Original Article

Retrograde Coronary Venous Ethanol Infusion for Ablation of Refractory Ventricular Tachycardia

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Background—Radiofrequency ablation (RFA) of ventricular tachycardia (VT) can fail because of inaccessibility to the VT substrate. Transarterial coronary ethanol ablation can be effective but entails arterial instrumentation risk. We hypothesized that retrograde coronary venous ethanol ablation can be an alternative bail-out approach to failed VT RFA.

Methods and Results—Out of 334 consecutive patients undergoing VT/premature ventricular contraction ablation, 7 patients underwent retrograde coronary venous ethanol ablation. Six out of 7 patients had failed RFA attempts (including epicardial in 3). Coronary venogram-guided venous mapping was performed using a 4F quadripolar catheter or an alligator-clip–connected angioplasty wire. Targeted veins included those with early presystolic potentials and pace-maps matching VT/premature ventricular contraction. An angioplasty balloon (1.5–2×6 mm) was used to deliver 1 to 4 cc of 98% ethanol into a septal branch of the anterior interventricular vein in 5 patients with left ventricular summit VT, a septal branch of the middle cardiac vein, and a posterolateral coronary vein (n=1 each). The clinical VT was successfully ablated acutely in all patients. There were no complications of retrograde coronary venous ethanol ablation, but 1 patient developed pericardial and pleural effusion attributed to pericardial instrumentation. On follow-up of 590±722 days, VT recurred in 4 out of 7 patients, 3 of whom were successfully reablated with RFA.

Conclusions—Retrograde coronary venous ethanol ablation is safe and feasible as a bail-out approach to failed VT RFA, particularly those originating from the left ventricular summit. **(*Circ Arrhythm Electrophysiol*. 2016;9:e004352. DOI: 10.1161/CIRCEP.116.004352.)**

Key Words: catheter ablation ■ ethanol ■ LV summit ■ premature ventricular contractions ■ tachycardia, ventricular

Radiofrequency ablation (RFA) is the standard of care for ablation of drug-refractory ventricular tachycardia (VT), particularly in the setting of ischemic heart disease.[1–3] Ablation success is far from uniform, in part because of technical challenges reaching the VT substrate with currently available technologies because all require some degree of tissue contact with the targeted tissue. Epicardial instrumentation[4] may allow reaching VT substrates refractory to endovascular approaches[5,6] but remains difficult in patients who have undergone previous cardiac surgery,[7] and it is not always helpful because many ventricular arrhythmias derive from deep intramural origins or in proximity to coronary vessels.[8–10] This is particularly true for VT originating from the left ventricular (LV) summit, where an intramural origin, proximity to coronary vessels, and inaccessibility to the epicardial approach limit RFA success.[11]

Transarterial coronary ethanol ablation (TCEA) as an alternative treatment modality has been reported extensively in the literature.[12–16] TCEA has become a modality of last resort in the treatment of VT not amenable to alternate contact-based ablation.[12,16] TCEA is limited by the risks of arterial instrumentation; the dependence on a feasible arterial anatomy, commonly affected by the ischemic disease that led to the VT substrate; the risk of unintended collateral damage; and the logistic challenges of requiring interventional cardiology support. To overcome these limitations, retrograde coronary venous ethanol ablation (RCVEA) has been described as an alternative to the arterial approach. Its initial application in canines showed feasibility and effective myocardial ablation.[17] We have reported feasibility in humans and acute procedural success of RCVEA in 2 cases.[18] The venous approach is uniquely suited for detailed activation mapping using an angioplasty wire. Here, we report its combination with venous wire mapping in a variety of VT substrates, particularly the LV summit, and report its chronic outcomes.

Methods

Data Collection

A total of 7 patients were included. All were counseled about the unconventional nature of venous ethanol ablation and gave informed consent to the intervention. Clinical data collection was performed under an institutional review board–approved protocol. Initial data

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WHAT IS KNOWN

- RFA of VT fails when the VT substrate is inaccessible as is common for those originating from the LV summit.
- RCVEA has been shown to be feasible, but human experience is limited.

WHAT THE STUDY ADDS

- RCVEA was acutely successful in 7 patients with difficult ventricular arrhythmias, 5 of which arose from the LV summit. Although VT recurred in 4, it was then controlled with RFA.
- There were no major complications attributable to ethanol injection.
- RCVEA is reasonable to consider when RFA fails and an appropriate coronary venous target can be identified.

relating 2 procedures performed in 2011 (n=2) were collected retrospectively from patient charts. Acute outcomes pertaining to the latter have previously been reported.[18] The subsequent 5 patients were included from a cohort of consecutive patients undergoing VT/premature ventricular contraction (PVC) ablation studied prospectively from January 2012 through February 2016. This data included medical history, procedural reports, and major postprocedural and follow-up events.

Procedural Approach: Vein Mapping

In all procedures, efforts were initially made to localize VT substrate within an area amenable to RFA. Electroanatomical maps were constructed using 3-dimensional mapping systems (NavX; St Jude Medical, St Paul, MN; n=3) or Carto3 (Biosense-Webster, Diamond Bar, CA; n=4). Mapping strategies included substrate maps to localize low-bipolar voltage areas in the presence of structural heart disease, activation maps, and pace-maps. Access to the epicardial space via a subxiphoid anterior puncture was undertaken when suitable for epicardial mapping and ablation (n=3).

