Objectives
This multicenter study sought to evaluate the long-term follow-up of patients ablated for idiopathic ventricular fibrillation (VF).

Background
Catheter ablation of idiopathic VF that targets ventricular premature beat (VPB) triggers has been shown to prevent VF recurrences on short-term follow-up.

Methods
From January 2000, 38 consecutive patients from 6 different centers underwent ablation of primary idiopathic VF initiated by short coupled VPB. All patients had experienced at least 1 documented VF, with 87% having experienced ≥2 VF episodes in the preceding year. Catheter ablation was guided by activation mapping of VPBs or pace mapping during sinus rhythm.

Results
There were 38 patients (21 men) age 42 ± 13 years, refractory to a median of 2 antiarrhythmic drugs. Triggering VPBs originated from the right (n = 16), the left (n = 14), or both (n = 3) Purkinje systems and from the myocardium (n = 5). During a median post-procedural follow-up of 63 months, 7 (18%) of 38 patients experienced VF recurrence at a median of 4 months. Five of these 7 patients underwent repeat ablation without VF recurrence. Survival free of VF was predicted only by transient bundle-branch block in the originating ventricle during the electrophysiological study (p = 0.0001). The number of significant events (confirmed VF or aborted sudden death) was reduced from 4 (interquartile range 3 to 9) before to 0 (interquartile range 0 to 4) after ablation (p = 0.01).

Conclusions
Ablation for idiopathic VF that targets short coupled VPB triggers is associated with a long-term freedom from VF recurrence. (J Am Coll Cardiol 2009;54:522–8) © 2009 by the American College of Cardiology Foundation

Ventricular fibrillation (VF) is the main cause of sudden cardiac death, which is responsible for approximately 300,000 deaths in U.S. alone (1). Although most of these deaths are associated with identifiable causes such as ischemic heart disease and cardiomyopathy (2), idiopathic VF still accounts for up to 8% of victims of sudden cardiac death (3) and represents a major health care issue.

The gold standard treatment for either primary or secondary prevention of VF is the insertion of an implantable cardiac-defibrillator (ICD) (2,4–7). However, although an ICD can deliver life-saving therapy at the time of an event, it does not prevent the event from occurring. Previous experimental and clinical studies have demonstrated the
The procedural end point was abolition of the culprit ventricular premature beat (VPB). Ablation targeting specific Purkinje potentials that precede the culprit VPB has shown encouraging short-term results (9–12,15). However, the long-term outcomes of patients after VF ablation are still unknown. Therefore, we sought to evaluate the long-term effect of targeted ablation of triggering VPB in patients with VF.

**Methods**

**Study population.** From January 2000, 38 consecutive patients from 6 centers underwent attempted ablation of primary idiopathic VF. Only patients with primary idiopathic VF without preceding monomorphic ventricular tachycardia were included. Patients were recruited if they had experienced at least 1 significant event (either syncope, electrical storm, documented VF, or aborted sudden cardiac death) with documented VPB-triggered VF on a 12-lead electrocardiogram (ECG). The definition of idiopathic VF was based on established criteria, including a normal physical examination and ECG, echocardiography, and right and left ventricular ejection fraction in all patients (16). Structural heart disease, myocardial ischemia, and catecholaminergic ventricular tachycardia (VT) were excluded by clinical history, Holter monitoring, exercise testing, coronary angiography, and infusion of isoproterenol and/or adrenaline in all patients as previously described (9). Furthermore, endomyocardial biopsy was performed in 8 patients and egonovine infusion in 7 patients. Abnormalities of ventricular repolarization were excluded in all patients based upon a corrected QT interval between 340 and 440 ms and the absence of QT prolongation after a pause by use of the Bazett formula. Brugada syndrome was excluded by normal QRS complexes in V$_1$ to V$_3$ leads in all ECGs before and after cardiac arrest and during oral or intravenous class IC drug administration in 24 patients. Channelopathies were excluded by genetic testing in 14 patients.

