PERSPECTIVES IN CONTRAST

Empiric catheter ablation of premature ventricular contractions when there is a >20% burden in an asymptomatic patient with normal left ventricular size and function—An argument for a conservative, do-less approach

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Premature ventricular contractions (PVCs) are common. Historically they have been considered benign in the setting of a normal heart, with long-term prognosis in asymptomatic healthy subjects with frequent PVCs showing a similar long-term prognosis to that of a healthy U.S. population, without an increased risk of death.[1]

However, in some patients without structural heart disease PVCs may be a sign of early preclinical cardiomyopathy (arrhythmogenic right ventricular dysplasia, sarcoid), a cause of sudden cardiac death in PVC-induced ventricular fibrillation, or progressive left ventricle (LV) dysfunction with heart failure in the setting of PVC-induced cardiomyopathy.[2–11]

Research has focused on patient and PVC characteristics to help us differentiate high-risk features to help elucidate the more malignant phenotypes. High-risk patient features include male sex, obesity, and asymptomatic nature, while high-risk PVC features include PVC burden, PVC origin (epicardial), QRS width, PVC coupling interval, duration of occurrence, arrhythmogenic right ventricular dysplasia risk score, ABC-VT score, etc.[3,8,12–18] Most clinicians focus on PVC burden as the leading indicator of progression to cardiomyopathy, with a burden of equal to or greater than 24% suggesting increased risk and little or no risk seen at less than 10%.[15] However, it is important to recognize that there is no universal PVC burden cutoff value that is perfect, and case studies and data from the Cardiovascular Health Study suggest that even lower burdens than previously thought may contribute to cardiomyopathy.[19,20] The good news is catheter ablation has been the treatment of choice for elimination of PVCs, with high acute success rates approaching 80%–90% with low recurrence rates.[6,9,10,21–23]

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Should we perform catheter ablation in an asymptomatic patient without structural heart disease with elevated PVC burden?

The ideal treatment strategy in asymptomatic patients without structural heart disease remains unclear. Fear of progression to cardiomyopathy along with high success rates with catheter ablation lead clinicians to contemplate an aggressive approach with upfront ablation. Before one chooses the perceived "best" intervention, a few comments and questions must be considered: (1) The ideal situation in an asymptomatic patient would be an intervention that would carry little or no risk and have a high rate of curing a risk factor that has imminent progression to a potential irreversible disease. (2) Specifically, do the benefits of catheter ablation in asymptomatic patients (ie, preventing risk of progression to cardiomyopathy) outweigh the risks of the intervention? (3) If the outcome does occur, is it reversible? (4) We also need to assess the question of spontaneous resolution of PVCs with no intervention. Who would sign up for an intervention with any risk if the asymptomatic risk factor may resolve on its own?

Spontaneous PVC resolution and risk of progression to cardiomyopathy

There are very few longitudinal studies that follow the natural history of asymptomatic PVC patients without underlying heart disease to address long-term burden and outcomes (Table 1).

The landmark study by Kennedy and colleagues[1] followed 73 asymptomatic healthy patients with ventricular ectopy from 1973 to 1983. "Healthy" was determined by extensive noninvasive cardiologic examination, although

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KEY FINDINGS

- Minimally and asymptomatic patients with frequent premature ventricular contractions (PVCs) and normal left ventricle (LV) size and function have a significant rate of spontaneous resolution without treatment (up to 44%).
- The rate to overall progression to LV dysfunction (LV ejection fraction <50%) appears to be low at approximately 4%–5%; and of those patients who exhibit a reduction in LV ejection fraction <50%, most are asymptomatic, without signs or symptoms of clinical heart failure or cardiomyopathy.
- Although success rates are high for catheter ablation and complication rates are low, no treatment approach has zero risk, and any complication in asymptomatic patients, the overwhelming majority (≈95%) of whom will not progress to any clinical cardiomyopathy or will even resolve spontaneously, is tragic.
- A conservative approach with clinical surveillance without offering catheter ablation in asymptomatic patients with PVCs and normal LV size and function should be preferred.

coronary angiography of a subsample disclosed serious coronary artery disease in 19%. The mean frequency was 566 PVCs per hour (78–1994) and included couplets in 60% and nonsustained ventricular tachycardia (VT) in 26%. Mean follow-up was 6.5 years (3.0–9.5 years). Over this time period they had 2 deaths (1 sudden cardiac death and 1 cancer). Calculation of a standardized mortality ratio at the time of 448 person-years indicated that 7.4 deaths were expected. Overall the long-term prognosis was similar to that of the healthy U.S. population and suggested no increased risk of death despite the complex ventricular ectopy seen. This *New England Journal of Medicine* publication set the scene for reassuring patients with PVCs for decades.

