Ablation-Induced Change in the Course of Fascicular Tachycardia

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ABSTRACT: **Background:** Multiform fascicular tachycardia (FT) was recently described as a ventricular tachycardia (VT) that has a reentrant mechanism using multiple fascicular branches and produces alternate fascicular VT forms. Ablating the respective fascicle may cause a change in the reentrant circuit resulting in a change in morphology. Ablation of the septal fascicle is crucial for successful treatment.

Objectives: To describe four cases of FT in which ablation induced a change in QRS morphologies and aggravated clinical course.

Methods: Four out of 57 consecutive FT cases at three institutions were retrospectively analyzed and found to involve multiform FT. These cases underwent electrophysiological study, fascicular potential mapping, and electroanatomical mapping. All patients initially had FT with right bundle branch block (RBBB) and superior axis morphology.

Results: Radiofrequency catheter ablation (RFCA) targeting the distal left posterior fascicle (LPF) resulted in a second VT with an RBBB-inferior axis morphology that sometimes became faster and/or incessant and/or verapamil-refractory in characteristics. RFCA in the upper septum abolished the second VT with no complications and uneventful long-term follow-up.

Conclusions: The change in FT morphology during ablation may be associated with a change in clinical course when shifting from one route to another and may aggravate symptoms. Targeting of the proximal conduction system (such as bifurcation, LPF, left anterior fascicle, high septal/auxiliary pathway) may serve to solve this problem.

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KEY WORDS: fascicular tachycardia (FT), multiform, ventricular tachycardia (VT), ablation, arrhythmia

Fascicular tachycardia (FT) is a common form of sustained idiopathic left ventricular tachycardia (VT). Detailed electrophysiological studies have shown that FT has a re-entrant mechanism, can be responsive to verapamil, involves various branches of the Purkinje network with differential conduction properties participating in the tachycardia, and can be successfully treated by localized ablation [1-4]. The verapamil-sensitive fascicular ventricular tachycardia is the most common form of idiopathic left VT. It was first recognized as an electrocardiographic entity by Zipes and colleagues in 1979 [1] and was demonstrated to be verapamil sensitive by Belhassen et al. in 1981 [2]. According to the QRS morphology, Nogami et al. [3,4] classified the verapamil-sensitive left fascicular VT into three subtypes: **(1)** the left posterior fascicular (LPF) VT, the QRS morphology that exhibits right bundle branch block (RBBB) configuration and a superior axis (SA); **(2)** the left anterior fascicular (LAF) VT, the QRS morphology that exhibits an RB configuration and right-axis (RA) deviation; and **(3)** upper septal FT, the QRS that exhibits a narrow QRS configuration and normal or RA deviation. This arrhythmia typically occurs in a heart with no structural disease, and its mechanism has proven to be reentry within the left-sided specialized conduction system that uses calcium currents [4-6].

Previous studies of FT have described predominantly monomorphic QRS morphology [7]. Kottkamp and co-authors [8] reported a patient who had two left VT configurations with right- and left-axis deviation [8]. Radiofrequency catheter ablation (RFCA) was delivered to a single site between the LAF and LPF in this patient, which eliminated both VTs. Sung and colleagues [9] published the first case series describing multiform fascicular VTs, with evidence supporting reentry with both morphologies using an auxiliary fascicle (possibly septal) in all cases.

We describe another case series of patients with multiform FT. In these patients we observed a change in clinical course along with change in the route of FT. This change in clinical course necessitated subsequent ablation of the second morphology VT.

*The first two authors contributed equally to this study

PATIENTS AND METHODS

STUDY POPULATION

We reviewed all of the FT cases performed in three Israeli medical centers (Barzilai Medical Center, Sheba Medical Center, Tel Aviv Sourasky Medical Center). The study was approved by the local research ethics committees of each institution, and all patients gave written informed consent to the procedures. Altogether, we retrospectively reviewed 57 FT cases conducted in our centers between January 2006 and December 2013. In four of these patients (7%) more than one morphology of QRS during VT was found. All patients were young, healthy males (age 24–57 years) with normal left ventricular function and no structural heart disease.