**Electrophysiological study.** We attempted to perform an invasive electrophysiology study during electrical storm. If this was not possible, patients were studied soon afterward or at a time of frequent VPBs. Multielectrode catheters (2 to 4) were introduced percutaneously through the femoral veins, including a 4-mm tip ablation catheter (Biosense Webster, Diamond Bar, California). Surface ECG leads and bipolar intracardiac electrograms filtered at 30 to 500 Hz were recorded simultaneously with a polygraph (model Lab system or Mias, 1- to 4-kHz and 10-kHz sampling rate, respectively, or Bard Electrophysiology, Lowell, Massachusetts) for off-line analysis. When left ventricular access was required, it was obtained by the transeptal or retrograde aortic method. After transeptal access, a single bolus of heparin (30 IU/kg) was administered.

**Ablation protocol.** The procedural end point was abolition of all clinical VPBs. These VPBs were localized by mapping the earliest electrogram relative to the onset of the ectopic QRS complex during a ventricular ectopy. During sinus rhythm, the location of the Purkinje network was indicated by initial sharp potentials (<10 ms in duration) preceding the QRS complex by ≤15 ms. Such electrograms were distinct from earlier electrograms (>15 ms before the QRS) that were taken to indicate proximal Purkinje fascicle activation. The absence of a Purkinje potential at the site of earliest activation indicated the ventricular myocardium as the origin of the VPB.

If required, VPBs were induced by the use of pacing maneuvers (ventricular burst or extrastimuli) and/or isoproterenol (1 to 4 μg/kg/min) or adenosine (up to 40 mg) by intravenous infusion. If these measures were ineffective, pace mapping was used to identify the site of origin of clinical VPBs (perfect match of at least 11/12 leads on the surface ECG).

Ablation was performed by the use of radiofrequency energy with a target temperature of 50°C and a maximum power of 50 W. In cases in which the desired power could not be delivered, an externally irrigated 3.5-mm tip catheter (Thermocool, Biosense Webster) was used. For this purpose, manual titration of the saline perfusate ranging from 10 to 60 ml/min was performed to achieve the required power. In all cases, ablation was extended approximately 1 cm$^2$ around the targeted site. No 3-dimensional mapping system was used during the ablation protocol.

**Follow-up.** All recruiting centers were contacted for each patient, and follow-up was completed by August 2008. In addition to records of clinical events, ECGs, and Holter monitoring, VF and associated intracardiac electrograms were documented by ICD interrogation. Thirty-seven of 38 patients received an ICD in the periablation period; 1 patient refused ICD implantation after ablation. Antiarrhythmic drugs were generally ceased after ablation except in the case of VF recurrence and unless otherwise decided by the referring cardiologist. A repeat ablation procedure was undertaken in the event of VF recurrence refractory to antiarrhythmic medication.

**Statistical analysis.** Continuous variables are expressed as mean ± SD except for count and time variables, which are expressed as median and the interquartile range (IQR). Statistical significance was assessed by use of the unpaired Student $t$ test or Mann-Whitney $U$ test if necessary. Categorical variables, expressed as numbers or percentages, were analyzed with the chi-square test or Fisher exact test. Differences between baseline and after VF ablation were tested by the paired Student $t$ test or Wilcoxon signed rank test for continuous variables. Univariate analysis of variables was performed. A $p$ value <0.05 was considered statistically significant.
Results

Population study. We studied 38 patients (21 men) ages 42 \(\pm\) 13 years. In sinus rhythm, the mean heart rate was 68 \(\pm\) 10 beats/min, and ECG results showed a PR interval of 164 \(\pm\) 24 ms, a QRS duration of 92 \(\pm\) 15 ms, and a corrected QT interval of 398 \(\pm\) 22 ms. The left ventricular ejection fraction was 67 \(\pm\) 9%, and the left ventricular end-diastolic dimension was 42 \(\pm\) 10 mm.

Before ablation, patients were refractory to a median of 2 (IQR 1 to 3) antiarrhythmic drugs. The median number of significant events before ablation was 4 (IQR 3 to 9) events. The median time from the first significant ventricular event to ablation was 4 months (IQR 1 to 36 months). Thirty-three of the 38 patients (87%) had at least 2 events in the year before the initial ablation procedure. The coupling interval of VPB was longer when originating from the right ventricular outflow tract compared with the Purkinje system (355 \(\pm\) 23 ms vs. 276 \(\pm\) 22 ms, \(p < 0.001\)). Clinical characteristics are summarized in Table 1.