Coronary vein mapping was performed by advancing a sheath in the coronary sinus via the right femoral vein (Preface; Biosense-Webster) or via the right internal jugular vein (CPS Sheath; St Jude Medical, Sylmar, CA). Coronary venograms were performed. A multipolar catheter was inserted in the coronary sinus and selected ventricular branches (4F quadripolar IBI; St Jude, or Deca-Nav; Biosense-Webster). Mapping and pacing from small coronary veins was performed by advancing an angioplasty wire (BMW 0.014"; Abbott) connected to an alligator clip in a unipolar configuration with reference electrode as a needle inserted in the thigh skin. This approach led to significantly reduced noise, compared with that produced when using Wilson's central terminal or an indifferent electrode in the inferior vena cava,[19] and provided exclusively local signals, compared with those provided when using a neighboring electrode. Selective wire cannulation of different targeted veins was achieved by introducing a left internal mammary artery angioplasty guide catheter and torquing it in the desired direction, or simply by guiding the angioplasty wire with the help of a torquing device. To obtain unipolar signals from selective portions of the targeted vein, the angioplasty balloon was advanced over the wire to cover it except for the most distal 3 to 5 mm, which acted as the active electrode. RCVEA was considered in the following situations: (1) when RFA failed at the best endocardial sites as guided by the earliest activation or best pace-mapping; (2) when feasible, epicardial RFA failed or was deemed not indicated because of proximity to coronary arteries or because of presence of the earliest activation site at a broad area; and (3) when optimal pace-mapping and earliest activation was obtained from within a coronary vein.

The bulk of our experience targeted LV summit VT, which we targeted by mapping septal branches of the anterior interventricular vein (AIV; n=5). Other targets included a posterolateral coronary vein (n=1) or the middle cardiac vein (n=1).

Before ethanol infusion, the presence of vein-to-vein collaterals was assessed by inflating the balloon (1.5–2 mm by 6 mm, depending on vein caliber) to achieve venous occlusion and injecting contrast.

Table 1. Patient Demographics and Clinical Outcomes

Patient	Age, y	Comorbidities	LVEF, %	Previous Ablations	AICD	Acute Success	Follow-up Interval, d	Procedure Time, h	Fluoroscopic Exposure Time, min	Recurrence Interval, d	Complications
1	70	HTN, DL, AF, CHF, mechanical aortic valve	35–39	3	Yes	Yes	1552	5:11	70.5	169	None
2	65	HTN, DL, DM II	57	3	Yes	Yes	1705	5:51	74.1	258	Pericarial effusion; Ethanol-induced myocardial injury
3	72	HTN, DM II, CHF s/p LVAD	<20	0	Yes	Yes	206	4:24	0.55	N/A	None
4	58	HTN, DL, AF, DMII, hypothyroid, CHF s/p LVAD	10	1	Yes	Yes	207	3:37	27.82	N/A	None
5	42	HTN, DL, DM II, CHF	40	2	No	Yes	404	5:26	47.03	224	None
6	52	HTN, DL, GERD, COPD, OSA, CAD	60–65	1	No	Yes	40	3:34	42.15	N/A	None
7	77	HTN, CAD	60–65	1	No	Yes	19	3:49	68.27	1	None

AF indicates atrial fibrillation; AICD, automatic implantable cardioverter defibrillator; CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; DL, dyslipidemia; DM II, diabetes mellitus II, GERD, gastroesophageal reflux disease; HTN, hypertension; LVAD, left ventricular assist device; and OSA, obstructive sleep apnea.

Ethanol infusion was injected only in the absence of vein-to-vein collaterals to deliver ethanol to the capillaries and the myocardium and avoid vein-to-vein shunting. Once a vein was selected, the balloon was inflated to 4 to 8 atmospheres (aiming to occlude the selected vein). In the first 4 cases, 1 cc of 98% ethanol were infused for 2 minutes. In the subsequent 3 cases, 2 to 4 injections were administered. Flushing with normal saline was performed after ethanol. Balloon occlusion time ranged from 2 to 8 minutes. An infusion of cold saline was attempted in 1 case, but it failed to terminate the VT, despite an eventual ethanol success, and cold saline was abandoned for subsequent cases.

Procedural Success

In PVC ablation (n=3), ablation success was defined as the cessation of spontaneous ectopy after 20 seconds of ethanol infusion. In VT ablation (n=4), attempts were made to induce the clinical tachycardia before and after ablation, and the procedure was considered successful if induction failed post ablation. The electrophysiology testing protocol used 400- and 600-ms drive trains followed by 1 to 3 ventricular extrastimuli that were 2 ms in duration at twice the diastolic threshold. Extrastimuli were decremented down to a coupling interval no shorter than 200 ms. If this protocol proved ineffective, rapid burst pacing up to a cycle length of 280 ms was used instead.

Clinical Follow-Up

All patients were hospitalized after the ablation procedure. They underwent continuous telemetry monitoring, 12-lead electrocardiography, and 24-hour ambulatory electrocardiography to document absence of VT/PVC recurrence before discharge. Echocardiograms were obtained if clinically indicated. Patients were later seen in the clinic at 1 week and 1 month post procedure. They were followed up on a biannual basis thereafter. Four patients had an implanted implantable cardioverter–defibrillator, and so interrogation and shock history were retrieved during follow-up. For the remaining patients, 12-lead electrocardiography and 24-hour ambulatory electrocardiographic monitoring were performed on follow-up.

Statistical Analysis

Gaussian continuous variables are reported as mean±SD and non-Gaussian variables as median (minimum–maximum). Qualitative findings were described as numbers and percentages. Analyses were performed using Sigmastat (version 3.11) and Stata software (version

