Divergent pattern: Pattern recognition or marker for adverse events

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SPECT imaging using Tc-99m-sestamibi has been a widely studied technique to evaluate infarct size, left ventricular volumes, and myocardial salvage after acute myocardial infarctions (AMI).^{1,2} These aspects have been shown to correlate with left ventricular function, as well as clinical outcomes (including cardiac mortality and morbidity related to heart failure), after reperfusion measures and adjunct therapies to limit infarct size.^{1–3} Specifically, the utility of Tc-99m SPECT early on, after an Anterior Myocardial Infarction, as an aid in prognostication has also been demonstrated.⁴ Infarct size as measured by Cardiac MRI or technetium-99m sestamibi SPECT within 1 month after primary percutaneous coronary intervention (PCI) is strongly associated with all-cause mortality and hospitalization for heart failure within 1 year. Therefore, the identification of patient subsets at higher risk of adverse cardiovascular events following anterior myocardial infarction is vital in improving overall patient outcomes.

In this edition of the Journal, Dr. Calabretta and colleagues⁵ explore the prognostic value of Divergent Pattern (DP) detection by SPECT among patients with Acute anterior Myocardial Infarction. Traditionally, divergent pattern recognition has been applied in the evaluation and management of ischemic cardiomyopathy but not in the setting of post-AMI patients.⁶ The presence of DP serves not only as a marker of significant LV dysfunction with apical remodeling but also as a

predictor of adverse cardiac events among patients with viability and ischemic cardiomyopathy.⁶ The application of this finding in the setting of acute myocardial infarction, specifically anterior myocardial infarction is a novel approach.

Their study⁵ enrolled 150 patients with anterior ST elevation myocardial infarction (STEMI) who were all successfully treated with primary percutaneous coronary interventions (PCI). All patients underwent perfusion gated SPECT prior to hospital discharge after the index event and a repeat study at 6-month follow-up. A total of 26 patients had evidence of DP in the study cohort. Patients demonstrating DP in comparison to those without DP on the initial SPECT study, had significantly larger infarct size ($28 \pm 19\%$ vs. $15.7 \pm 17\%$, $P < 0.02$), and lower ejection fraction ($33 \pm 7\%$ vs. $41 \pm 10\%$, $P < 0.001$) as would be expected. This finding was also corroborated by the peak Troponin values which were significantly higher among patients exhibiting DP.

Interestingly, at the 6-month follow-up gated SPECT, the infarct size among patients with DP did not decrease as much as among those without DP. Consequently, there remained a significant difference in the infarct size ($27.3 \pm 16\%$ vs. $9.7 \pm 12.5\%$, $P < 0.0001$) between DP patients and those without DP. In fact, the residual infarct size difference increased between the 2 groups by virtue of the improved recovery among patients without DP. Further, patients who demonstrated DP initially had significantly larger end diastolic volumes (EDV) (156 ± 54 vs. 107 ± 44 mL, $P < 0.0001$), end systolic volumes (ESV) (104 ± 47 vs. 59 ± 36 mL, $P < 0.0001$), and lower ejection fraction (EF) ($35 \pm 12\%$ vs. $48 \pm 13\%$, $P < 0.0001$) upon follow-up SPECT imaging. Therefore, more patients with DP manifested adverse LV remodeling compared to those without DP.

A total of 17 adverse cardiac events (cardiac death and heart failure hospitalizations) were noted during the study period. In this relatively small study population,

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the adverse events occurred more frequently in patients with DP compared to those without (27% vs 9%; $P < 0.02$). Kaplan–Meier cumulative survival analysis showed a worse prognosis for patients with DP.

Accordingly, the authors concluded that “The detection of DP early after AMI can be useful to predict the occurrence of LV remodeling in the short-term follow-up and has more general unfavorable prognostic implications.”

The authors are to be congratulated as the study examines an interesting concept in a sub-population at high-risk of adverse cardiac events following AMI.⁴ The utility of SPECT to study LV function remains its reliable reproducibility as well as the objective measurement of LV volumes and wall motion independent of observer variability. It also permits the evaluation of microvascular function. The identification of microvascular damage/edema and/or microvascular dysfunction that persist despite epicardial stenosis correction has been shown to result in unfavorable LV remodeling and increased infarct size. Studies have shown that myocardial salvage might be suboptimal despite sustained culprit vessel patency achieved by primary PCI.^{7,8} Mechanisms attributable to this finding include delayed reperfusion, microcirculatory dysfunction, or no reflow phenomenon. In the current study, the time from symptom onset to PCI was comparable across both groups which suggests that delayed reperfusion is an unlikely factor affecting the outcomes. The study was also notable for the thorough follow-up of all patients, albeit for a shorter term, that nonetheless provided accurate data and consistent results.

While objective measures of LV function are available with SPECT, the visual criteria used to define DP and the absence of methodological comparisons with alternative imaging techniques, particularly echocardiography or cardiac MRI, are significant limitations of this study. The findings of DP (essentially akinesis/dyskinesis of the apex) and remodeling should be adjusted for regional wall motion abnormalities. These aspects can be more reliably demonstrated by echocardiography with contrast.

Patients demonstrating DP compared to those without were also characterized by poorer pre-PCI TIMI flow of 0/1 (85% vs 69%) and were less often found to have multivessel CAD (21% vs 48%). The small study population likely resulted in these differences not reaching statistical significance. These findings would also point to ischemic preconditioning among patients without DP which cannot be adequately accounted for in analyzing the extent of myocardial injury and consequent remodeling given the study size. The relatively small patient sample and the curtailed study period make it underpowered for detailed statistical analysis. Thus,

the study serves to be hypothesis generating rather than confirmatory in nature.

In summary, this study demonstrates that DP is not infrequent in the early post-AMI period even after successful treatment with primary PCI. DP noted early after AMI can be useful to predict the occurrence of LV remodeling which in general has unfavorable prognostic implications. DP determined through SPECT is valuable to learn whether the LV dysfunction is due to simply myocardial stunning or more permissive transmural necrosis. The latter would, therefore, result in increased adverse cardiac events. These findings would also inform the decision to pursue more aggressive medical therapy with aldosterone antagonists in addition to angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blocker (ARB) therapy. While the study was underpowered to definitively predict LV recovery in the presence of DP, there undoubtedly was a signal that the absence of DP indicates improved LV function and recovery following AMI. This is meaningful as early detection of patients less likely to have LV recovery permits better management of patients with consequent cardiomyopathy. Further, it would also help guide earlier adoption and patient acceptance of secondary prevention measures such as ICD placement. It is known that fewer than 1 in 10 eligible patients with low EF received an ICD within 1 year after MI⁹ despite the knowledge that ICD implantation is associated with lower risk-adjusted mortality at 2 years. Thus, the detection of DP would be valuable in such patients. It provides an evidence-based approach in identifying patients with large infarcts who should have continued EF assessment to determine their eligibility for ICD placement.

Declarations

Disclosures

Dr. Gokhale—none

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