ELECTROPHYSIOLOGICAL STUDY AND MAPPING OF LEFT VENTRICLE

For each study we used three 5F or 6F quadripolar catheters (St. Jude Medical, Minneapolis, MN, USA) that were introduced via femoral vein access and were placed in the high right atrium, His-bundle region, and right ventricular apex. To access the left ventricle (LV), the retrograde aortic approach or an antegrade trans-septal approach was employed, using a BRK needle, Safe-Sept J-shaped-guidewire, and an SL0 long sheath (St. Jude Medical) that was further exchanged for an Agilis steerable sheath (St. Jude Medical). An irrigated tip ablation catheter (Biosense Webster, Diamond Bar, CA, USA) was used for ablation. The procedure was conducted under an infusion of intravenous (IV) heparin with a target activated clotting time of 300–350 seconds. In all patients, induction of VT was achieved by programmed electrical stimulation (PES) from the atrium or ventricle with the ability to entrain the tachycardia from the LV. Electrophysiological study (EPS) included detailed mapping of the left-sided fascicles during sinus and during the various VTs and three-dimensional (3D) electroanatomic activation mapping (EAM) using the CARTO system (Biosense Webster).

CASE DESCRIPTIONS

Case 1

A 40 year old healthy male presented with palpitations following exercise, multiple premature ventricular contractions (PVCs), and a VT episode at 200 beats per minute (bpm) lasting 2.5 minutes. His baseline electrocardiogram (ECG) showed mild RA deviation; echocardiograph exam was normal. Beta blockers aggravated the PVCs. All PVCs and VT had a relatively narrow QRS with RB SA morphology. Assuming FT, he had an EPS where the clinical VT could be induced with atrial pacing and isoproterenol, and could demonstrate a short HV interval during VT (VT1) [Figure 1A1]. Target points of the Purkinje potentials at the posterior apical septum were ablated with no success, as were areas of earliest activation identified by CARTO 3D mapping close to previous points. A line of ablation was then applied across the LPF, midway between the apex and base, from mid-septum to posterior wall, following which there was a mild widening of the QRS in sinus. Isoproterenol induced a different VT, with RB RA morphology (VT2) [Figure 1A1] that alternated with the original VT1. VT2 was mapped by earliest activation on CARTO to an anterolateral LV site (presumably LAF) and was ablated there with temporary success. There was a later recurrence of a non-sustained third type of VT and PVCs, the morphology of which was very similar to the native QRS morphology (VT3) and was responsive to verapamil. Over the following day he had multiple PVCs and recurrent VT episodes that lasted several hours (VT3 morphology) [Figure 1A1] and partially responded to amiodarone.

Five months later the patient had another procedure (retrograde aortic approach) due to persisting symptomatic PVCs of the VT3 morphology. Left ventricular CARTO mapping showed an exit point at the apical low septal area. Ablation there caused a change in VT morphology similar to the original VT1. A re-map of that VT showed an exit point and a pre-potential (earlier

Table 1. ECG characteristics

Patient #	Arrhythmia	Baseline ECG in SR	QRS width during VT (ms)	VT axis	Precordial QRS configuration during VT[§]	False tendon (Yes/No)
1	VT1 VT2 VT3	S–I, aVL Q–II,III,aVF; S–I,aVL Q–II,III, aVF; S–I, avL, T↓-II, III, aVF	80 90 85	RBLA RBIA Similar to sinus	– Sinus type Sinus type	No
2	VT1 VT1 post ablation VT2	S–aVL Q–III, aVF; S–avL, T↓-II, III, aVF Q–III, aVF; S–avL, T↓-II, III, aVF	80 90 90	RBSA RBSA RBIA	– – ICRBBB type[‡]	No
3	VT1 VT2 VT3 after 2 years	S–aVL S–aVL Normal	90 90 90	RBSA RBIA RBLA: 30°	– ICRBBB type ICRBBB type	No
4	VT1 VT2 VT1 after 8 years VT2 after 8 years	S–III S–I, aVL; T↓-II, III, aVF S–I, aVL S–I, aVL	90 90 105 125	RBSALA RBRA RBSALA RB normal axis	– ICRBBB type ICRBBB type	No