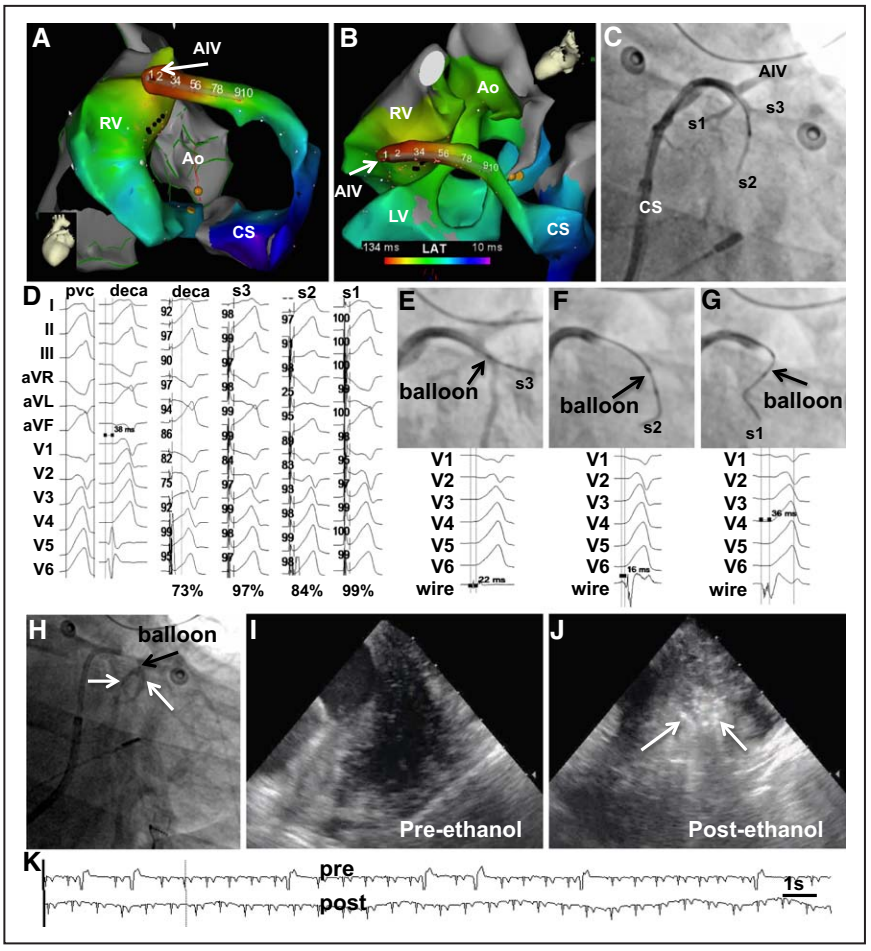

Figure 1. Mapping of septal branches of the anterior interventricular vein (AIV) in a patient with left ventricular (LV) summit premature ventricular contractions (PVCs) and successful venous ethanol ablation. **A**, Three-dimensional activation map (Carto; Biosense-Webster, Sylmar, CA) of the right ventricle (RV), coronary sinus (CS, using a decapolar [deca] catheter), and AIV. The aortic cusps and LV outflow activation map are included in **B**. **C**, Venogram of the distal CS demonstrating 3 septal branches denoted s1, s2, and s3, at the origin of the AIV. **D**, Surface ECG of the PVC, including signals recorded from the decapolar catheter, and pace-maps (% matching with PVC) obtained with unipolar pacing via an angioplasty wire in each of the 3 septal branches. S1 has a perfect pace-map match. **E–G**, Angioplasty wire position and unipolar signals obtained from septal veins s1 through s3, respectively. Signal from s1 precedes QRS by 36 ms. **H**, Balloon occlusion of s1 and selective s1 venogram showing myocardial staining (white arrows). **I** and **J**, Intracardiac echocardiogram images of the LV outflow tract before and after ethanol, showing increased echogenicity of the ethanol-injected myocardium (white arrows). **K**, ECG before and after ethanol, showing elimination of PVCs.

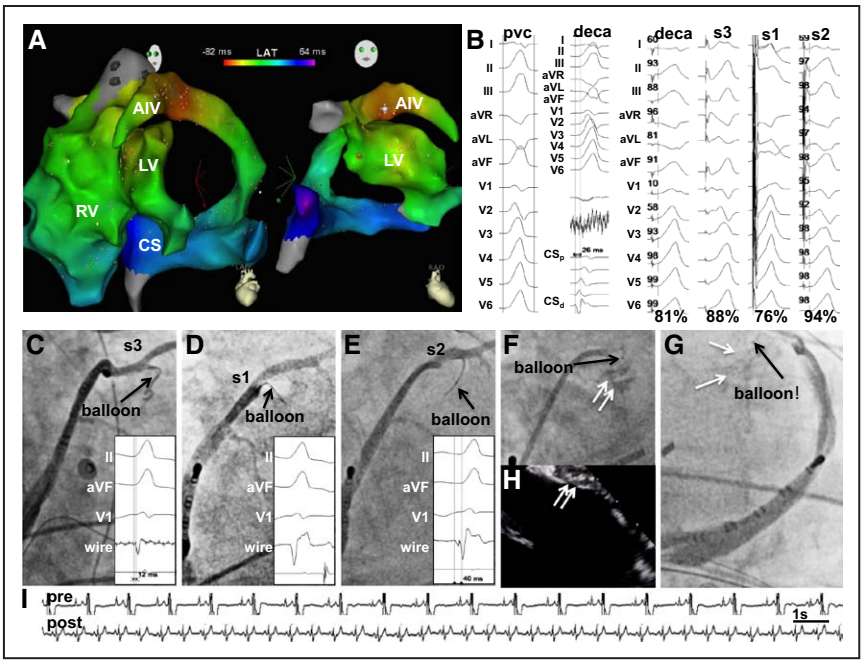

Figure 2. Septal vein mapping and ethanol ablation of LV summit premature ventricular contractions (PVCs). **A**, Activation maps (Carto) of the right ventricle (RV), left ventricle (LV), coronary sinus (CS), and anterior interventricular vein (AIV), showing earliest site in the AIV. **B**, ECG and pace-maps of the PVCs (including AIV signals, recorded from the distal CS, CSd), obtained from 3 different septal branches: s1, s2, and s3. A near-perfect pace-map is obtained from s2. **C–E**, Angioplasty wire cannulation of s1, s2, and s3 and their respective unipolar signals, which were earliest in s2. **F** and **G**, Myocardial staining during selective contrast injection in s2, shown in right (**F**) and left (**G**) anterior oblique (AO) projections. **H**, Increased echo density in the basal LV septum after ethanol injection. **I**, ECG before and after ethanol injection, with elimination of extrasystoles. This case had not received any previous ablation and radiofrequency ablation of the AIV was not feasible because of its small size.

