Is myocardial viability related to left ventricular dyssynchrony?

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The role of cardiac dyssynchrony in coronary artery disease (CAD) is still not well defined. Several studies have evaluated the relation of left ventricular dyssynchrony (LVD) with myocardial ischemic and/or scar burden,^{1–4} CAD extent,⁵ and LV contractile function.⁶ However, there are conflicting data in the literature about the effect of different patterns of perfusion abnormality on LVD in CAD patients. On initial stress-rest Tc99m-MIBI study, no significant relation between LVD and stress-induced ischemia was observed and this was attributed to delayed image acquisition after stress.³ So, it was proposed, that stress-induced changes in LVD may be better evaluated using Thallium-201 (Tl-201) MPS, as the post-stress images are acquired within 10 minutes of stress in Tl-201 study. Chen *et al* evaluated this aspect on stress-rest Tl-201 MPS and suggested that stress-induced ischemia causes dyssynchronous contraction in the ischemic region, leading to worsening of LVD, whereas normal myocardium showed more synchronous contraction during stress.⁴ However, in a similar study, Singh *et al* found that LVD parameters were smaller on post-stress as compared to rest study on Tl-201 MPS, regardless of the perfusion pattern. Stress-induced worsening of LVD was observed only in patients with perfusion abnormalities, but this is not related to the type of perfusion abnormality.² Therefore, there is still a lack of clarity on the exact relationship of the LVD with the type of perfusion abnormalities.

The present study addresses the same issue but with a view to explore the relation between viable myocardium and LVD, taking into consideration, that LVD is related to ischemia^{1–4} and regional scar.^{7,8} Further, the authors have extrapolated from the conventional stress-rest study wherein ischemic segments are associated with worsening of dyssynchrony and hypothesized that improvement in perfusion of ischemic segments post-nitroglycerine (NTG) at rest can be associated with improvement of dyssynchrony.

In this issue of the Journal of Nuclear Cardiology, Padron *et al* have reported that in patients with ischemic dilated cardiomyopathy (IDC) and depressed left ventricular ejection fraction (LVEF), the myocardial viability detected by rest/NTG GSPECT MPI, might determine LVD improvement. The authors conducted a non-randomized study, by enrolling fifty-four consecutive patients with IDC and depressed LVEF. Patients with severe proximal stenosis > 70% in at least one main coronary artery on invasive coronary angiography and LVEF of < 40% were included in the study. They underwent a two-day rest/NTG GSPECT MPI to determine the myocardial viability. The patient received sublingual NTG before the radiotracer injection and sublingual NTG was also administered before acquisition to evaluate the effects of NTG on function and LVD parameters.

The author divided the patients into two groups, viable and non-viable. Patients with a nitrate-induced increase in uptake of > 10% vs. baseline, in atleast, two consecutive dysfunctional segments, were considered viable as well as those who showed no improvement in the uptake but the uptake was > 50% on post-NTG study. Patients with no nitrate-induced increase of uptake and uptake of < 50% were considered non-viable. A semi quantitative assessment on 17 segment model was also performed and the perfusion defects were scored at baseline and after NTG administration. Left ventricular contraction dyssynchrony was assessed by phase analysis, as evaluated by two variables, phase

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standard deviation (PSD) and phase histogram bandwidth (PHB).

The authors reported viability in 25 patients, of which 13 (52%) showed a nitrate-induced uptake increase of > 10% and 12 (48%) had no improvement in the uptake but the uptake was > 50% after NTG administration. Uptake of < 50% after NTG and no increase in uptake post NTG was found in 29 patients (non-viable group). Perfusion, function and LVD were compared in 25 viable patients vs. 29 non-viable patients at baseline and post-NTG. There was a statistically significant improvement in LVEF ($P = 0.001$) and reduction in end systolic volume (ESV) ($P = 0.006$) in the viable group compared to the non-viable group. The viable group patients also experienced a significant reduction in the LVD variables: PSD reduced from $57.77^\circ \pm 19.47^\circ$ to $52.02^\circ \pm 17.09^\circ$ and PHB from $190.20^\circ \pm 78.83^\circ$ to $178.0^\circ \pm 76.14^\circ$ ($P < 0.05$) in post-NTG study. However, LVD variables showed no improvement in the non-viable group ($P > 0.05$). The authors concluded that in patients with IDC and depressed LVEF, the myocardial viability detected by rest/NTG GSPECT MPI determined LVD improvement.

