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.

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.

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. 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%. 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.

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.

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 (i.e., 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 followed 73 asymptomatic healthy patients with ventricular ectopy from 1973 to 1983. “Healthy” was determined by extensive noninvasive cardiologic examination, although...
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.

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.

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.

Tsui and colleagues 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 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, 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 | 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 pseudoaneurism 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 colleagues27 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.8,6,14,21,25,28 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 fleca-
References

1. Kennedy HL, Whitlock JA, Sprague MK, Kennedy LJ, Buckingham TA, Goldberg RJ. Long-term follow-up of asymptomatic healthy subjects with frequent and complex ventricular ectopy. N Engl J Med 1985;312:193–197.

2. Haissaguerre M, Shah DC, Jais P, et al. Role of Purkinje conducting system in triggering of idiopathic ventricular fibrillation. Lancet 2002;359:677–678.

3. Hoffmayer KS, Bhave PD, Marcus GM, et al. An electrocardiographic scoring system for distinguishing right ventricular outflow tract arrhythmias in patients with arhythmogenic right ventricular cardiomyopathy from patients with idiopathic tachycardia. Heart Rhythm 2013;10:477–482.

4. Haissaguerre M, Shoda M, Jais P, et al. Mapping and ablation of idiopathic ventricular fibrillation. Circulation 2002;106:962–967.

5. Knecht S, Sacher F, Wright M, et al. Long-term follow-up of idiopathic ventricular fibrillation ablation: a multicenter study. J Am Coll Cardiol 2009;54:522–528.

6. Marcus GM. Evaluation and management of premature ventricular complexes. Circulation 2020;141:1404–1418.

7. Nogami A, Sugiyasu A, Kubota S, Kato K. Mapping and ablation of idiopathic ventricular fibrillation from the Purkinje system. Heart Rhythm 2005;2:646–649.

8. Latchamsetty R, Bogun F. Premature ventricular complexes and premature ventricular complex induced cardiomyopathy. Curr Probl Cardiol 2015;40:379–422.

9. Luebbert J, Auberson D, Marchlinski F. Premature ventricular complexes in apparently normal hearts. Card Electrophysiol Clin 2016;8:503–514.

10. Hoffmayer KS, Gerstenfeld EP. Diagnosis and management of idiopathic ventricular tachycardia. Curr Probl Cardiol 2013;38:131–158.

11. Bogun F, Crawford T, Reich S, et al. Radiofrequency ablation of frequent, idiopathic premature ventricular complexes: comparison with a control group without intervention. Heart Rhythm 2007;4:863–867.

12. Hoffmayer KS, Machado ON, Marcus GM, et al. Electrocardiographic comparison of ventricular arrhythmias in patients with arhythmogenic right ventricular cardiomyopathy and right ventricular outflow tract tachycardia. J Am Coll Cardiol 2011;58:831–838.

13. Voskoboinik A, Hadjas A, Alhede C, et al. Predictors of adverse outcome in patients with frequent premature ventricular complexes: The ABC-VT risk score. Heart Rhythm 2020;17:1066–1074.

14. Latchamsetty R, Bogun F. Premature ventricular complex-induced cardiomyopathy. JACC Clin Electrophysiol 2019;5:537–550.

15. Baman TS, Lange DC, Ilg KJ, et al. Relationship between burden of premature ventricular complexes and left ventricular function. Heart Rhythm 2010;7:865–869.

16. Del Carpio Munoz F, Syed FF, Noheria A, et al. Characteristics of premature ventricular complexes as correlates of reduced left ventricular systolic function: study of the burden, duration, coupling interval, morphology and site of origin of PVCs. J Cardiovasc Electrophysiol 2011;22:791–798.

17. Kawamura M, Badhwar N, Vedantham V, et al. Coupling interval dispersion and body mass index are independent predictors of idiopathic premature ventricular complex-induced cardiomyopathy. J Cardiovasc Electrophysiol 2014;25:756–762.

18. Yokokawa M, Kim HM, Good E, et al. Relation of symptoms and symptom duration to premature ventricular complex-induced cardiomyopathy. Heart Rhythm 2012;9:92–99.

19. Dukes JW, Dewland TA, Vittinghoff E, et al. Ventricular ectopy as a predictor of heart failure and death. J Am Coll Cardiol 2015;66:101–109.

20. Shanmugam N, Chua TP, Ward D. ‘Frequent’ ventricular bigeminy—a reversible cause of dilated cardiomyopathy. How frequent is ‘frequent’? Eur J Heart Fail 2006;8:869–873.

21. Latchamsetty R, Yokokawa M, Morady F, et al. Multicenter outcomes for catheter ablation of idiopathic premature ventricular complexes. JACC Clin Electrophysiol 2015;1:116–123.

22. Lee D, Hoffmayer KS, Iusu JC, et al. Long-term mode and timing of premature ventricular complex recurrence following successful catheter ablation. J Interv Card Electrophysiol 2019;53:153–160.

23. Zhong L, Lee YH, Huang XM, et al. Relative efficacy of catheter ablation vs antiarrhythmic drugs in treating premature ventricular contractions: a single-center retrospective study. Heart Rhythm 2014;11:187–193.

24. Tsuji A, Nagashima M, Hasegawa S, et al. Long-term follow-up of idiopathic ventricular arrhythmias in otherwise normal children. Jpn Circ J 1995;59:654–662.

25. Niwano S, Wakisaka Y, Niwano H, et al. Prognostic significance of frequent premature ventricular contractions originating from the ventricular outflow tract in patients with normal left ventricular function. Heart 2009;95:1230–1237.

26. Lee AKY, Andread J, Hawkins NM, et al. Outcomes of untreated frequent premature ventricular complexes with normal left ventricular function. Heart 2019;105:1408–1413.

27. Whitman IR, Gladstone RA, Badhwar N, et al. Brain emboli after left ventricular endocardial ablation. Circulation 2017;135:867–877.

28. Gopinathannair R, Etheridge SP, Marchlinski FE, Spinale FG, Lakkireddy D, Olshansky B. Arrhythmia-induced cardiomyopathies: mechanisms, recognition, and management. J Am Coll Cardiol 2015;66:1714–1728.

29. Yokokawa M, Good E, Crawford T, et al. Recovery from left ventricular dysfunction after ablation of frequent premature ventricular complexes. Heart Rhythm 2013;10:172–175.

30. Krittayaphong R, Bhuripanyo K, Punlee K, Kangkagate C, Chaithirapan S. Effect of atenolol on symptomatic ventricular arrhythmia without structural heart disease: a randomized placebo-controlled study. Am Heart J 2002;144:e10.

31. Hyman MC, Mustin D, Supple G, et al. Class IC antiarrhythmic drugs for suspected premature ventricular contraction-induced cardiomyopathy. Heart Rhythm 2018;15:159–163.