CI: 0.46-0.86, p < 0.001)	COR, 8% vs. MV-PCI, 9.4% (p = 0.06)	Staged PCI, 2.3% vs. COR, 9.2% (RR: 4.10, 95% CI: 1.93-8.86, p < 0.001)	MV-PCI vs. COR (OR: 1.17, 95% CI: 0.86-1.58, p = 0.31)	MV-PCI vs. COR (OR: 0.78, 95% CI: 0.54-1.11, p = 0.018, I ² = 50.9%)	Data not available because maximal follow-up for this study was in-hospital only
Other outcomes	Not reported	Not reported	Not reported	Recurrent ischemia, reinfarction, acute heart failure, and in-hospital mortality. MV-PCI, 16.7% vs. COR, 52% (p = 0.0001)	MACE at 1 yr: staged PCI, 13.4% vs. COR, 18.1% (RR: 1.42, 95% CI: 0.96-2.10, p = 0.08)	Revascularization at 1 yr: MV-PCI vs. COR (OR: 0.47, 95% CI: 0.28-0.78, p = 0.31)	Long-term MACE: MV-PCI vs. COR (OR: 0.60, 95% CI: 0.33-1.08, p for interaction < 0.001, I ² = 80.5%)	Not reported

APEX-AMI = Pexelizumab in Conjunction With Angioplasty in Acute Myocardial Infarction; CS = cardiogenic shock; HORIZONS-AMI = Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction; NCDR = National Cardiovascular Data Registry; RR = relative risk; other abbreviations as in Table 1.

with an absolute risk reduction of 14% (hazard ratio: 0.35, 95% CI: 0.21 to 0.58, $p < 0.001$). The benefit was similar in magnitude and remained statistically significant when the analysis was limited to the combined endpoint of cardiac death and nonfatal MI (hazard ratio: 0.36, 95% CI: 0.20 to 0.57, $p = 0.004$), although the absolute number of deaths was small (4 in the preventive PCI group and 10 in culprit vessel intervention alone). Procedure time, fluoroscopy dose, and contrast volume were increased in the preventive PCI group, but complication rates (e.g., procedure-related stroke, bleeding requiring transfusion or surgery) and contrast-induced nephropathy requiring dialysis were similar between the 2 groups. Additionally, despite concerns regarding the prothrombotic and inflammatory milieu present in the early phase of STEMI, there was no difference in the stent thrombosis rate (9,13).

SUMMARIZING THE LITERATURE

Despite worse outcomes in patients with STEMI and MV-CAD, no clear benefit of complete revision over culprit lesion revascularization only has been demonstrated thus far. Because of the observational and retrospective nature of these studies, revascularization strategies were chosen using varying criteria that were not prospectively defined and are undoubtedly influenced by patient and operator characteristics. This may lead to significant selection bias. The prospective literature is scant, but evolving. A recent meta-analysis by Sardar et al. (32) that incorporates 3 randomized trials including the PRAMI trial revealed that an MV-PCI strategy significantly reduced the risk of MI (OR: 0.33, 95% CI: 0.16 to 0.69, $p = 0.003$, number needed to treat [NNT] = 17), repeat revascularization (OR: 0.28, 95% CI: 0.18 to 0.45, $p < 0.0001$, NNT = 6.6) and major adverse cardiac events (OR: 0.26, 95% CI: 0.17 to 0.38, $p < 0.00001$, NNT = 4) versus culprit vessel-only intervention. ORs for all-cause mortality and cardiac mortality showed a trend toward benefit (32). The most recently published meta-analysis on this topic by Zhang et al. (28) included 14 randomized and nonrandomized studies and showed worse short- (OR: 0.50, 95% CI: 0.32 to 0.77, $p = 0.002$) and long-term (OR: 0.52, 95% CI: 0.36 to 0.74, $p < 0.001$) mortality with MV-PCI, thus supporting current guidelines. However, a number of the included studies were suboptimally designed and had considerable confounding. Although the PRAMI trial is the largest prospective study to date, it was highly selective in its enrollment with 2,428 patients screened and only 465 enrolled over a 5-year period. The lack of a staged arm after the primary

intervention is a significant difference between the PRAMI trial and previous observations. Due to heterogeneous designs, populations, outcome measures, and follow-up times, comparison of existing literature is difficult.

