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RESEARCH LETTER

Prevalence of Short-Coupled Ventricular Fibrillation in a Large Cohort of Dutch Patients With Idiopathic Ventricular Fibrillation

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In patients with idiopathic ventricular fibrillation (IVF), the cause of ventricular fibrillation (VF) remains unknown after extensive diagnostic testing. With increased knowledge, several disease entities have been identified during the past decades resulting in targeted treatment options.

In a recent article from Canada,[1] a specific IVF subtype was described and referred to as short-coupled IVF (SCVF), resembling earlier reports[2] and also known as short-coupled variant of torsade de pointes. The correct terminology is still a matter of debate. Because we report on patients with IVF, we adhere to SCVF. In patients with SCVF, short-coupled premature ventricular complexes (PVCs) with a coupling interval <350 ms initiate polymorphic ventricular tachycardia/VF. SCVF is malignant with frequent arrhythmia recurrences. SCVF prevalence of only 6.6% was reported in the Canadian IVF cohort. However, data on the percentage of patients with documentation of the VF onset was not provided. We aimed to investigate the prevalence and the SCVF phenotype in our Dutch IVF registry (Figure).

Patients were included in our IVF registry after cardiac arrest, with documented VF, when no cause was identified after comprehensive assessment.[3] We assessed SCVF by retrospectively reviewing telemetry, Holter, ECG, and implantable cardioverter defibrillator interrogations, using the proposed definition of VF or polymorphic ventricular tachycardia/VF initiated by a PVC with a coupling interval <350 ms.[1] As by IVF definition, patients with QTc prolongation, pause-dependent torsades, structural heart disease, or primary electrical disorders were excluded. The study data are available from the corresponding author on reasonable request. The study was approved by the institutional review committee and the subjects gave informed consent. Comparisons between continuous variables were performed by using independent sample *t* test or Mann-Whitney *U* test; categorical variables were compared using the Fisher exact test; and incidence rates were compared using an exact Poisson test.

In total, 228 patients with IVF were included. Median follow-up duration was 6.4 (interquartile range, 2.6–12.5) years. Altogether, 57 of 228 (25%) patients experienced VF recurrence (including 9 during hospitalization and 48 during follow-up). In 34 of 57 (60%) of these patients, the initiation of VF was documented. It is important to note that, in 31 of 34 (91%) patients with documented VF onset, the arrhythmia was triggered by a short-coupled PVC, resulting in an SCVF prevalence of 14% (31/228) for the entire cohort and 91% (31/34) for those with documented arrhythmia initiation. There were no significant differences between patients with SCVF and patients with IVF regarding age (51±10 versus 53±17 years) or sex distribution (55% versus 60% male). The occurrence of the *DPP6* IVF haplotype[4] was higher in patients with SCVF than in patients with IVF (n=15 [48%] versus n=15 [8%], $P<0.0001$). The median VF-initiating coupling interval in patients with SCVF was 288 ms (interquartile range, 251–316). Patients with SCVF showed a higher

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Nonstandard Abbreviations and Acronyms

IVF	idiopathic ventricular fibrillation
PVCs	premature ventricular complexes
SCVF	short-coupled idiopathic ventricular fibrillation
VF	ventricular fibrillation

shock burden (median 8 versus 3 shocks in patients with at least 1 recurrence, $P<0.0001$) and a higher incidence of electrical storm (32% versus 4%, $P<0.0001$) than in patients with IVF. Quinidine was frequently prescribed to patients with SCVF (n=19/31 [61%]; median dose, 733 mg). The incidence of VF recurrence on-quinidine was significantly lower than off-quinidine (0.1 versus 1.2 event/y, $P<0.0001$). Quinidine was effective in patients with and without *DPP6*. Six patients with SCVF also had VF episodes initiated by PVCs with a coupling interval >350 ms. In only 3 patients, VF-initiating PVCs always had a coupling interval >350 ms (range, 360–560).

In this article, we report a high prevalence of SCVF, of 91% for patients with IVF with documented arrhythmia onset and 14% for the entire IVF cohort. We confirm the malignant phenotype of this subset of patients with IVF. A limitation of the proposed definition for SCVF is the arbitrary and circular-thinking nature of the description. First, our data confirm that SCVF is a distinct phenotype in IVF, but we believe that it is too early to recognize SCVF as a distinct primary arrhythmia syndrome. One could argue that if the vast majority (91%) of documented VF recurrences have short-coupled initiations, then SCVF might not be a subtype of IVF but rather the common phenotype in true IVF. Furthermore, in our cohort, we found patients with IVF with both short and longer VF-initiating coupling intervals. Because the cutoff value for SCVF is debatable, it is unclear if these patients should be classified as patients who have