[§]QRS during VT presumed to be upper septal – identical to sinus or ICRBBB type

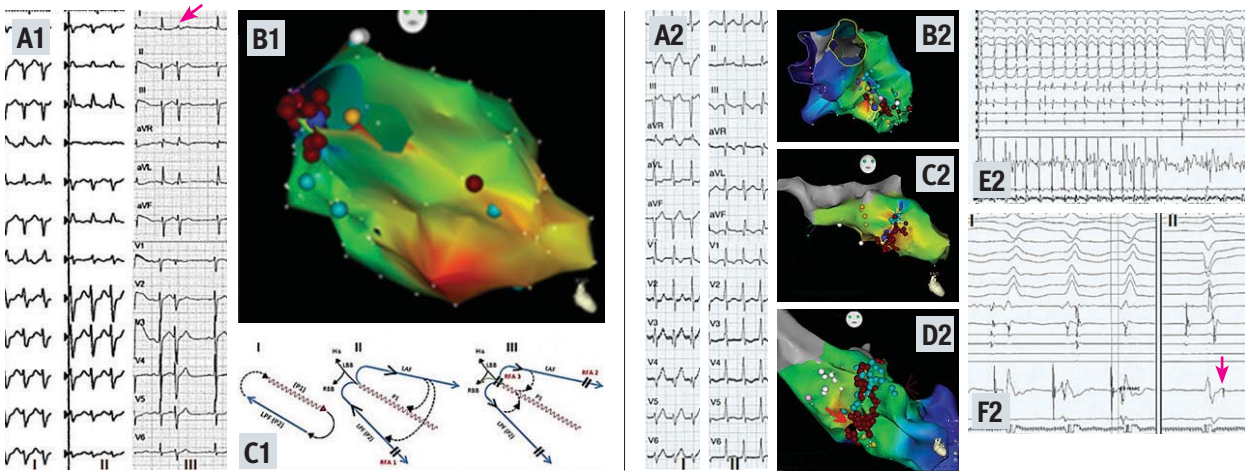
[‡]Correlated with type II (less basal) upper-septal FVT [10].

ICRBBB = incomplete right bundle branch block, ECG = electrocardiogram, VT = ventricular tachycardia, RBLA = right bundle left axis, RBIA = right bundle, inferior axis, SR = sinus rhythm, RBSA = right bundle superior axis, RBSALA = right bundle superior axis left axis

Figure 1. Patient 1 (A1–C1) and patient 2 (A2–F2)

Patient 1: **[A1]** ECG of VT1 (I) and VT2 (II) and PVCs of VT3 morphology (III-arrow). **[B1]** CARTO map of successful ablation site (red dots) close to His-bundle region (yellow). **[C1]** Schematic representations of a suggested intraventricular activation sequence during the ablation-induced change in the route of fascicular VTs. **I.** During common FVT (VT1), the impulse propagates antegradely from the basal to the apical site, down the mid septum (diastolic pre-potential, P1), then the activation goes retrogradely to the LPF (pre-systolic pre-potential, P2). **II**. After RFA of the distal LPF, probably distal to the circuit, blocking antegrade activation of the LV down the septum, the exit activates the proximal LPF retrogradely and then the LAF antegradely, then the proximal LPF or septal fascicle retrogradely (VT2). **III.** Ablation at the distal LAF changed the tachycardia circuit into VT3, a narrow complex variant that was finally ablated at a high septal location. VT3 used the remaining proximal LAF as an antegrade limb and the septum as the retrograde limb with simultaneous conduction to the right ventricle over the RBB; or VT3 used the remaining fibers of both the LPF and LAF as simultaneous antegrade limbs and the septal fascicle as retrograde limb that was successfully ablated

