Since the earliest days of the thrombolytic era, maximizing myocardial salvage by reperfusion of the myocardial region at risk for myocardial infarction has been the most important immediate objective in management of ST-segment elevation myocardial infarction (STEMI) (1). The roles of time to reperfusion and collateral flow to the infarct territory and their impact on early and late post-infarct ventricular function were recognized in those early days. However, tools for quantitation of myocardial salvage have been scarce and difficult to use. A few studies have been done with radionuclide imaging, using immediate injection of sestamibi before reperfusion to depict the risk region, with scanning after reperfusion, combined with a later reinjection and scan post-reperfusion to depict the reperfused viable myocardium (2–4). The difference in size between the initial perfusion defect and the post-reperfusion perfusion defect then represents myocardial salvage, whereas the perfusion defect on the post-reperfusion scan represents infarct size. However, this approach has been difficult to implement on a large scale. In this issue of *JACC*, a potentially important study by Ortiz-Pérez et al. (5) applies a recently developed approach using the BARI (Bypass Angioplasty Revascularization Investigation Myocardial Jeopardy Index) score (6) for estimation of the size of the myocardial risk region, expressed as percent left ventricular myocardium, while using cardiac magnetic resonance (CMR) delayed enhancement imaging to quantitate infarct size (7–9). A myocardial salvage index (MSI) is then calculated as the ratio of myocardial salvage to total LV wall volume (MSI = [myocardial salvage/total left ventricular wall volume] × 100). Use of the BARI score to determine the size of the risk region has been previously validated by this group in an analysis of results in 83 patients undergoing percutaneous coronary intervention (PCI) for STEMI with a completely occluded culprit vessel (Thrombolysis In Myocardial Infarction [TIMI] flow grade 0) (10). In that study, there were 35 subjects with transmural infarction by CMR, in whom the risk region was presumably completely infarcted. In those subjects, there was an excellent correlation between BARI score–predicted risk region size and infarct size. In addition, the endocardial surface area of the infarct by CMR in all subjects with time to reperfusion over 1 h correlated well with the BARI score risk region size, independent of collateral flow or time to reperfusion. Both early reperfusion and the presence of visible collateral were associated with reduced infarct transmurality and trends to smaller infarct size. Other investigators have found less agreement between BARI score and endocardial infarct surface area, but this is likely due to inclusion of patients with substantial antegrade flow in the infarct vessel in their analysis (11).

In the present study, the authors have apparently added to the previously evaluated cohort an additional 38 patients with residual antegrade flow in the culprit vessel, TIMI flow grade 1 to 3 at the time of angiography, and reanalyzed the data with a
focus purely on determinants of salvage, not validation of the methods. They have assessed the impact of pre-reperfusion antegrade flow, collateral flow, time to reperfusion, and CMR microvascular obstruction on the MSI and have also examined the relationship of these variables to wall motion score, to major adverse cardiac events (MACE) (cardiac death, admission for heart failure, or need for heart transplantation), and to changes in wall motion score at follow-up.

The results demonstrate that, in contrast to patients with TIMI antegrade flow 0 to 1, initial TIMI flow grade 2 to 3 was associated with smaller infarcts, more myocardial salvage, and less infarct transmurality, as well as lower wall motion scores and fewer MACE events. In patients with initial TIMI flow grade 0 to 1, those with good collaterals (grade ≥2) also had higher ejection fraction, better wall motion score, less infarct transmurality, and a trend toward higher MSI than those with poor collaterals (grade ≤1, n = 65). As expected, increasing time to reperfusion was associated with reduced myocardial salvage and increased infarct transmurality, but only in patients with poor residual flow (TIMI flow grade 0 to 1) and no collaterals. In a multivariate analysis, symptom-to-balloon time, residual TIMI flow grade 2 or more, collateral flow, and microvascular obstruction by CMR were significantly and independently associated with MSI and infarct transmurality, whereas BARI score per se was only associated with MSI. Further, the impact of antegrade flow prior to reperfusion in limiting infarct size appears greater than that of collateral flow. Unfortunately, the methods used do not permit rigorous quantitation of either antegrade or collateral flow in the risk region.

These findings underscore the complex interplay of multiple determinants of myocardial salvage in PCI for STEMI. Clearly, symptom-to-balloon time remains a dominant factor, but it is most determinative in the setting of little residual antegrade or collateral flow. The preponderant role of antegrade as opposed to collateral flow and a reduction in endocardial surface extent of necrosis relative to the BARI score risk region in patients with TIMI flow grade 2 or more at presentation are notable and clearly delineated. Overall, the results presented offer the clinician some additional tools in the estimation of both the benefit of reperfusion in a given patient with STEMI and the infarct extent.

There are, however, some important limitations. The number of patients with TIMI 2 to 3 antegrade flow is small, and they have smaller infarcts and much less multivessel disease, so that multivariate analysis in a larger population would be needed to convincingly differentiate effects of antegrade flow from those of infarct size and multivessel disease. In addition, the number of MACE events is very small, and given the multiple differences between the groups compared, caution must be observed in drawing any conclusions from that analysis. Further, one wonders whether expression of myocardial salvage only as percent left ventricular myocardial volume is really the best approach. Using this approach, vessels with smaller risk regions will inevitably show less salvage than vessels with larger risk regions. But we also want to know what proportion of the risk region itself has been salvaged in order to better evaluate treatment success. Thus, an additional salvage index based on the ratio of viable myocardium at risk to total risk region size would also be extremely helpful.

Finally, although the methods used in the study have served the investigators very well, they may have been overtaken by recent developments in CMR. In particular, CMR imaging of myocardial edema in both the infarct itself and the reversibly injured, but viable, risk region surrounding it, using T2-weighted CMR sequences has now become sufficiently reliable to provide an alternative, more direct method than the BARI score technique for risk region quantitation (11–15). Although evidently not available at the time of initiation of data collection for this study, CMR edema imaging now appears to be the preferred method for determination of risk region size and is easily added to a CMR study that includes imaging ventricular size and function by cine CMR and infarct size by delayed enhancement. Indeed, the combination of T2-weighted and delayed enhancement imaging has already provided a very compelling demonstration of the impact of time to reperfusion on myocardial salvage (15). Thus, although the present study provides valuable information on myocardial salvage, newer methods and evaluation of additional salvage indexes appear likely to further advance our understanding of this important problem in the near future.

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