EDITORIAL COMMENT

Multivessel Intervention During Primary Angioplasty

Too Greedy?*

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Primary angioplasty is the therapy of choice for patients with ST-segment elevation myocardial infarction (STEMI) (1). Continuous advancements in adjuvant antithrombotic strategies coupled with refinements in interventional techniques have led to significant improvement in procedural success and long-term clinical outcomes (1). However, STEMI patients with multivessel disease remain a major challenge. In this setting, different studies have shown that multivessel disease is a major *independent* predictor of adverse prognosis (2). Current clinical practice guidelines recommend that in STEMI patients, only the culprit vessel should be initially treated unless hemodynamic compromise is present (1). In fact, a Class III recommendation is provided for elective interventions on noninfarct-related arteries during the index procedure (1).

In the fibrinolytic era, noninvasive ischemia-detecting tests were commonly indicated to gain useful prognostic insights for the triage of patients requiring invasive procedures. Currently, however, even when fibrinolysis is selected for logistic reasons, most STEMI patients undergo routine early angiography to evaluate coronary anatomy (1). Thus, we are entering into a completely new scenario, where important early clinical decisions are made—in a growing number of stable post-STEMI patients—to ensure complete coronary revascularization. Notably, many of these patients with severe multivessel disease would have been considered ideal surgical candidates had they presented in a relatively stable clinical condition. However, the recent STEMI episode, and above all, the fact that the infarct-related artery has already been "*fixed*," usually shift the decision toward repeated percutaneous interventions. Many

times, this *paradoxical* clinical decision-making process (by which percutaneous revascularization is systematically offered to complex patients with multivessel disease and impaired ventricular function) is not substantiated by firm evidence. In addition, the dilemma of whether complete revascularization should be obtained during hospitalization in a staged procedure, or rather some time after discharge, remains unsettled.

Recent data suggest that with currently available technologies, multivessel stenting can be readily and safely performed during primary angioplasty procedures (3–6). In fact, some provocative studies challenge current recommendations and suggest that this strategy is indeed superior to the classic approach of staged elective procedures (4,5). Most of these studies, however, are relatively small (i.e., underpowered to detect differences in major clinical events) and did not evaluate the influence of a widespread drug-eluting stent utilization.

Present Study

In this issue of the *JACC: Cardiovascular Interventions*, Hannan et al. (7) examine the large database of the mandatory New York State's Percutaneous Coronary Interventions Reporting System Registry (NY-PCIRS) to gain further insight into appropriate revascularization strategies in STEMI patients with multivessel disease. New York's vital statistics data were used to follow up local residents for up to 42 months. Patients with prior thrombolytic therapy and those in cardiogenic shock were excluded. A total of 4,024 STEMI patients with multivessel disease undergoing primary angioplasty within 24 h were analyzed. Multivessel intervention during the index procedure was performed in 503 (12.5%) patients. Of the remaining 3,521 patients, staged interventions during admission were performed in 259 patients (7.4%), whereas staged procedures within 2 months of STEMI were indicated in 538 (15.3%) patients. Interestingly, drug-eluting stents alone were used in nearly two-thirds of cases. However, data on the use of thrombus aspiration devices or glycoprotein IIb/IIIa inhibitors were not presented. To account for imbalances in baseline characteristics and potential confounders, patients were propensity score-matched. For patients without hemodynamic compromise, culprit-vessel-only intervention during the index procedure was associated with significantly lower in-hospital mortality than multivessel intervention. Furthermore, patients undergoing staged multivessel intervention within 2 months after STEMI, but not during the index procedure, had a significantly lower mortality rate than patients undergoing culprit lesion intervention alone. This series represents the largest systematic study with long-term clinical follow-up ever performed to address this issue. Results indicate that, whenever possible, multivessel intervention should be initially avoided during primary angio-

plasty, and also that in STEMI patients with multivessel disease, a strategy aimed to achieve complete revascularization, when addressed in staged elective procedures, is associated with long-term clinical benefit.

Previous Studies

Many studies have suggested the benefit of multivessel intervention in patients with acute coronary syndromes. However, data on STEMI patients with multivessel disease undergoing primary angioplasty are sparse and results are conflicting (2–6). Two small randomized studies focused on this topic. Di Mario et al. (4) assigned 69 STEMI patients with multivessel disease to unbalanced randomization with culprit lesion treatment only (n = 17) versus complete multivessel intervention (n = 52). The multivessel intervention group required longer procedures and larger amounts of contrast, but only had a trend for lower revascularization requirements at 12 months. In a more recent trial, Politi et al. (5) randomized 214 STEMI patients with multivessel disease to culprit vessel angioplasty alone (n = 84), simultaneous treatment of nonculprit vessels (n = 65), or culprit vessel only followed by staged revascularization (n = 65). In-hospital mortality, unplanned rehospitalization, and repeat revascularization occurred more frequently in the culprit-vessel-only group (all p < 0.05). Further, the culprit-vessel-only strategy emerged as an independent predictor of adverse events. Although the results of these 2 randomized studies are provocative, some may consider that the requirement for repeat revascularization in the culprit-only strategy should not be considered a major adverse event, but rather interpreted within a global strategy in which closer clinical follow-up is needed. Likewise, the sample size of these studies was grossly underpowered to detect differences in death or recurrent myocardial infarction.

