Short or Long-Coupled Idiopathic Ventricular Fibrillation: Does the Coupling Interval Really Matter?

Bernard Belhassen[1] and Oholi Tovia-Brodie[2]

[1]Hadassah Medical Center
[2]Shaare Zedek Medical Center

January 22, 2023

Abstract

I am not sure this editorial comment deserves an abstract. Plesae advise.

EDITORIAL COMMENT

Short or Long-Coupled Idiopathic Ventricular Fibrillation:

Does the Coupling Interval Really Matter?

Bernard Belhassen MD[a,b] and Oholi Tovia-Brodie, MD[c]

From the [a]Heart Institute, Hadassah Medical Center, Jerusalem, Israel [b]Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel [c]Jesselson Integrated Heart Center, Shaare Zedek Medical Center, Jerusalem, Israel

Text: 1317 words References: 12

None of the authors has a conflict of interest to declare

Address for correspondence:

Bernard Belhassen, MD Heart Institute, Hadassah Medical Center, Kyriat Hadassah, PO Box 12000, 91120, Jerusalem, Israel

Email: bblhass@gmail.com, bblhass@hadassah.org.il Telephone: 972.3.52.426.6856 Fax: 972.153.52.426.6856

Idiopathic ventricular fibrillation (IVF) is responsible for approximately 5-7% of cases of aborted cardiac arrest (1). Multiple case reports and series published during the last 70 years have shown that short-coupled premature ventricular complexes (SCPVCs) (coupling interval < 350ms) usually precede the onset of VF in these patients (1-4). In a recent review, however, we found that PVCs with "not-so-short" coupling intervals (> 350 ms) preceded VF onset in 15 (17.4%) of 86 patients (1). Coupling intervals ranging from 400 to 450ms were found in 5 patients. Two of these patients had their arrhythmias originating from the right ventricular outflow tract while the arrhythmias originated from the left posterior fascicle, the left anterior fascicle and presumably the right ventricular moderator band in 1 patient each (1).

In the present issue of the Journal, Surget and associates reviewed the data from 5 French arrhythmia referral centers including 79 consecutive patients with IVF (5). Among these patients, 12 (15.2%) had documented late-coupled PVCs (LCPVCs) defined as PVCs falling after the end of the T wave, with a normal QTc interval. Sustained polymorphic ventricular tachycardia (PVT)/VF initiation by LCPVCs was documented only in 1 of the 12 patients, whereas nonsustained (NS) PVT, couplets or single PVCs were documented

in 8, 2 and 1 patients, respectively. In 10 of 12 patients, PVCs were recorded showing both long and short coupling intervals of 418±46 ms and 304±33 ms, respectively.

The authors should be commended for reporting these results and especially the ECG tracings documenting these LCPVCs. We would like to bring the following comments:

1) While the vulnerable period of the T wave has been involved in most initiations of IVF, this study showed that LCPVCs initiating repetitive PVCs or sustained VF had coupling intervals ranging from 360 to 500mg, including 9 having LCPVCs > 400ms and 2 who had LCPVCs of 500ms. In other words, the PVC falls after the end of the T wave as attested by a coupling interval/QT ratio longer than 1 in all patients. Although such VF initiation may look surprising, the electrophysiologic recordings during LCPVC provided by the authors in 2 patients enable a comprehensive understanding of the underlying mechanism which involved the Purkinje system in both cases. Two types were identified: a) Type 1: an early Purkinje activity is conducted to the ventricle with a long delay; b) Type 2: a late Purkinje activity is conducted with no delay to the ventricle. A review of 10 additional cases of the literature of LCPVCs in which electrophysiologic study was performed confirmed that their mechanism was either of type 1 (n=4), or type 2 (n=5), or both types (n=1) (unpublished data).

2) The definition of LCPVC used in the present paper (PVCs falling after the end of the T wave) is different from that adopted by us (1) and Groeneveld et al. (6) (initial PVC having a coupling interval> 350ms). The latter definition was indirectly based on the definition of short-coupled IVF (SCIVF) (coupling interval <350ms) made by Steinberg et al. (7). Their new definition may be a simpler practical diagnostic tool, and mostly more accurate than that the one currently used, especially in case of sinus tachycardia. For example, a PVC having a coupling interval of 320ms may have less clinical significance when the sinus cycle length is 600ms than when it is 800ms. Harmonization and optimization of the cut-off coupling interval for defining long and SCIVF is needed for future studies on the topic.