13). Statistical significance could not be attributed because of the inherent limitation imposed by the small sample size.

Results

Baseline Characteristics

A total of 334 consecutive patients underwent VT/PVC ablation in a single tertiary center between January 2011 and February 2016. Of these, 7 cases were considered suitable for RCVEA and underwent the intervention accordingly (Table 1). Three patients underwent ablation for PVC, and 4 for VT. Six patients were men, and mean age at procedure time was 62.2±12.6 years. Patient clinical characteristics and comorbidities are detailed in Table 1. Of particular relevance, 6 out of the 7 patients had undergone previous VT ablation with recurrence, including epicardial ablation in 3 cases (1.8±1.0 previous ablations). In 1 patient with LV summit VT, an attempt to advance an ablation catheter into the AIV failed because of the small vein caliber, which made it impossible to reach the targeted site. Two patients had previously been implanted with a LV assist device (LVAD) as well (Figures 1 and 2), which precluded epicardial access. One LVAD patient had recurrent VT in the setting of ischemic cardiomyopathy. The second LVAD patient had incessant VT in the setting of a nonischemic cardiomyopathy, which recurred after LVAD implant despite maximum tolerated doses of pharmacological therapy including amiodarone and mexiletine. Four patients were diagnosed with nonischemic cardiomyopathy and had an implantable cardioverter–defibrillator implanted, whereas 1 was diagnosed with tachycardia-induced cardiomyopathy. Mean LV ejection fraction was 41.1±20.6%.

LV Summit VT: Ethanol Infusion in Septal Veins

Six cases had incessant PVC/VT ablated via ethanol infusion in septal veins. Five had PVCs arising from the LV summit (Figures 1 through 4)—1 has been previously reported.[18] In all cases, extensive endocardial mapping in both sides of the septum was initially performed, as well as mapping from the great cardiac vein and AIV with a multipolar catheter. In 3 out of 7 cases, RFA had been previously delivered via the right ventricular endocardium and LV endocardium without success. Epicardial mapping, performed in 2 cases with LV summit PVC/VT (1 each), revealed earliest activation over a broad area of the LV anterior base. In 1 case, no suitable ablation targets were found in either right ventricular or LV, and the ablation was performed exclusively with ethanol (Figure 2).

After mapping the great cardiac vein and AIV with a multipolar catheter showed a promising signal from the AIV, selective AIV venograms were performed to identify septal branches. Then, detailed unipolar septal vein mapping was performed with the angioplasty wire, which could be used to selectively obtain unipolar signals and pace-maps from the different septal branches (Figures 1 through 3). The septal branch with perfect pace-map match and earliest unipolar signals was selected for ethanol infusion. Figure 1 shows septal vein mapping in a patient with LV summit PVCs in whom the first septal branch was chosen to deliver ethanol after mapping and pacing with the angioplasty wire in other veins. In Figure 2, 3 septal

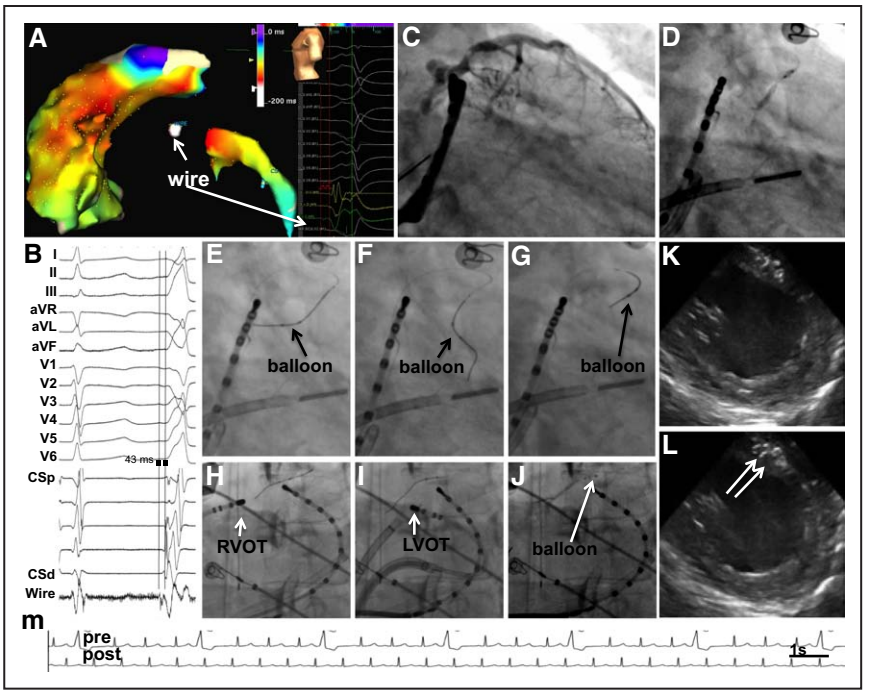

Figure 3. Septal venous mapping and ethanol ablation of LV summit VT. **A**, NavX (St Jude, St Paul, MN) map of the activation time in the right ventricle (RV) and coronary sinus (CS). The wire tip was localized by NavX using an alligator clip. The left ventricle (LV) and epicardium were also mapped (not shown) but showed later activation. The unipolar signal from the septal AIV branch precedes all other signals. **B**, ECG and unipolar wire signal in sinus rhythm and during a premature ventricular contraction. Wire signal obtained from the proximal septal branch (**G**) preceded QRS by 43 ms. **E–G**, Angioplasty wire mapping of different branches of the septal vein (RAO). **H–J**, LAO views of the wire location relative to earliest sites in the RV outflow tract (RVOT, **H**), LVOT (**I**), and septal vein (**J**). **K** and **L**, Intracardiac echocardiography images before and after ethanol infusion, showing echogenicity of the LV basal septal septum (arrows). **M**, ECG before and after ethanol infusion.