Tsuji and colleagues[24] prospectively followed 163 children, mean age 8.9 (± 3.4) years without underlying heart disease and ventricular arrhythmias. They evaluated children with PVCs only (78 patients), PVCs including couplets (39 patients), and PVCs including runs of ventricular tachycardia (46 patients). The children were followed long term (71.7 ± 32.1 months in PVC, 65.9 ± 32.8 months PVCs including couplets, and 84 ± 31.9 in VT group). The overall PVC burden was an average of 10% ± 8.9%. In all groups they had complete resolution or disappearance in a significant portion. PVCs disappeared during the follow-up period in 22 of the 78 children (28%) in the PVC-only group. In the PVC-couplets group, couplets disappeared in 15 (38%) and overall PVCs disappeared in 9 (23%). In the 46 children in the VT group, VT disappeared in 30 (65%) and PVCs disappeared in 17 (37%). The mean time until the disappearance of PVCs in the 163 patients was estimated to be 115.2 ± 4.3 months.

Niwano and colleagues[25] prospectively followed 239 patients with frequent outflow tract PVC (>1000 beats/day) with normal LV function seen on echo and cardiac magnetic resonance imaging (MRI). The mean age was 43 years (± 13 years) and PVC burden was 12,289 (approximately 12%). During a mean follow-up of 5.6 (± 1.7) years there was no significant change in the mean LV ejection fraction (EF) and mean LV diastolic dimension (LVDD). There was a small population of patients (5.4%) that exhibited a subclinical decrease in LVEF and increase in LVDD without any clinical heart failure symptoms. The overwhelming majority of patients (95%) had no meaningful change in their EF or LVDD. In this cohort they did not report any cases of spontaneous resolution. Looking exclusively at minimally symptomatic or asymptomatic patients, they found no clinical events such as syncope, new-onset VT / ventricular fibrillation, or heart failure.

Perhaps the most striking research in this arena that assesses both spontaneous resolution and risk of cardiomyopathy progression comes from Lee and colleagues,[26] who prospectively evaluated 100 patients with a mean PVC burden of 18.4% and normal LV size and function for a median of 29.3 months not receiving intervention in the British Columbia PVC registry. They were followed with serial electrocardiography (ECG) monitoring and echocardiography. Patients also underwent cardiac MRI and any patients showing delayed gadolinium enhancement consistent with scar were excluded. The primary arrhythmic outcome was PVC resolution, defined as a reduction of burden to <1% per 24 hours. The primary nonarrhythmic outcome was reduction in LVEF <50% by echocardiography. The mean age was 51.8 ± 16.5 years and 57% were female. The most common symptom was palpitations. Incredibly, reduction of PVC burden spontaneously occurred in 44 of the 100 patients (44%), all without any intervention, with median time to PVC resolution of 15.4 months (2.6–64.3 months). No clinical predictors of spontaneous resolution were found, including the initial PVC burden. Of the 44% that showed spontaneous resolution, the majority sustained the resolution. Only 9 (20.5%) encountered subsequent increase in PVC burden ≥1%, and only 4 exhibited a burden >5%. Of the 100 total patients, only 4 (4%) developed left ventricular dysfunction (EF <50%). The median time to recorded LVEF <50% was 60.9 months (52.7–74.8 months). Of the 4 patients who developed LV dysfunction, only 1 developed clinical heart failure symptoms.

Complications of Catheter Ablation

Before consideration of any treatment option in asymptomatic patients, it is important to consider any potential risks, as any serious complication would be tragic. Catheter ablation risks will differ based on PVC location, with left-sided and epicardial locations having higher risk. Like most catheter ablation procedures, overall complication rate is

Table 1 Studies evaluating the natural history of asymptomatic premature ventricular contractions

Study	Patients (n)	Ventricular ectopy forms	Origin location	Burden	Follow-up, years (± years)	Spontaneous PVC resolution	Cardiomyopathy (%)	Comments
Kennedy et al 1985	73	Isolated PVC, couplets, and NSVT	All	566/h (78–1994)	6.5 (±1.8)	Not reported	1 (1.4%) report of CHF	Overall the long-term prognosis was similar to that of the healthy U.S. population and suggested no increased risk of death despite the complex ventricular ectopy seen.
Tsuji et al 1995	163	Isolated PVC, couplets, and NSVT	All	10% (± 8.9%)	6.0 (± 2.7)	28% of isolated PVC group 23% PVC couplet group 37% PVC/VT group	0%	Followed children with 3 groups of PVC forms. In all groups they had complete resolution or disappearance in a significant portion.
Niwano et al 2009	239	Isolated PVC, couplets, and NSVT	Outflow tract	>1000 beats/day	5.6 (± 1.7)	Not reported	5.4% exhibited a subclinical decrease in LVEF and increase in LVDD without any CHF	During a mean follow up of 5.6 (± 1.7) years there was no significant change in the mean LVEF and mean LV diastolic dimension (LVDD). The overwhelming majority of patients (95%) had no meaningful change in their EF or LVDD.
Lee et al 2019	100	Not reported	All	18.4% (range 5.4%–49.8%)	2.42	44%	4%	No clinical predictors of spontaneous resolution were found, including the initial PVC burden. Of the 44% that showed spontaneous resolution the majority sustained the resolution. Only 1 of the 4 patients with a change in LVEF was below 40%.