The results of the present study show that more the extent of viable myocardium, lower the dyssynchrony parameters, which also means that more the extent of scarred myocardium higher the dyssynchrony. In this context, the results of the present study are consistent with the previous studies that have shown similar relation between extent of scarred myocardium and LVD.⁷⁻¹⁰ Ludwig *et al* reported higher LVD among IDC than non-ischemic patients ($57 \pm 17^\circ$ vs. $35 \pm 13^\circ$) ($P < 0.001$) and concluded that PSD values increased with extent of scarred myocardium.⁷ Samad *et al* have demonstrated that in a population of patients with IDC, a reduced LVEF, increasing QRS duration, severity and extent of myocardial scar are independent predictors of mechanical dyssynchrony.⁸ In another study, Malhotra *et al* have also shown that summed rest score (SRS) is the independent predictor of LVD.⁹ Bios *et al* demonstrated that dyssynchrony parameters by SPECT MPI can be employed to detect scar. All the three phase analysis (PA) parameters—entropy, PHB, and PSD, were associated with scar on univariable analysis and were progressively higher (indicating greater dyssynchrony) as SRS increased, indicating greater extent and severity of the perfusion defect.¹⁰ In the present study also, the non-viable group had higher SRS score at baseline compared to the viable group. It suggests that the extent and severity of perfusion defect was higher in this group. Hence non-viable group showed lower LVEF and higher dyssynchrony on baseline study and showed no change in LVEF, SRS, and LVD post-NTG. On other hand, the viable group patients had lower SRS, higher

LVEF and lower dyssynchrony on baseline study and that these showed improvement in post-NTG study. The authors have also acknowledged that the high prevalence of LVD in their study population is because all the patients had IDC and the non-viable group with more extensive scarred areas had significantly higher dyssynchrony. If the present study had assessed relation of LVD with extent of scarred instead of viable myocardium then the results would have been consistent with the previous studies that evaluated this aspect. It can also be inferred that more the extent of viability, better the synchrony which is consistent with the results of this study.

The important aspect of the present study is that the authors have demonstrated improvement in dyssynchrony post NTG in the viable group. Interestingly, the authors administered short-acting, sublingual NTG at the time of acquisition to evaluate the effects of NTG on function and LVD parameters. The improvement in LVD was noted in viable group both in the patients who showed nitrate-induced increase in uptake and also in patients who showed no increase but uptake was > 50%. But there was no significant difference between the two, as nine (69%) patients with a nitrate-induced increase in uptake and eight (67%) without improvement but uptake > 50% experienced LVD improvement after NTG study ($P > 0.05$). This study tried to establish the role of dyssynchrony in context of viability study performed with nitrate augmentation. However, viability as determined on NTG study cannot be simplified into two groups of viable and non-viable. A rest nitrate-augmented MPI in IDC patients can have ischemic but viable myocardial segments, non-ischemic viable segments, scarred segments and segments with non-transmural infarction (mixed scar and viable). The interplay of these segments and its association with dyssynchrony is very complex and can present contrasting findings similar to the results of many studies that observed the effect of perfusion abnormalities and dyssynchrony on conventional stress-rest protocol.¹⁻⁴

Patients are selected for revascularization on the basis of viability but the data in this study are not strong enough to suggest that change in dyssynchrony can be used as criteria to select or predict response in patients undergoing revascularization. The improvement in perfusion and hence the improvement in viability is the primary effect post-NTG, which results in the improvement in the dyssynchrony. Although, PET has relatively limited availability compared to SPECT but its utility in assessment of viability is strongly established. Unless the prognostic value of improvement in dyssynchrony in viability is proved in selecting patients for revascularization and predicting functional recovery, the clinical relevance of this finding is debatable. A

larger randomized study with follow-up post revascularization may show its clinical utility.

Disclosure

The authors declare no conflict of interest.

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