branches were mapped as well, and the second one was shown to have earliest unipolar signals with perfect pace-maps. In both Figures 1 and 2, the septal branches were relatively short, and the angioplasty wire only advanced ≈2 cm deep into the septum. Figure 3 illustrates a case in which a large septal vein was identified and cannulated (Figure 3C and 3D), and after

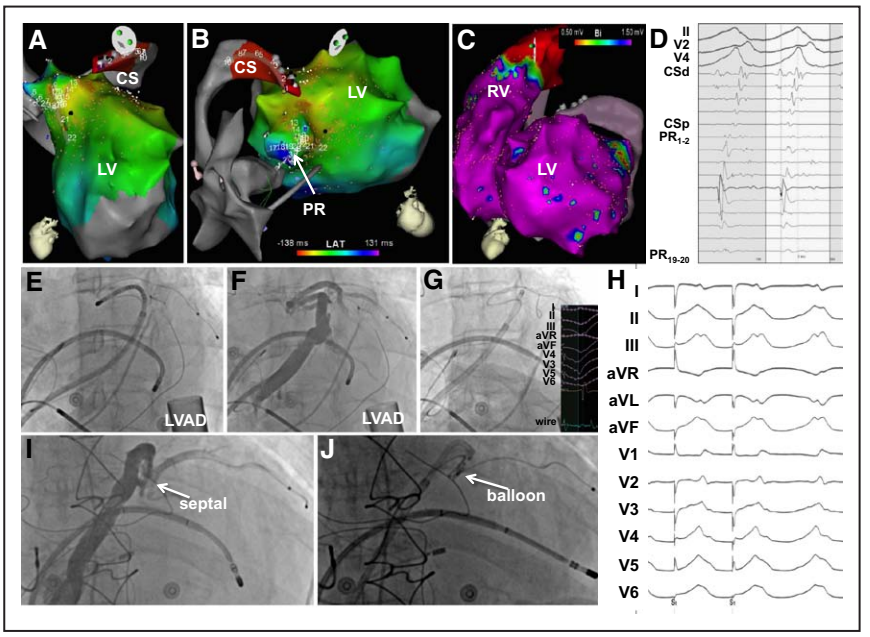

Figure 4. Mapping and ablation of left ventricular (LV) summit ventricular tachycardia (VT) in the context of nonischemic cardiomyopathy. **A** and **B**, Activation maps of VT, obtained with a PentaRay catheter (PR; Biosense-Webster) in the LV and a decapolar catheter in the coronary sinus (CS). The distal CS signals (CSd in **D**) are earliest. **C**, Absence of endocardial low-voltage areas in either LV or RV. **E**, CS cannulation with a decapolar. **F**, CS venogram. **G**, Septal vein wire cannulation and unipolar wire signals during paced rhythm, showing late, post-QRS activations. **H**, Pace-map from the angioplasty wire from a septal vein branch. **I** and **J**, Septal vein balloon cannulation for ethanol infusion showing perfect QRS match.

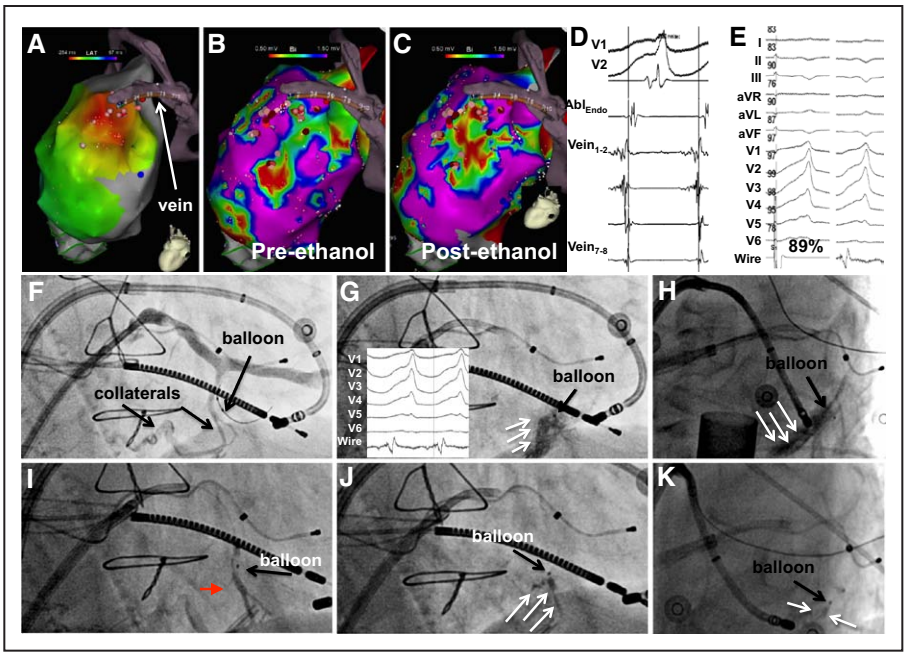

Figure 5. Posterolateral vein mapping and ethanol infusion in ischemic cardiomyopathy-related ventricular tachycardia (VT) in a patient with an LV assist device (LVAD). **A**, Activation map showing earliest site arising from the LV posterolateral base, adjacent to a scar shown in **B**. Radiofrequency ablation failed to terminate the VT at those sites (pink dots). **D**, A posterolateral vein on the epicardial side of the scar was mapped with a decapolar catheter and showed signals earlier than the earliest endocardial site. **E**, Angioplasty wire mapping the LV vein shows pace-map match (**left**) and mid-diastolic signals (**right**), obtained from the wire position shown in **F**, which also shows the vein anatomy (with an LV pacing lead in situ) and vein-to-CS collaterals. **G**, Selective contrast injection in a vein branch without collaterals (RAO view). Myocardial staining without collateral flow shunting is seen (white arrows). Inset shows signals from the wire that vein. **H**, LAO view. This vein was injected with ethanol. **I**, Additional targeted vein included a small branch without collateral shunting (red arrow). **J** and **K**, Selective contrast injection in that same small branch showing no collateral flow and myocardial staining (white arrows, RAO and LAO, respectively). This vein was also targeted with ethanol. **C**, Postethanol endocardial scar map.

mapping with the angioplasty in different locations within the vein (Figure 3E through 3J), the most proximal region of the septal vein (Figure 3G) offered the best signal and was used for ethanol infusion with successful elimination of PVC.