3) In contrast to the IVF Dutch Registry where only 6 (19.3%) of their 31 patients with SCIVF had LCPVCs (6), 7 (70%) of the 10 patients with SCIVF in the present study also had LCPVC. In addition, when both short and LCPVCs were recorded in an individual, they presented a different morphology in most cases which indicates a different ventricular exit.

In a multicenter study (58 centers and 1 multicenter, 22 countries) we are presently conducting, which involves 287 IVF patients in whom arrhythmia onset was documented in 231 patients, 72 (31.2%) of the study patients showed a LCPVC initiating PVT/VF (single or couplets LCPVCs were not accounted). Interestingly, 30 of these 72 patients also had SCPVCs initiating VF, as found by Surget al. in their study (5).

4) In the present study, the authors found that 92% of LCPVCs were found to originate from the left Purkinje system. In our review, we found that in patients with long-coupled PVT/VF, there was a tendency for higher incidence of Purkinje ectopy origin in the left ventricle (1). Whether this is related to the complexity the left multifascicular fiber network following the division of the left bundle branch block has not been established.

4) In a previous study involving 83 consecutive patients with Purkinje-initiated IVF from 4 arrhythmia referral centers, Surget and coworkers (9) found that Purkinje extrasystoles triggering idiopathic VF originate predominantly from the right ventricle in men and from the left ventricle or both ventricles in women. Although not specifically indicated, that study mainly included patients with SCIVF.

In the present study mainly dealing with LCPVC (n=12), 7 (64%) of the 11 patients with Purkinje ectopy triggering NSPVT were females and in all these 7 patients the left Purkinje system was involved. Triggered activities—as early afterdepolarization or delayed afterdepolarization— are the main mechanisms of Purkinje ectopy and well known to be increased by estradiol (9). This may explain some increase in female prevalence. However, their predominance in the left Purkinje system in women is unclear.

5) Idiopathic fascicular PVCs mainly originating in the left anterior and posterior fascicles have been reported in Chinese patients (10,11). These arrhythmias almost always consisted of single LCPVCs. They can be ablated at usual left anterior and posterior fascicles but also in the right coronary cusp for left anterior

fascicular arrhythmias. Although one may suspect that such arrhythmias represent the initial manifestation of malignant Purkinjopathy, their presence has not been reported in patients who later suffered from syncopal events or PVT/VF. In addition, in the Chinese series, no case of syncope or sudden death has been observed before or after ablation of the arrhythmias (10,11). Therefore, we do recommend patient reassurance policy in asymptomatic or mildly symptomatic patients (i.e., palpitations) displaying these arrhythmias after extensive work-up including repeat 12 leads ECG Holter and maybe pharmacologic drug testing as recommended by the Bordeaux group (12). In contrast, if such arrhythmias are documented in a patient who suffered one or more "true syncopal" events, extensive work-up should be performed with high suspicion that the syncope might be related to aborted malignant tachyarrhythmias. Fortunately, we have never observed such cases in our experience.

Study limitation. A limitation of the current study is that sustained PVT/VF initiation by LCPVCs was documented only in 1 of the 12 patients, whereas NSPVT, couplets or only single PVCs were documented in 8, 2 and 1 patients, respectively. Hence, the mechanistic and causal relationship between LCPVCs and VF initiation remains to be further elucidated. Albeit, this study provides further validation to the results of the review, making it clear that not all LCPVCs are benign.

Conclusion. Documentation of SCPVCs in a VF patient who has normal ECG and no structural heart disease, after exclusion of other types of inherited arrhythmias, should highly suggest the diagnosis of IVF and an arrhythmia origin in the Purkinje system. We believe that the present study as well as the results of our review (1) should lead to the same conclusion in case of LCPVCs, especially those suggesting a left Purkinje origin. In other words, the value of the coupling interval should not matter when VF is documented in the presence of normal heart. Both "short-coupled" and "long-coupled" PVT/VF likely represent "Purkinje arrhythmias" in the setting of "Purkinjopathy" (8) that may be treated with ablation or quinidine (1). Further characterization of these LCPVCs in a larger patient cohort in attempt to identify markers of malignant arrhythmias is needed.