Ablation procedure. The median duration of radiofrequency energy delivered, fluoroscopy, and total ablation procedural time were 14 min (IQR 9 to 24 min), 28 min (IQR 18 to 52 min) and 135 min (IQR 100 to 215 min), respectively. Thirty patients (81%) had clinical VPB at the time of the procedure, whereas 8 patients (19%) did not. Clinical VPBs triggering VF arose from the right Purkinje system in 16 patients, the left Purkinje in 14 patients, in both the left and right Purkinje system in 3 patients, and in the myocardium in 5 patients (including the right ventricular outflow track in 4 patients) (Fig. 1). A mean of 1.7 \(\pm\) 2.0 VPB morphologies were targeted per patient. The QRS duration of VPBs was shorter when originating from the left than the right Purkinje system (130 \(\pm\) 24 ms vs. 162 \(\pm\) 19 ms, \(p = 0.002\)), but the QRS duration of VPBs was not significantly different between VPBs originating from the left Purkinje system and the myocardium (130 \(\pm\) 24 ms vs. 150 \(\pm\) 16 ms, respectively, \(p = 0.11\)). When VPBs were

![Figure 1](image.png)

**Figure 1** Triggered VF

Twelve-lead electrocardiograms (left) and their corresponding location in the anteroposterior fluoroscopic view (right, red asterisks). The origin of ventricular premature beat (VPB) triggering ventricular fibrillation (VF) was the left Purkinje either at the posterior (A) or the anterior (B) insertion, the right Purkinje (C), and the right ventricular outflow track (D). Related fluoroscopic views with a decapolar catheter inserted in the left ventricle (E and F), an ablation catheter inserted in the right ventricle (G), and a quadrupolar catheter inserted at the His position (E to G). Ventricular premature beat originating in the left Purkinje system (A and B and related anteroposterior fluoroscopic view) produce more variable 12-lead electrocardiogram (ECG) patterns, reflecting the more complex and extended Purkinje arborization on the left. VPBs originating in the right Purkinje system (C and related anteroposterior fluoroscopic view) typically have a left bundle-branch block pattern with left superior axis. Ventricular premature beat originating from the right ventricular outflow track (D) have the classical aspect with a left bundle-branch block pattern and an inferior axis.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline Characteristics of Patients Undergoing Ablation</th>
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<tbody>
<tr>
<td>Age (yrs)</td>
<td>42 (\pm) 13</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>21/38 (55%)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>67 (\pm) 9</td>
</tr>
<tr>
<td>Left ventricular end-diastolic diameter (mm)</td>
<td>42 (\pm) 10</td>
</tr>
<tr>
<td>Implantable cardiac-defibrillator</td>
<td>37/38 (97%)</td>
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<tr>
<td>Time from initial VF to ablation (months)</td>
<td>4 (IQR 1–36)</td>
</tr>
<tr>
<td>Number of significant events before ablation</td>
<td>4 (IQR 3–9)</td>
</tr>
<tr>
<td>Antiarrhythmic medication before ablation</td>
<td>2 (IQR 1–3)</td>
</tr>
<tr>
<td>Coupling interval of VPB (ms)</td>
<td>291 (\pm) 39</td>
</tr>
</tbody>
</table>

IQR = interquartile range; VF = ventricular fibrillation; VPB = ventricular premature beat.
present at the time of the procedure, catheter ablation was successful in abolishing VPB in all patients.

Ablation at successful sites typically resulted in multiple VPBs leading to polymorphic VT and/or VF (Fig. 2). After ablation, 1 patient developed transient left bundle-branch block. Six other patients developed nonspecific intraventricular conduction defects not meeting formal criteria for a bundle-branch block.

Results on clinical follow-up. During a median follow up of 63 months (IQR 40 to 80 months), 7 (18%) of 38 patients experienced a recurrence of VF. This occurred after a median of 24 months (IQR 1 to 60 months). VF recurrence was detected by the ICD and did not lead to syncope or clinical sudden cardiac arrest in any of the patients. Ablation was repeated in 5 of these 7 patients (1 patient had 2 repeat procedures). Four of these 5 patients had other VPB morphologies as compared with the initial procedure, whereas 1 patient had the same clinical VPB recurrence triggering VF. These 5 patients had no subsequent recurrence of VF or documented VPBs for 28 months (IQR 24 to 72 months).