In 1 patient with nonischemic cardiomyopathy and previous LVAD implant, endocardial activation mapping of incessant VT revealed a large component of the VT cycle length contained in the area of the LV summit (Figure 4A and 4B), and AIV mapping with a decapolar catheter showed earliest activations (Figure 4A through 4D). Venograms of the AIV were used to navigate an angioplasty wire into the veins and obtain optimal pace-maps (Figure 4G and 4H). A septal vein was then selected for ethanol infusion (Figure 4I and 4J).

In 1 patient, the third septal branch of the middle cardiac vein was cannulated and subjected to ethanol infusion with elimination of VT originating from an inferoseptal myocardial infarction.[18]

Lateral LV Vein Ethanol

In a patient with ischemic cardiomyopathy, severe heart failure, and previous LVAD implant, endocardial mapping revealed a patchy basal inferolateral scar, from which the exit site of the VT was mapped (Figure 5A through 5C). Mapping of a LV vein with a decapolar catheter revealed earlier signals on the epicardial aspect of the scar (Figure 5D), which prompted more detailed mapping with the angioplasty wire. Venograms demonstrated ample postcapillary collaterals (Figure 5F). To deliver ethanol to the myocardium, small venules without such collaterals were selected. Recording from the angioplasty wire revealed mid-diastolic signals and optimal pace-maps (Figure 5E through 5I). Ethanol was infused in 2 such venules (Figure 5F through 5K).

Capillary and Vein Obliteration by Ethanol

Targeted veins were selected based on the electrogram timing and pace-mapping. Once a targeted vein was cannulated with the angioplasty balloon, selective contrast injection through the inflated balloon was performed. In 6 out of 8 targeted veins, myocardial staining was obtained. In 1 case, the optimal signal was obtained from the proximal aspect of a septal vein (Figure 3), whereas mapping from more distal in the vein yielded suboptimal signals and pace-maps. Ethanol was delivered in the proximal aspect of the vein, which led to PVC elimination and septal vein obliteration (Figure 6A and 6B). In 1 case, selective septal vein contrast injection opacified a collateral vein returning to the coronary sinus, and on ethanol injection, all contrast was directed to the myocardium (Figure 6B and 6C). In 2 cases, initial pre-ethanol selective venograms led to myocardial staining, whereas postethanol contrast injection demonstrated enhanced collateral flow as well (Figure 6D through 6I).

Procedural Parameters and Outcomes

Overall, mean procedure time was 273±56 minutes, 47±26 minutes of which were spent under fluoroscopic exposure. Three out of 7 procedures included some degree of intraprocedural failed RFA before RCVEA, averaging 10±8 applications

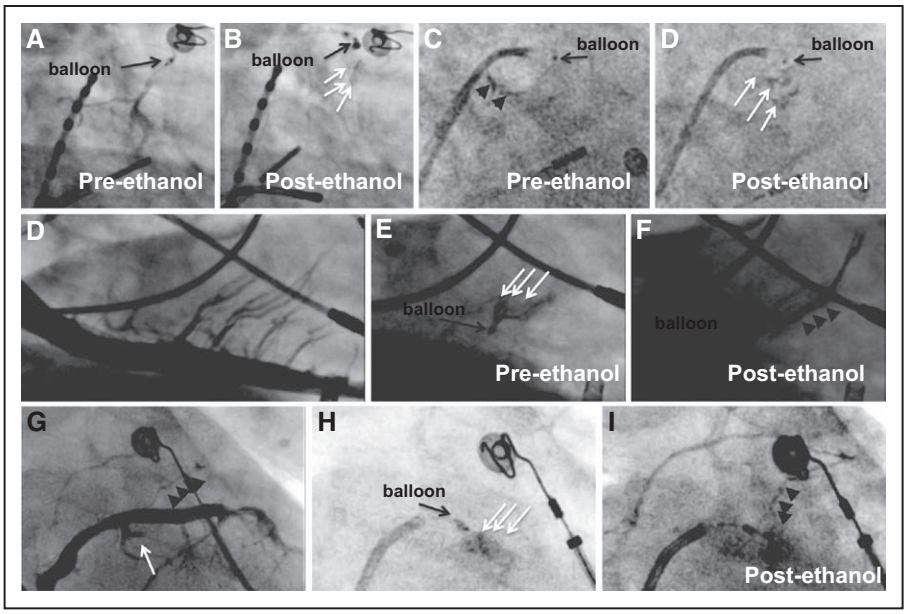

Figure 6. Coronary venograms before and after ethanol injection. **A** and **B**, Septal vein obliteration after ethanol. A large septal vein is shown in **A**. Wire mapping showed best signals from its proximal portion (Figure 3). Ethanol was delivered proximally at a slow rate to allow retrograde flow to keep ethanol close to the injection site, achieving premature ventricular contraction elimination. Post ethanol ablation (**B**), the septal vein was obliterated and contrast injection showed myocardial staining (white arrows). **C** and **D**, Elimination of postcapillary collaterals with ethanol. A septal vein was selectively cannulated (s2 in Figure 2). Selective contrast injection opacified a collateral vein shunting blood back to the coronary sinus (CS; arrowheads in **C**). After ethanol infusion, contrast injection lead to myocardial staining (arrows in **D**) and no opacification of the collateral. **D–F**, New collateral shown after ethanol infusion in a septal branch of the middle cardiac vein (MCV). MCV venogram showed multiple septal branches (**D**), one of which was selectively cannulated (**E**) and contrast injection led to myocardial staining (white arrows). After ethanol infusion, contrast injection showed new collateral flow aside from myocardial staining. **G–I**, New collateral flow after anterior interventricular vein (AIV) septal ethanol injection. **G**, Nonselective AIV venogram. A first septal branch was targeted (white arrow). A collateral vein is shown (black arrowheads). **H**, Selective septal vein venogram shows myocardial staining (arrows). **I**, After ethanol injection, repeated venogram shows enhanced flow to the collateral (black arrowheads).

during a span of 1062±827 seconds. (An additional 3 patients had previous failed RFA procedures and had no further RFA attempts during RCVEA, and 1 patient only had RCVEA as the sole ablative technique; Figure 2).