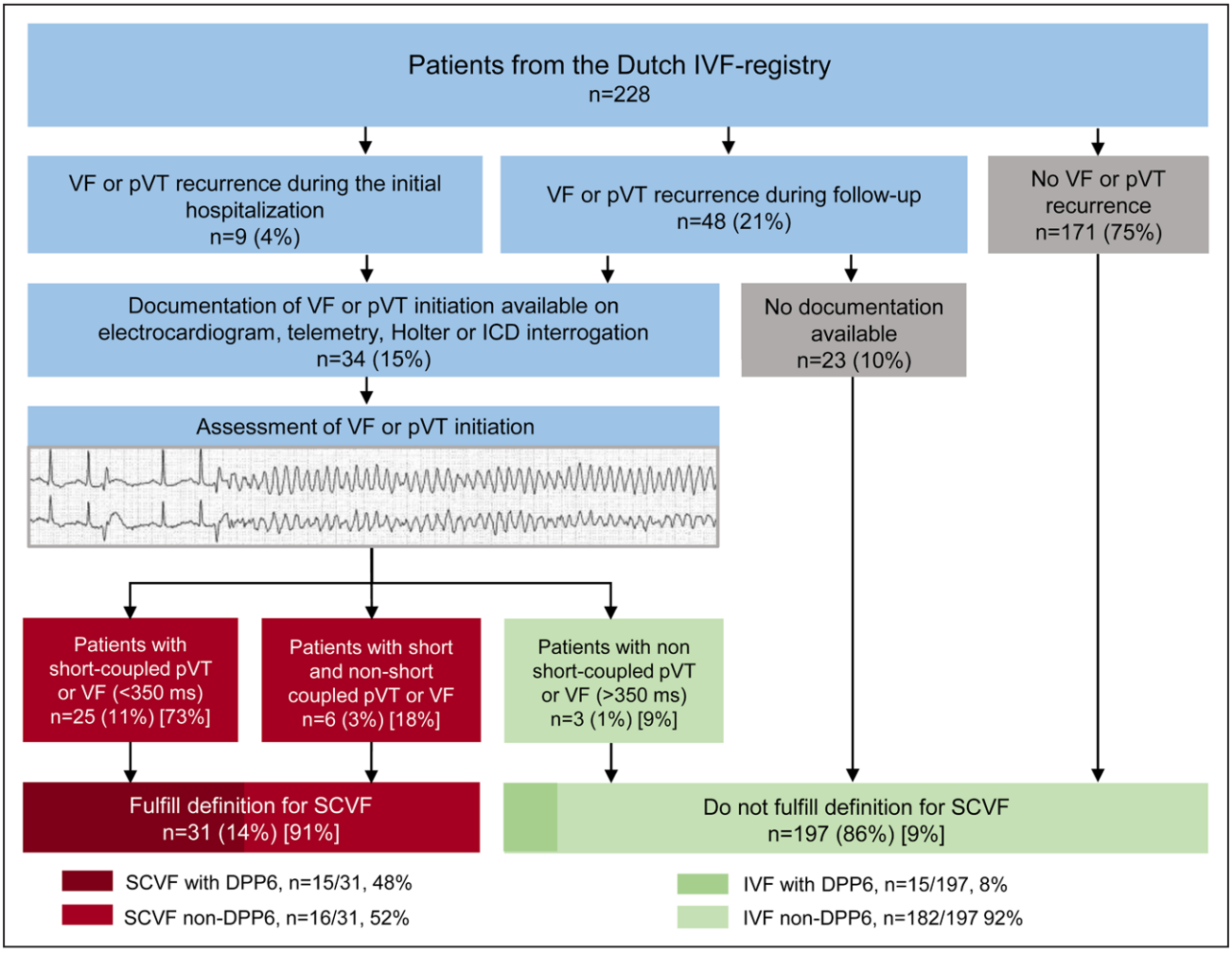

Figure. Flowchart of the diagnostic assessment for SCVF (see text for explanation).
Parentheses show percentages for the entire cohort (n=228) and square brackets show percentages for those with documented initiations of VF (n=34). *DPP6* indicates *DPP6* IVF risk-haplotype (a genetic subset of patients with IVF who have arrhythmias initiated by short-coupled PVCs); ICD, implantable cardioverter defibrillator; IVF, idiopathic ventricular fibrillation; PVC; premature ventricular complex; pVT, polymorphic VT; SCVF, short coupled ventricular fibrillation; VF, ventricular fibrillation; and VT, ventricular tachycardia.

IVF or who have SCVF.[5] Second, the SCVF diagnosis is fully dependent on documenting initiating PVCs. For this reason, SCVF can only be diagnosed in patients with arrhythmia recurrences, because the initiation of VF during the index event is typically not documented, potentially introducing bias toward a more malignant phenotype. Last, in The Netherlands, a hereditary subset of patients who have IVF with arrhythmias initiated by short-coupled PVCs exists (the *DPP6*-haplotype),[4] which contributes to our higher SCVF prevalence. The appropriate terminology for arrhythmias triggered by short-coupled PVCs also remains unsettled because different terms are used interchangeably.

To conclude, our data confirm that short-coupled idiopathic ventricular fibrillation (SCVF) is a malignant phenotype but also indicates that its prevalence may be higher than recently reported, depending on the study population, the cutoff value for SCVF, and the availability of VF documentation. As such, the incidence, underlying mechanisms, heritability, and SCVF treatment require further scrutiny. Because quinidine and verapamil have been reported to be effective in SCVF, a future randomized trial is needed to evaluate these findings.

ARTICLE INFORMATION

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Disclosures

None.

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