Two patients with VF recurrence were not reablated. In these 2 patients, clinical VPB morphology triggering VF recurrence could not be analyzed because there was no 12-lead ECG recording of the events. Of these 2 patients, 1 was treated with quinidine. This treatment had been ineffective before ablation and was discontinued without medical advice after ablation; after reinitiation of quinidine, there have been no VF recurrences (for 6 months). The second patient who did not receive reablation had a single asymptomatic short run of polymorphic VT 2 years after the ablation, which terminated spontaneously (without ICD therapy) and which did not recur for 5 years.

Before ablation, 12 patients (32%) experienced VF electrical storm 3 months (IQR 1 to 6 months) beforehand, whereas after ablation, only 3 patients (8% of all patients) had a recurrence of electrical storm (p = 0.03) that occurred 1, 48, and 60 months after ablation. Three patients experienced clinical recurrence of the initial clinical VPB after the initial ablation procedure, which did not result in malignant ventricular arrhythmia. One symptomatic patient has been reablated without recurrence of VPB, and the 2 other patients never experienced malignant ventricular arrhythmia recurrence on verapamil and quinidine therapy despite persistence of VPB.

Overall results for this strategy. Ablation significantly reduced the number of significant events (confirmed VF/VT or sudden death) from 4 (IQR 3 to 9) before ablation to 0 (total range 0 to 4, p = 0.01) afterwards. After a mean

![Figure 2](image-url) 12-Lead Electrocardiogram During Radiofrequency Ablation at the Right Purkinje System

The start of ablation (arrow) typically resulted in ventricular tachycardia followed by sinus rhythm, as shown in this example.
follow-up of 52 ± 28 months after the last procedure, 36 of 38 patients are free from VF after a mean of 1.28 ± 0.6 procedures. Five (13%) of the 38 patients are currently on antiarrhythmic therapy, including 2 who experienced VF recurrence and 2 with VPB recurrence.

**Predictors of VF recurrence.** The only parameter that was associated with an adverse outcome was the presence of bundle-branch block in the targeted ventricle before ablation as the result of mechanical trauma “bumping” (p < 0.0001; hazard ratio: 0.0325, 95% confidence interval: 0.00001 to 0.00006) (Fig. 3). Technically, this is related to the fact that such bundle-branch block obscured ipsilateral Purkinje potentials during sinus rhythm, thus complicating subsequent ablation. Notably, the frequency of VPB at the time of EP study and a greater frequency of previous events did not predict adverse outcome in this study.

**Discussion**

**Main findings.** This multicenter study confirms that ablation for idiopathic VF, targeted at its potential ventricular ectopic triggers, may effectively prevent VF recurrence in a high-risk population. With rigorous follow-up for more than 5 years, with the use of both clinical information and data from ICD interrogations in all but 1 patient, we found that only 18% of individuals had a recurrence of VF or polymorphic VT. In these patients in whom structural disease and other proarrhythmic syndromes had been excluded, the only parameter that predicted ablation success was ipsilateral intraventricular conduction delay at electrophysiological study.

**Ablation of VF.** The feasibility of VF ablation has already been demonstrated in populations with idiopathic VF (9), long-QT syndrome, Brugada syndrome, and ischemic heart disease (10–12,15). Although mechanisms for VF have yet to be defined for each syndrome, the basis may be scar and re-entry in ischemic disease (17), focal ectopy and re-entry in the long-QT syndrome (18), and conduction slowing (19) with repolarization dispersion (20) in Brugada syndrome. Patients with idiopathic VF, such as those in our study, lack many of these substrates. Indeed, increasing evidence suggests that the Purkinje network may have a primary role in both initiating and perpetuating VF in these patients (8,9,21).

**Role of the Purkinje network in idiopathic VF.** The specialized conduction system of the Purkinje network, localized endocardially in the human heart, consists of a single branch on the right that penetrates a limited portion of the right ventricle, and 2 larger branches on the left that ramify more intricately to supply a greater area of the left ventricle (22,23). There is a growing body of evidence that the Purkinje network plays a pivotal role in both the initiation and perpetuation of VF. In experiments performed in isolated canine hearts, multielectrode mapping of the endocardial left ventricle have shown a focal initiating mechanism for VF in 34% of cases, of which 42% arose from Purkinje fibers (24). Moreover, endocardial activation involved the Purkinje network in >84% of cases (24). The Purkinje system has been shown to be capable of very rapid burst activity suggestive of its potential role in being a driver of VF (9). Finally, studies also suggest the existence of re-entry involving the Purkinje-myocardial junction, at least in the early stages of VF (8).