Acute procedural success was documented in all patients immediately after venous ethanol ablation. In the 3 cases of LV summit PVC ablation, ectopy was completely abolished after the first 30 seconds of ethanol infusion (Figures 1 through 3). In one of them, PVCs recurred during the patient's hospitalization. In 2 LV summit VT ablations[18] (Figure 4), there was acute success because attempts to induce the arrhythmia failed after ethanol ablation. In the LV summit VT patient with an implanted LVAD, after ethanol infusion, a separate VT was inducible but not the clinical VT. No major complications occurred during the course of intervention in any patient. One patient developed a small pericardial effusion—attributed to concomitant pericardial access—and 250 mL of bloody fluid was drained from the pericardium at the end of the procedure from the preexistent pericardial access.[18] The patient underwent cardiac magnetic resonance imaging 48 hours post procedure. It revealed significant expansion of basal anteroseptal hyperenhancement, indicative of ethanol-induced injury. Cardiac magnetic resonance images demonstrating this outcome are previously published.[18] One patient developed a coronary sinus dissection that resolved spontaneously and did not prevent AIV cannulation. There were no other adverse events attributable to the venous ethanol infusion protocol.

Chronic Outcomes

Overall, follow-up interval was 590±722 days. The first 3 patients to undergo the intervention 1113±711 days ago have all suffered recurrence of VT/PVC 217±45 days after the ethanol ablation, albeit with a subtly different QRS morphology in all 3. All 3 underwent repeat ablation, this time using RFA: 2 LV summit PVCs were successfully treated with RFA delivered at the left pulmonary artery, and 1 had inferoseptal RFA. After RFA, all 3 patients remain free of VT recurrence to date. One patient had recurrence of his PVCs 1 day after the procedure. All recurrences occurred in cases in which only 1 cc of ethanol was infused: none of the patients in which more than 1 cc ethanol was delivered recurred. No patients suffered any adverse events related to the procedure during the follow-up interval.

Discussion

The salient results of our experience are as follows: (1) coronary venous ethanol is useful as a bail-out strategy in refractory PVC/VT, particularly when originating from the LV summit; (2) detailed coronary venous mapping is helpful in delineating the origin of RFA refractory PVC/VT and can be achieved by unipolar mapping with an angioplasty wire; (3) capillary obliteration occurs after venous ethanol infusion; and (4) despite uniform acute success, recurrence can occur that seems to decrease with repeated (≤4) injections.

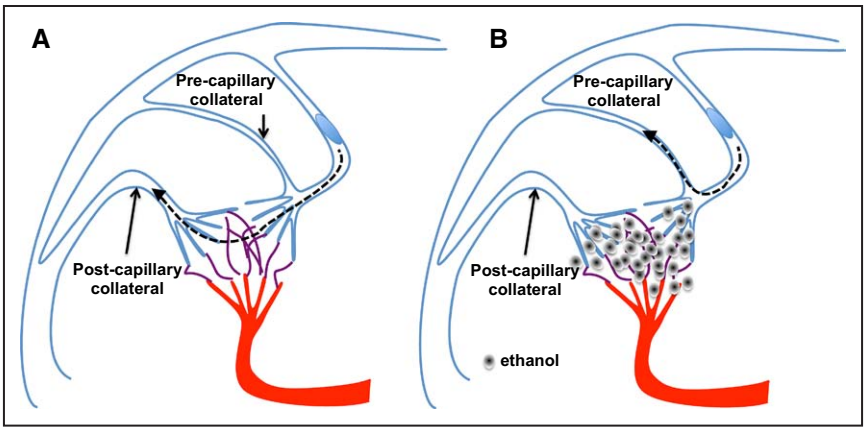

Figure 7. Schematic of coronary venous flow and proposed effects of ethanol. **A**, Redundant epicardial coronary veins show vein branches followed by venules leading to capillaries. Precapillary collaterals and postcapillary collaterals exist. Not shown are Thebesian veins draining into left ventricle (LV) and right ventricle (RV) cavity. Selective retrograde contrast injection shows flow into the capillaries (myocardial staining) and through postcapillary collaterals (as in Figure 6C). **B**, After ethanol infusion, capillaries are obliterated, and repeated retrograde contrast cannot reach postcapillary collaterals (as in Figure 6D). If precapillary collaterals exist, flow through them is enhanced after ethanol (as in Figure 6D–6I).

Current Pitfalls in Standard Treatment

The most commonly used modality for VT ablation remains RFA. It has been proven to be 81% effective in the acute abolition of VT,[20] but only ≈49% of patients will remain free of disease during medium-term follow-up.[1] Other modalities that have been gaining popularity in this regard include cryoablation, laser, and high-intensity focused ultrasound.[21–28] All of these interventions, as is the case of RFA, are limited by a need for adequate tissue contact. VT substrate often presents in the epicardium.[7] Although pericardial access through a subxiphoid technique is useful, this approach remains difficult in patients who have undergone previous cardiac surgery,[7] particularly in post-LVAD patients. Furthermore, many ventricular arrhythmias derive from deep intramural origins that are difficult to target with contact-based instrumentation.[9,29,30] PVC/VT originating from the LV summit remain particularly challenging because they combine both an intramural origin and inaccessibility to epicardial approaches.[11] Proximity to coronary vessels is another factor that limits local application of radiofrequency.[8,10] Surgical cryoablation or TCEA has been reported.[31] Strategies such as ablation in the AIV[32] and bipolar ablation[33] have been proposed, but catheter size, proximity to coronary arteries, or impedance rises limit the former,[34] and the latter is not universally available. Other approaches have been described, such as hot saline or direct ethanol injections.[35,36] Novel approaches, such as needle radiofrequency irrigation,[37] facilitated radiofrequency with gadolinium, or selected irrigants,[38,39] are not available or fully developed. Septal coronary venous mapping and ethanol ablation seem uniquely suited for LV summit VTs.