REFERENCES

1. Belhassen B, Tovia-Brodie O. Short-Coupled Idiopathic Ventricular Fibrillation. A literature review with extended follow-up. *JACC Clin Electrophysiol* . 2022;8:918-936.

2. Leenhardt A, Glaser E, Burguera M, Nürnberg M, Maison-Blanche P, Coumel P. Short-coupled variant of torsade de pointes. A new electrocardiographic entity in the spectrum of idiopathic ventricular tachyarrhythmias. *Circulation* . 1994;89:206-15.

3. Viskin S, Lesh MD, Eldar M, Fish R, Setbon I, Laniado S, Belhassen B. Mode of onset of malignant ventricular arrhythmias in idiopathic ventricular fibrillation. *J Cardiovasc Electrophysiol.*1997;8:1115-20.

4. Haïssaguerre M, Shoda M, Jaïs P, Nogami A, Shah DC, Kautzner J, Arentz T, Kalushe D, Lamaison D, Griffith M, Cruz F, de Paola A, Gaïta F, Hocini M, Garrigue S, Macle L, Weerasooriya R, Clémenty J. Mapping and ablation of idiopathic ventricular fibrillation. *Circulation.*2002;106:962-7.

5. Surget et al. Idiopathic ventricular fibrillation associated with long-coupled Purkinje ectopy. *J Cardiovasc Electrophysiol*XXXXXXXXXXXXXX

6. Groeneveld SA, van der Ree MH, Mulder BA, Balt J, Wilde AAM, Postema PG, Hassink RJ. Prevalence of short-coupled ventricular fibrillation in a large cohort of Dutch patients with idiopathic ventricular fibrillation. *Circulation* . 2022;145:1437-1439.

7. Steinberg C, Davies B, Mellor G, Tadros R, Laksman ZW, Roberts JD, Green M, Alqarawi W, Angaran P, Healey J, Sanatani S, Leather R, Seifer C, Fournier A, Duff H, Gardner M, McIntyre C, Hamilton R, Simpson CS, Krahn AD. Short-coupled ventricular fibrillation represents a distinct phenotype among latent causes of unexplained cardiac arrest: a report from the CASPER registry. *Eur Heart* J. 2021;42:2827-38.

8. Haïssaguerre M, Duchateau J, Dubois R, Hocini M, Cheniti G, Sacher F, Lavergne T, Probst V, Surget E, Vigmond E, Welte N, Chauvel R, Derval N, Pambrun T, Jais P, Nademanee W, Bernus O. Idiopathic

ventricular fibrillation: role of Purkinje system and microstructural myocardial abnormalities. *JACC Clin Electrophysiol* . 2020;6:591-608.

9. Surget E, Cheniti G, Ramirez FD, Leenhardt A, Nogami A, Gandjbakhch E, Extramiana F, Hidden-Lucet F, Pillois X, Benoist D, Krisai P, Nakatani Y, Nakashima T, Takagi T, Kamakura T, André C, Welte N, Chauvel R, Tixier R, Duchateau J, Pambrun T, Derval N, Jaïs P, Sacher F, Bernus O, Hocini M, Haïssaguerre M. Sex differences in the origin of Purkinje ectopy-initiated idiopathic ventricular fibrillation. *Heart Rhythm* . 2021;18:1647-54.

10. Zhang J, Tang C, Zhang Y, Su X. Catheter ablation of premature ventricular complexes arising arising from the left fascicular system. *Heart Rhythm* . 2019 ;16:527-535.

11. Chen S, Lu X, Peng S, Xue Y, Zhou G, Ling Z, Wei Y, Yang K, Fu W, Cai L, Xu J, Ouyang F, Liu S. Ablation at right coronary cusp as an alternative and favorable approach to eliminate premature ventricular complexes originating from the proximal left anterior fascicle.

Circ Arrhythm Electrophysiol . 2020;13:e008173.

12. Escande W, Gourraud JB, Haissaguerre M, Gandjbakhch E, Lavergne T, Martins R, Cheniti G, Krisai P, Hermida JS, Maury P, Merino JL, Pasquié JL, Combes N, Surget E, Duchateau J, Pambrun T, Derval N, Hocini M, Jaïs P, Postema PG, Nademanee K, Vigmond E, Bernus O, Sacher F, Probst V. Malignant Purkinje ectopy induced by sodium channel blockers.*Heart Rhythm* . 2022:19:1595-1603.