In a previous multicenter study, conduction delay from the Purkinje network to the myocardium were shorter in the
right than left ventricle, with variable conduction delays and dissociated Purkinje potentials in some patients (9). Ectopy arising from the Purkinje system produces a characteristic 12-lead ECG pattern; VPBs originating in the right Purkinje system typically have a left bundle-branch block pattern with left superior axis. Ventricular premature beats originating in the left Purkinje system produce more variable 12-lead ECG patterns, reflecting the more complex and extended Purkinje arborization on the left (Fig. 1).

**Practical considerations for ablation.** A previous report suggested that the success of VF ablation improves when patients have clinical ectopy at the time of the procedure (9), yet the absence of frequent VPB at the time of ablation did not predict an unfavorable outcome in our study. Nevertheless, when clinical VPBs are infrequent or absent at the time of the procedure, localizing the Purkinje network remains of primary importance for procedural success. Notably, ipsilateral intraventricular conduction delay was the only independent predictor of success because once this occurs, it masks ipsilateral Purkinje potentials in sinus rhythm. The specificity of this index awaits further study.

Interestingly, a recurrence of clinical VPBs was observed in 2 patients that no longer resulted in malignant ventricular arrhythmia despite the extended follow-up. Speculatively, this finding suggests that modulation of the Purkinje system and its surrounding tissue may be sufficient in some cases to avoid VF initiation.

**Clinical implications.** Implantation of a cardiac defibrillator is the gold standard treatment for both primary and secondary prevention of sudden cardiac death (2,4–7). Although the long-term results of the present study are very encouraging, ablation of triggering VPBs for VF does not replace ICD implantation. This finding is re-enforced by the present study because some patients who had a recurrence of VF had a new morphology of VPB triggering VF, suggesting an evolution of the disease for these patients. However, repeated ICD shocks for electrical storm may occur in 10% to 25% of patients (25,26). Because ICD therapy may not fully protect against VF and electrical storm (27,28), adjunctive VF ablation may be useful in reducing mortality in patients with recurrent VF. Moreover, ICD therapy has its drawbacks. The use of ICDs does not provide absolute protection against death due to ventricular arrhythmia, with a risk for sudden death among patients who do not have a response to ICDs of approximately 5% (29). In addition, ICD discharges are painful, whereas syncope may occur before delivery of a shock. Clinically significant anxiety and depression as a result of recurrent ICD shocks occur in >50% of patients (30–32).

The results of this study demonstrate the feasibility of catheter ablation for patients with idiopathic VF, targeting short coupled VPBs that may trigger arrhythmogenic episodes. This strategy may reduce the morbidity of patients with idiopathic VF implanted with an ICD. It may also decrease the mortality from arrhythmic storm for these patients, although this requires further prospective trials.

**Study limitations.** This is an observational study with no control group; however, this was a high-risk population that experiences multiple events and that has been shown to be associated with a poor outcome (26,27). Another important limitation is the fact that VF episodes are sporadic, and it is difficult to state with certainty that the absence of VF recurrence was due to ablation. However, the patients in the study had frequent clinical events before ablation, yet very few afterwards, rendering this criticism less important. Nevertheless, further studies with a control group of ICD recipients without adjunctive ablation would help to address this issue prospectively. Third, it is impossible to exclude the impact of additional antiarrhythmic agents in suppressing the arrhythmias. However, all patients had already failed antiarrhythmic medications, whereas multivariate analysis failed to reveal that post-ablation drug was a confounder. Because of the often-dramatic presentation of these patients, it was difficult to implement uniform ICD programming between centers. However, by definition, idiopathic VF was not preceded by VT. Furthermore, in the 7 patients who experienced post-ablation recurrence, VF was not preceded by VT or by an acceleration of a tachycardia into VF by antitachycardia pacing.

**Conclusions**

Ablation of idiopathic VF, targeted to its VPB triggers, is feasible and results in an excellent long-term outcomes. Short coupled VPB triggering VF originates predominantly from the Purkinje system and the right ventricular outflow track.

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**REFERENCES**


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