Does the location of perfusion defects matter? An old question with a new answer

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Coronary artery disease (CAD) remains the leading cause of death in the USA. Since effective management of this disease is available, it is crucial to properly risk stratify these patients and to provide aggressive treatment to the high-risk patients.

Epidemiologic data have previously shown that the majority of the ST elevation myocardial infarctions (STEMIs) occur in the territories of left anterior descending (LAD) artery followed by the right coronary artery (RCA).^{1,2} In many studies, the site of infarction was an important predictor of outcomes. More specifically, the proximal LAD territory was found to be associated with the highest risk and thus its involvement in CAD was incorporated into various prognostic risk models.^{3–5} Whether this worse prognosis is due to the larger size of the infarct or the location of the infarct is still debatable. However, some data of the pre-revascularization era showed that there is an independent contribution of location of infarct, independent of the size of the infarction.^{3,6} This association ranged from marginal⁷ to overt^{8,9} in subgroup analysis of randomized controlled trials and observation studies. In the revascularization era, the association of worse clinical outcomes with LAD infarcts continued to be observed.

Proximal LAD infarcts are also associated with worse, not only short-term but also long term, outcomes. It was initially thought that because the degree of

myocardial necrosis is greater in patients with LAD artery involvement, they would eventually have worse outcomes. Conversely, more recently, it was demonstrated that it is not the amount of myocardial necrosis that leads to worse outcomes, but it is the degree of remodeling and resulting left ventricular dysfunction associated with these large infarcts, which predicts the worse long-term outcomes.^{10–13}

Single photon emission computed tomography (SPECT) is a functional imaging study that provides a visual demonstration of regional perfusion of myocardium. The utility of SPECT in risk stratification for CAD has been well established.¹⁴ SPECT imaging has good overall accuracy to differentiate perfusion defects due to stenosis in different vascular territories. However, the prognostic value of different perfusion defects locations was not evaluated before.

DOES LOCATION OF PERFUSION DEFECT ON SPECT MPI PREDICT OUTCOMES?

In this issue of *the Journal*, Slim et al¹⁵ evaluated the prognostic importance of location of perfusion defects in a cohort of 4,937 patients who underwent exercise and pharmacological SPECT. In the 4,937 patients with single-vessel perfusion defects, 1,774 (35.9%) had LAD defects, 2,864 (58%) had RCA territory defects, and 299 (6.1%) LCx territory defects, while in the two-vessel perfusion defect group of 2,907 patients, 1,232 (52.4%) had LAD involvement with another vessel territory. Those authors showed that the cardiac deaths and non-fatal myocardial infarction (MI) did not differ in patients with LAD defect compared with non-LAD defect.

On a first glance, these data appear contradictory to prior coronary angiography and acute MI registry data. The coronary angiography data from the Duke database have shown that the revascularizing left main and the proximal LAD arteries are associated with a significant mortality benefit, while revascularizing other lesions might not impact mortality.¹⁶ A similar relation was shown in the coronary computed tomography angiography (CCTA) literature, where the proximal LAD lesions were associated with worse outcomes, compared with the lesions in other vessels.¹⁷

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The discrepancy that we see here can be explained as follows:

1. SPECT myocardial perfusion imaging is a physiological study that provides functional and prognostic assessment of hemodynamically significant stenosis as compared to coronary angiography and CCTA, which only provide limited functional and prognostic data, and it may miss hemodynamically non-significant lesions. Nearly two-thirds of the vulnerable plaques that lead to MI were found to be non-flow limiting and hemodynamically insignificant in previous studies.
2. In patients with known CAD (who were not excluded from this analysis), the defect localization might not be as accurate due to the presence of collateral circulation, micro-vascular obstruction, left bundle branch block or bypass grafts, etc. Thus, the localization of defects in these patients and correlating with anatomical sites may not be as accurate compared with patients without known CAD. Moreover, in patients with diffuse multi-vessel disease, the extent of disease can be underestimated by 30-50%.¹⁸ Thus, underestimation of LAD disease may happen, especially if higher degree of ischemia is present in other vascular territories.

DOES LOCATION OF CORONARY ARTERY PREDICT SITE OF MI?

Another logical question arises: Are perfusion defects observed on SPECT associated with cardiac events in the same territory where they were observed? In two small studies, researchers found that the site of perfusion defect did not correlate with the site of subsequent MIs. Later on, larger studies found similar results.¹⁹⁻²² This could be because a high degree stenosis might lead to a better collateral circulation, and hence better survival.²³ The agreement was found to be in the range of 22-64% in these studies. Based on the autopsy data, Kanei et al.²⁴ found that although the scintigraphic defects did not correlate with the site of future AMI, they predicted increased risk of future STEMI. This implies that a higher atherosclerotic plaque burden acts as a surrogate marker of future cardiac events.

Another important finding in this study is that the degree of stress-induced perfusion abnormalities is more important than the location of the perfusion defect. The prognostic value of perfusion abnormalities has been well documented before.²⁵ This analysis emphasized this further and clearly showed that the severity of perfusion defect is more important than the location of defect. Thus, the lack of outcome difference between the different groups in this study is most likely due to the

absence of significant differences in ischemia burden. Some could argue that patients with proximal LAD lesions may be associated with a higher ischemic burden than those with an RCA or LCx lesion which in turn may result in worse long-term outcome. However, this specific case scenario was not evaluated in this analysis, and further research is needed.

CONCLUSION

In conclusion, in a clinical setting, it is important to also adopt a holistic approach in determining the risk of future cardiovascular mortality, while taking into account risk factors for CAD, patient-based characteristics and high risk predictors on MPI and just not rely on the location of the coronary artery involvement on a myocardial perfusion imaging. It should be also kept in mind that even though the agreement between morphological and functional studies is not great, the complimentary information provided by both the studies has an incremental value in the management of CAD patients.

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