Coronary Arterial Ethanol Ablation

The use of alcohol as an ablative solution preceded the development of RFA and has been reported extensively in the literature.[12–15] Intra-arterial injection of ethanol classically delivered cytotoxic injury through the vasculature supplying target myocardial tissue. In 1989, Brugada et al[40] performed the intervention on 3 patients with incessant VT postmyocardial infarction. They described acute procedural success in all 3, with recurrence in 1 patient after collateral flow developed and temporary complete atrioventricular block requiring pacemaker implantation in 1. Similarly, Kay et al[15] reported TCEA in 10 patients, with 90% acute success and 50% recurrence. Adverse events were common, however, including complete atrioventricular block in 40% and pericarditis in 10% of patients. More recently, intracoronary ethanol injection has become limited to arrhythmogenic foci that are not amenable to contact-based ablation.[12,41] Noninducibility of VT after intracoronary ethanol ablation is reported between 56% and 84%, with a recurrence rate of ≈33% to 64%.[1,31,41,42] Unfortunately, adverse events are not uncommon, most notably coronary arterial dissection, thrombosis, and myocardial infarction.[13–15] Furthermore, ethanol infusion may spill over to nontargeted myocardium, resulting in infarction or conduction block.[15] Additionally, in patients with coronary artery disease, the technique is limited by difficulty in localizing a terminal arrhythmia-related vessel, especially in the presence of coronary stenosis.[12] Another limitation stems from the variability of vessel size and flow rate, which influence the cytotoxicity of ethanol and make its outcomes difficult to predict.

Retrograde Venous Ethanol Ablation

To overcome some of these limitations, retrograde venous infusion of ethanol has been described as an alternative to the arterial approach. Its initial application in canines showed promise in circumventing arterial damage, thereby avoiding the risk of coronary arterial dissection and myocardial infarction.[17] Furthermore, off-target myocardial injury created by ethanol leak is not a concern of RCVEA because retrograde flow allows dilution of the ethanol into the coronary sinus rendering it harmless. Still, an occlusive balloon is necessary because given the retrograde direction of ethanol infusion, the normal blood flow direction naturally tends to wash out ethanol from the targeted tissue. In our experience, RCVEA has proven to be acutely effective in suppressing ventricular arrhythmias,[18] including 1 case in which long-term elimination

of VT was achieved by RCVEA alone without the use of any other ablative technology (Figure 2).

The coronary venous approach offers logistical advantages to the operator as well. Particularly, when combined with venous mapping, which entails coronary sinus access and selective vein branch cannulation, adding an angioplasty balloon does not contribute increased logistical complexities to the case. Most centers using intra-arterial ethanol for VT recruit an interventional cardiologist for this procedure, which adds such logistical complexities. Most electrophysiologists are thoroughly familiar with the coronary venous anatomy, and its instrumentation is aided by tools developed for LV lead placement in coronary veins.

The coronary venous anatomy is extremely redundant. Aside from venous return to the coronary sinus, Thebesian veins can drain directly into the LV cavity.[17] Within the epicardial venous system, collateral veins abound, communicating epicardial veins with one another and the coronary sinus (Figure 5). When targeting the myocardium with ethanol, it is important to use a vein with direct connection to capillaries to avoid ethanol shunting. Collateral veins may be present at baseline injection. In some cases, collateral veins disappeared after ethanol, whereas in others, they became more prominent. We hypothesize that ethanol obliterates capillaries. Collateral veins arising after the capillary territory obliterated by ethanol would disappear after ethanol (Figure 6B and 6C), whereas those collateral veins arising before the capillaries may become more prominent (Figure 6D through 6I). Figure 7 shows a schematic illustrating this concept.

Long-term outcomes remain challenging because we observed recurrence in 4 out of 7 cases. The fact that the nonrecurrent cases underwent repeated ethanol injections (≤4 cc versus only 1 cc in the recurrent cases) suggests that successful myocardial ablation may require higher ethanol doses. Other potential reasons for failure include inaccurate localization, inadequate tissue destruction, or perhaps other mechanisms.

Limitations

This is a small, observational case series. As long as the intervention is considered a bail-out strategy of last resort, and in the presence of alternative bail-out modalities, recruitment of large numbers of clinically indicated patients will be difficult. Patients enrolled in this series host exceptionally drug- and ablation-resilient arrhythmias, so recurrence outcomes cannot be generalized to all treatment-indicated LV summit cases. We cannot compare outcomes with other bail-out techniques, but the advantages are appealing. Furthermore, all procedures in this series were performed by a single operator who is experienced in ethanol ablation (M.V.). Hence, additional experience with a larger cohort of patients and by multiple operators will be necessary to assess the global clinical safety, efficacy, and practicality of RCVEA. Moreover, the specific mechanism of capillary obliteration enforced by this technique remains ill defined and should ideally be explored through histological data derived from animal models. Although the technique is promising, it is not without limitations, including the need for a suitable vein without collateral shunting, the technical challenges of vein cannulation, the uncertain mechanisms, and dosing of ethanol.

Conclusions

RCVEA seems to be safe and feasible as a bail-out approach in the treatment of failed VT RFA, particularly for LV summit VT.

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Disclosures

None.

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