Therefore, data from large registries are also of major interest and complementary value. A subanalysis of the CADILLAC (Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complication) trial (2) showed that in patients with multivessel disease undergoing primary angioplasty, subsequent revascularization of noninfarct-related arteries conferred a clear prognostic benefit. More recently, Cavender et al. (6) examined the large dataset of the U.S. National Cardiovascular Data Registry to identify STEMI patients with multivessel disease undergoing primary angioplasty. In-hospital mortality of 3,134 patients (10.8%) with multivessel intervention was compared with that of the remaining 25,802 patients undergoing single-vessel intervention only at the index procedure. Patients with multivessel intervention during primary angioplasty were at higher risk and more likely presented in cardiogenic shock. Overall, the mortality rate was higher in patients undergoing multivessel intervention. This increased mortality persisted after adjustment for potential confound-

ers, and surprisingly, when only patients in cardiogenic shock were analyzed. Nevertheless, clinical follow-up was not obtained and only in-hospital mortality was assessed. In addition, adjustment was performed using classical multivariate logistic regression models but not propensity score matching, so residual selection biases cannot be excluded.

Further Insights and Clinical Perspective

Coronary artery disease is a diffuse process, and one-half of STEMI patients have concomitant multivessel disease (2). However, data from the "real world" registry of Hannan et al. (7) suggest that only 1 in 4 patients with STEMI and multivessel disease (>70% stenosis in ≥2 major vessels) receive nonculprit-vessel interventions within 2 months. Therefore, actually most of these patients had incomplete revascularization. Further studies are warranted to determine whether additional efforts to obtain complete revascularization in a larger number of STEMI patients may translate into improved clinical outcomes.

During primary angioplasty procedures, interventions are usually confined to the infarct-related artery. However, some consider this an incomplete approach. Proponents of initial multivessel interventions argue that STEMI patients have a heightened inflammatory milieu and multiple plaque disruptions. Plaque instability is not limited to the culprit lesion, and lack of therapy of the other lesions is associated with adverse events. Additionally, severe disease in nonculprit vessels may hamper the compensatory contractility of remote myocardial regions characteristic of STEMI patients. Finally, early discharge may be contemplated in patients with complete revascularization (2–6). Alternatively, proponents of a culprit-vessel–only strategy emphasize that multivessel intervention is not initially required because it may lead to prolonged interventions, contrast overload, heart failure, and renal impairment. In addition, nonculprit lesion severity may be exaggerated as the result of circulating catecholamine-mediated vasoconstriction, and precise evaluation of revascularization requirements may be hampered. Furthermore, jeopardizing remote myocardial territory would be of special concern in the acute phase. Finally, multivessel stenting might be associated with higher rates of periprocedural myocardial infarction, and eventually, with increased rates of late revascularizations secondary to restenosis (2–6) (Table 1).

In the study by Hannan et al. (7) and in most previous observational studies alike, the final reasons to perform nonculprit vessel interventions during the index procedure and proceed against current recommendations remain elusive. Despite elegant and rigorous adjustments using complex statistical analyses, the potential for residual bias caused by unmeasured confounders cannot be fully discarded. Two opposite clinical scenarios may explain the performance of additional interventions on nonculprit lesions. Firstly, this

Table 1. Potential Consequences of Multivessel Intervention During Primary Angioplasty

Favorable
Ensuring adequate, complete, early revascularization
Revascularization of remote ischemic myocardial territory
Lower requirement of repeated procedures
Improvement of left ventricular function
Stabilization of additional disrupted plaques
Reduction of hospital stay
Reduction in hospital costs
Improving long-term clinical outcome (?)
Unfavorable
Prolonged procedures
Larger amount of contrast media (heart failure, renal failure)
Concerns of jeopardizing remote but critical myocardium in the acute phase
Higher rates of procedure-related myocardial infarction
Higher requirement of late procedures as the result of restenosis from multivessel stenting
Inaccurate assessment of lesion severity/revascularization requirements
Shadowing in-hospital and long-term prognosis (?)

strategy may be selected in a favorable setting. This would be the patient in whom successful culprit vessel stenting has been readily accomplished during a smooth procedure, leading to Thrombolysis In Myocardial Infarction (TIMI) coronary flow grade 3 and nearly complete ST-segment resolution. If another easy/attractive target is identified in this patient, the *temptation* to finish the procedure achieving complete revascularization might be high. Conversely, a complex, prolonged procedure required to open the culprit lesion will likely discourage the operator from further attempts in other vessels. In the study by Hannan et al. (7), patients' multivessel interventions during the index procedure had less frequently an abnormal coronary flow (TIMI flow grade ≤2) in the culprit lesion, suggesting easy lesions. However, additional data on lesion characteristics or stenoses severity were not provided. Secondly, this aggressive strategy also may be selected in an unfavorable setting. For instance, additional procedures might be pursued in hemodynamically stable patients with persisting chest pain or significant residual ST-segment elevation. Indeed, the performance of multivessel stenting during primary angioplasty may be more likely in the patient in whom procedural success is not apparent. Identification and treatment of the culprit lesion is not always easy in patients with multivessel disease, especially in the presence of small culprit vessels or total occlusions receiving collateral circulation. In some patients, a chronic occlusion may be attempted first, and subsequently another vessel will be attempted when the error is recognized. All of these may cause delayed or unsuccessful reperfusion and contribute to adverse prognosis. Eventually, we should acknowledge that the mindset of the operator during primary angioplasty and the myriad of variables interfering with procedure course are very difficult to measure and account for.

Conclusions

The present study strongly suggests that complete revascularization should be pursued in STEMI patients with multivessel disease. However, as recommended by current guidelines, the culprit lesion only should be attempted during the index primary angioplasty procedure and complete revascularization should be deferred to be achieved later on during staged elective procedures. Current data suggest that during primary angioplasty, perfect is the enemy of the good. Therefore, in this challenging scenario, a heuristic, *greedy*, multivessel approach does not seem to be justified unless hemodynamic compromise is present.

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