CHF = congestive heart failure; EF = ejection fraction; LVDD = left ventricular diastolic dimension; LVEF = left ventricular ejection fraction; NSVT = nonsustained ventricular tachycardia; PVC = premature ventricular contraction; VT = ventricular tachycardia.

reported at approximately 5%, with major complications around 3%.[9,21] Groin access sites continue to be the highest offender, with pseudoaneurysm and arteriovenous fistula attributing for more than half of the complications. However, more severe complications, including death, tamponade requiring pericardiocentesis or surgical repair, coronary artery injury and myocardial infarction, valve injury, and stroke, may also occur at less than 1%. Recent concern for brain microemboli from left-sided LV ablations have also been reported. Whitman and colleagues[27] demonstrated that pre and post brain MRI showed 58% of left-sided LV ablations had demonstration of microembolic infarcts within a week of ablation. Of course, the clinical significance of these lesions is unknown, and it is critical that future studies determine if any long-term consequences result. However, I think we can all agree most of us would rather not have these findings post ablation.

PVC-induced cardiomyopathy prognosis

The overall prognosis in these patients who do develop cardiomyopathy is good, as catheter ablation has a high acute success rate.[8,9,14,21,25,28] Successful catheter ablation and elimination of the PVCs restores LV function and restores normal LV dimensions in most patients within 4–6 months.[11,29] For these reasons PVC-induced cardiomyopathy has largely been considered a favorable and highly reversible cardiomyopathy.

Clinical surveillance if no intervention is pursued

At the minimum, patients should be seen in clinic annually and screened for PVC and heart failure symptoms. Annual ECG monitoring for PVC burden and echocardiograms to evaluate for LV dilatation and EF should also be performed. If there is any concern for LV dilatation or reduction in EF, a conservative approach should no longer be entertained.

Symptoms arise or concern for PVC-induced cardiomyopathy

If symptoms arise during active surveillance or if there is concern for PVC-induced cardiomyopathy, then a treatment strategy with catheter ablation or pharmacotherapy can be pursued. Catheter ablation has been the treatment of choice for elimination of PVCs, with high acute success rates approaching 80%–90% and low recurrence rates.[6,9,10,21–23] In patients who wish not to pursue catheter ablation, the use of beta-blockers or L-type calcium channel blockers can alleviate symptoms and provide a reduction in PVC burden of about 10%–24%.[6,14,30] Class IC agents have shown effective suppression of PVCs in patients refractory to ablation, leading to LVEF recovery in the majority of patients suspected of having PVC-induced cardiomyopathy.[31]

In situations where the diagnosis of PVC-induced cardiomyopathy is unclear, some centers offer a trial of PVC suppression with antiarrhythmic agents such as flecainide or amiodarone short term, as these can not only help alleviate symptoms but can help restore cardiac function by PVC suppression and help solidify the diagnosis of PVC-induced cardiomyopathy before proceeding with catheter ablation.

Summary recommendations

The data show that in minimally and asymptomatic patients with frequent PVCs and normal LV size and function the rate of spontaneous resolution is common (up to 44%) and the rate to overall progression to LV dysfunction (LVEF $<50\%$) appears to be low, at approximately 4%–5%. Of these patients who exhibit a reduction in LVEF $<50\%$, most are asymptomatic, without signs or symptoms of clinical heart failure or cardiomyopathy. Although success rates are high for catheter ablation and complication rates are low, no treatment approach has zero risk, and any complication in asymptomatic patients, of whom the overwhelming majority ($\approx 95\%$) will not progress to any clinical cardiomyopathy or will even resolve spontaneously, is tragic.

A conservative approach with clinical surveillance without offering catheter ablation in asymptomatic patients with PVCs and normal LV size and function should be preferred. If a more robust risk stratification existed, then early intervention may make sense and further investigation to identify the low percentage (4%–5%) that develop cardiomyopathy is needed. One also cannot underestimate the need for long-term registry outcome data, as most of the data are from small patient series.

Conclusion

The management of asymptomatic PVCs in patients with normal LV size and function with high PVC burden remains controversial and the optimal treatment strategy remains unknown. Patients should be screened for high-risk ECG features and prognosis and treatment options should be discussed. Asymptomatic patients without structural heart disease with high PVC burdens have a low risk of progression to cardiomyopathy, and a significant amount will resolve spontaneously. If concern for cardiomyopathy arises, then catheter ablation has been proven effective at elimination of PVCs and reversing the cardiomyopathy in the majority of patients. Given these factors, a conservative approach without offering upfront catheter ablation is preferred with clinical surveillance in these asymptomatic patients.

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