TIMING OF PCI

Only a few published analyses have examined the optimal timing strategy for MV-PCI in patients with STEMI. In the randomized study performed by Politi et al. (30), staged revascularization of the noninfarct artery was performed at 56.8 ± 12.9 days after the index procedure. There was no significant difference in mortality rate or MACE rate between staged PCI and the complete revision during culprit vessel intervention, although the sample sizes studied were too small to draw meaningful conclusions. Ochala et al. (33) compared MV-PCI with staged PCI in 92 patients with findings suggesting a quicker improvement in left ventricular function with MV-PCI during the index procedure compared with staged revascularization. Much of the literature is neutral, with no outcomes showing benefit of simultaneous MV-PCI over a staged procedure (15,18). However, other studies have demonstrated that a staged PCI strategy is associated with improved short- and long-term outcomes including all-cause mortality compared with simultaneous revascularization (10,13).

PRACTICAL AND FUTURE CONSIDERATIONS

If a decision to intervene is made, the appropriate and optimal timing of a nonculprit vessel preventive procedure is unknown. Emergent MV-PCI may be necessary in some STEMI patients who have complex CAD with cardiogenic shock and who do not improve after culprit lesion PCI, a strategy supported by the current guidelines (7). Evidence supporting this strategy, however, is lacking. The SHOCK (SHould we emergently revascularize Occluded Coronaries in cardiogenic shock?) trial suggests that culprit lesion revascularization alone is superior to MV-PCI in terms of 1-year survival (55% vs. 20%, $p = 0.048$) (34). What about the patient inadequately stabilized by culprit vessel PCI alone? Certainly consideration must be given to the clinical context, patient comorbidities, and the coronary anatomy if a strategy of preventive PCI is chosen. Although the PRAMI trial demonstrated that immediate MV-PCI offers a clinical benefit compared with only culprit vessel intervention, the findings have been met with skepticism among the medical community about a variety of concerns. The study did not compare immediate with staged PCI.

The generalizability of the results is questionable given that the majority of infarctions were of the inferior wall, and nonculprit vessel intervention was predominantly performed on the left anterior descending artery. It is also unclear whether the culprit vessel-only PCI group had appropriate follow-up. This may have affected outcomes because these patients probably stood to benefit most from closely monitored medical therapy. Furthermore, the angiographic criteria for nonculprit vessel intervention are considerably more inclusive than the conventional criteria (>70% stenosis) used in most studies. Finally, we are left to speculate about the causal relationship between residual lesions in the control group and events.

Without this information, a mechanistic explanation remains elusive. If using a more conservative strategy, can we apply what is known about the natural history of nonculprit lesion obstructive CAD? The literature is clear in its view of PCI in stable, obstructive CAD. Data from the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial in support of optimal medical therapy suggest that a noninvasive management strategy is preferred in patients with stable disease (35). The FAME (Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention) trials, by demonstrating a reduction in risk of repeat revascularization and decreasing angina, encourage the use of PCI for hemodynamically significant stenoses, defined by fractional flow reserve (36,37). The COURAGE, FAME, and FAME-2 (Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention-2) trials included patients with recent STEMI, so concluding that patients with STEMI possess otherwise typical CAD in nonculprit vessels may be presumptuous.

Last, the feasibility of identifying specific lesions for which preventive PCI in the context of STEMI may lead to improved outcomes is undetermined. Perhaps hemodynamic assessment of nonculprit lesions with fractional flow reserve or an anatomic evaluation of plaque vulnerability with intravascular ultrasound or optical coherence tomography may offer an advantage over angiography alone in guiding preventive PCI during STEMI.

CONCLUSIONS

Patients with STEMI and MV-CAD are at significant risk of future adverse cardiovascular events. Whether MV-PCI affects the natural history and prognosis of these high-risk patients remains controversial. The current practice guidelines do not advocate the practice of MV intervention at the time of primary PCI in the absence of hemodynamic compromise (7). However, the literature from which the guidelines are derived is largely retrospective and nonrandomized trial data. The recent PRAMI investigation suggests that an aggressive approach with preventive PCI may lead to improved cardiovascular outcomes in STEMI patients with MV-CAD, but this trial did not allow for a strategy of staged PCI of nonculprit lesions. Thus, the question remains: which patients with significant residual disease should have additional interventions on an elective basis? Larger randomized clinical trials are needed to further address the question of the timing of nonculprit lesion PCI in this clinical context and to help clarify which patients may derive the most benefit.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Rishi Handa, 100 Franklin Street, Apt. H304, Morristown, New Jersey 07960. E-mail: rishi.handa@atlantichhealth.org.

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