Speckle tracking echocardiography for management of patients with PVCs and normal ejection fraction

1. Editorial comment

Premature ventricular complexes (PVCs) are common in patients with and without structural heart disease. Although PVCs used to be considered as mostly benign, long-term frequent PVCs may be associated with PVC-induced cardiomyopathy [1,2]. Possible mechanisms include alteration of membrane ionic currents and intracellular calcium handling, alteration in autonomic tone, ventricular dyssynchrony during PVCs, shortened coupling intervals, and post-extrasystolic potentiation [3–6]. PVC ablation has been shown to reverse PVC related LV dysfunction [7–9]. PVC-induced cardiomyopathy is classified as an indication for catheter ablation therapy by European Heart Rhythm Association/Heart Rhythm Society/Asia Pacific Heart Rhythm Society Expert [10]. However, the diagnosis of PVC-induced cardiomyopathy continues to be done by exclusion or retrospectively with no definite criteria to prospectively guide the clinical diagnosis. It also remains controversial whether ablation therapy is required for patients with high burden of PVCs who are asymptomatic and have a normal left ventricular ejection fraction (LVEF). PVCs may induce impairment in radial, longitudinal, and circumferential strain. These changes are not able to be detected by standard imaging and newer techniques, such as speckle tracking, may be needed to detect early presence of PVC cardiomyopathy [11]. Two-dimensional speckle-tracking echocardiography has been shown to detect early left ventricular systolic dysfunction before overt changes in conventional echocardiographic measures and could be an indicator of early subclinical myocardial dysfunction in patients with normal LVEF [12]. The presence of abnormal strain measures in patients with frequent PVCs and normal LVEF could potentially be the impetus to treat these PVCs in order to prevent progression to overt LV dysfunction cardiomyopathy.

In this issue of the Indian Pacing and Electrophysiology Journal, Fonseca et al. provide the results of a small comparative retrospective study of 21 patient with right ventricular outflow tract PVCs without structural heart disease referred for ablation and 13 matched controls without PVCs who underwent AVNRT ablation [13]. Global and free wall longitudinal strain measurements (GLS and FW-LS) using 2D speckle tracking echocardiography 30–60 days after ablation were compared between the 2 groups. While LV-GLS stayed in the normal range, RVFW-LS and RV-GLS were lower in the PVC group and with a mean lower than the normal range. These findings suggested subclinical myocardial dysfunction in patients with right ventricular outflow tract PVCs. Several aspects of this study warrant emphasis to place the findings in perspective.

First, while the mean RVFW-LS and RV-GLS were significantly lower in patients with PVCs compared to study controls and fell below the lower range of normal (−22 or −23% for RVFWLS and −20% for RSV-GLS as defined by Muraro et al.), the respective standard deviations of these measurements indicate that some patients would still be within the normal range of these parameters [14]. While the larger standard deviations could be due to the low number and heterogeneity of the patients included, it might also mean that a good proportion of patients might not truly have any measurable feature of cardiomyopathy. A recent study using 2D strain imaging was done on 29 pediatric patients (≤21 years) with PVC (>5% burden) found normal RV-GLS and LV-GLS values [15]. This finding could be driven the lower PVC burden, the lower age and the lack of controls. Furthermore, the reference values of RV strain vary significantly between studies depending on the demographics of the population studied and the technique and software used [16,17]. Larger, more longitudinal multi-ethnic and age stratified studies are needed to better classify the normal range of RV strain measurements.

One should also keep in mind that the feasibility of RV strain imaging is sometimes limited due to smaller thickness, larger excursion, and lower quality of speckles compared to the LV. The feasibility of RV strain imaging has been in the order of about 85% [14]. In the current study, 3 patients had poor quality images to perform strain imaging, which is consistent with previously reported studies.

Second, the patients included in this study are patients referred for PVC ablation and not all comers with PVCs. The incidence of PVC-induced cardiomyopathy varies widely between studies with 6%–7% of patients with greater than 10 PVCs per hour followed prospectively but is typically higher (up to 38%) in patients referred for catheter ablation [18–20]. While selecting this population might give the authors a better chance of finding subclinical ventricular dysfunction, it also might overestimate its prevalence compared to all comers with PVCs.

Third, in patients presenting with frequent PVCs and ventricular dysfunction, whether overt or subclinical, it is difficult to ascertain whether the dysfunction is the consequence of the PVC or an independent condition. In short-term animal studies with pacing-induced PVCs, no fibrosis was detected and normalization of LV function occurred within 2 weeks after the cessation of pacing-induced PVCs [2]. Another study done by Wijnmaalen et al. found...
that strain measurements for both the RV and the LV improved in patient with successful PVC ablation in patients with baseline normal LVEF but remained unchanged in untreated patients with PVCs [11]. While these findings argue that the subclinical ventricular dysfunction is the consequence of the PVCs, the findings of the present study by Fonseca et al. argue for the opposite [13]. The lower RV-GLS, RVFW-LS and LV-GLS in patients with PVCs were not correlated with the PVC burden before ablation nor with the success of the ablation procedure. These results suggest that the sub-clinical myocardial dysfunction is not a consequence of the PVCs.

In patients with overt LV dysfunction, a reduction of PVC burden by more than 80% or below 5000/day have shown a significant improvement in their LV function with various times to recovery, mostly within 4 months after ablation, but sometimes up to 45 months [7,9]. A long term remodeling process in some patients suggests that there could be structural changes triggered by prolonged exposure to PVCs. However, up to 35% of patients do not show a significant improvement in their LV function after PVC ablation [8].

The most common factor of lack of response is a wider PVC QRS duration [7–9]. Although dysynchrony may play a role with wider PVC QRS, the study by Deyell et al. did not demonstrate that PVCs with narrower QRS durations were less likely to be non-responders compared to other sites [8]. This favors the hypothesis that VPD QRS duration is a manifestation of the underlying substrate, whether myofibril disarray and more advanced fibrosis. A longitudinal study with long term follow-up of all comers with PVCs, without fibrosis on cardiac magnetic resonance imaging would help determine whether the mechanical abnormalities seen are the result or the cause of the PVCs.

Finally, the PVC burden threshold associated with PVC-induced cardiomyopathy varies greatly between studies, with most between 16% and 26%, but sometimes less than 10% [18,20,21]. Although widely used, PVC burden alone remains a limited tool for predicting the risk of developing PVC-induced cardiomyopathy. Recent studies have attempted to determine other markers: lack of symptoms and longer exposure, epicardial location and wider QRS duration [7]. However, this study remains only an indicator of the underlying substructure. Myofibril disarray and more advanced fibrosis.

Despite its limitations, the study by Fonseca et al. suggests that strain echocardiographic imaging may offer a more direct assessment of early PVC-induced cardiomyopathy [13]. While the presence of normal standard and strain echocardiographic measurements may assist physicians in avoiding potentially unnecessary medical or interventional therapies, strain echocardiography has also the potential of predicting future overt ventricular dysfunction. However, this study remains only an indicator of the potential of these measurements and it still is too early to draw final conclusions. More longitudinal prospective studies that include all comers with PVCs are needed to bring this methodology to clinical practice in this patient population.

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