Patient 2: **[A2]** ECG of VT1 (I) and VT2 (II). **[B2]** Site of ablation #1 on CARTO map (red dots). **[C2]** Site of ablation #2. **[D2]** Site of ablation #3 (His-bundle cloud [white], LAF [light blue], LPF and LBB [yellow], ablation sites [red], VT terminated [black dot and arrow]). **[E2]** VT terminated during ablation. **[F2]** P1 signal before (I) and after (II) ablation. After the ablation P1 signal (arrow) was seen after the QRS complex during sinus rhythm



ECG = electrocardiogram, FT = fascicular tachycardia, FVT = fascicular ventricular tachycardia, LAF = left anterior fascicular, LPF = left posterior fascicle, LV = left ventricular, PVC = premature ventricular contractions, RFA = radiofrequency ablation, VT = ventricular tachycardia

*CARTO (Biosense Webster, Diamond Bar, CA, USA)

than His-bundle recording) in high septum close to the His-bundle area and under the aortic cusp [Figure 1B1]. Catheter bumping caused a temporary discontinuation of the tachycardia. Further cryoablation in this location caused a gradual slowing and discontinuation of the VT. Recurrence of VT necessitated RF application in the same location, causing termination of the arrhythmia with no residual arrhythmia of any morphology. Follow-up of more than 1 year (clinical and holter recordings) off medications was uneventful and free of arrhythmia.

Case 2

A 34 year old healthy male with no structural heart disease had recurrent symptomatic VT episodes at 220 bpm with narrow complex QRS and RB SA morphology, which were suspected to be of LPF origin (VT1) [Figure 1A2]. During EPS (a retrograde approach), the VT was easily induced and entrained from the LPF area. Using CARTO 3D for mapping the earliest activation as well as Purkinje and fascicular signals (P1 and P2) during tachycardia, the LPF was ablated at a distal-apical area [Figure 1B2]. The VT was still inducible at the end of the procedure, but due to the prolonged procedure time and multiple applications, the procedure was discontinued. Overnight in the hospital the patient had the same VT1 episodes, but slower (150 bpm) and persistent. They became incessant, very symptomatic, and could not be terminated by verapamil or flecainide or by recurrent DC cardioversion. Only after the infusion of intravenous amiodarone did the patient return intermittently to normal sinus rhythm (NSR).

The next day a redo procedure was conducted using an antegrade transseptal approach and CARTO 3D mapping. PES from the atria induced similar VT1. Ablation at the distal LPF location had terminated the VT during ablation with non-inducibility of the arrhythmia thereafter [Figure 1C2].

ECG during NSR post-procedure demonstrated T wave inversion in inferior leads and V4–V6. One hour later the VT recurred; this time the axis was changed to a more inferior axis (IA) and ICRBBB vs. ECG during sinus rhythm. It became incessant despite IV verapamil, amiodarone, beta blockers, and

Table 2. Electrophysiological characteristics

Patient #	Arrhythmia	VTCL (ms)	VT Axis	HV during sinus vs. VT (ms)	Mechanism (reentry or micro-reentry/ focal)	Entrained from ablation site (Yes/No)	FP was seen on ablation site (Yes/No)	Wobble confirmed role of potentials§ (Yes/No)	Ablation sites
1	VT1	300	RBSA	50/10	?	No	Yes	No	LPF, midway between the apex and base, from mid-septum to posterior wall
	VT2	286	RBIA	NA/negative	?	No	Yes	No	LAF
	VT3	330	RBRA	NA/NA	?	No	Yes	No	High septum close to and above His-bundle, below aortic cusp (cryo)
2	VT1	274	RBSA	NA	Reentry	Yes	Yes	No	LPF-distal apical
	VT1 post ablation	381	RBSA	59/negative	Reentry	Yes	Yes	No	Distal LPF
	VT2	375	RBIA	65/15	?	Not attempted	Yes	No	Distal LBB, proximal LPF, LAF, and midway
3	VT1	261	RBSA	42/negative	?	No	Yes	No	LPF= earliest PP and pace-map
	VT2	261	RBIA	42/ 10	?	No	Yes	No	LAF = close to His-bundle (caused LBBB)
	VT3 after 2 years	286	RBLA-30°	NA	NA	NA	NA	NA	Not ablated
4	VT1	375	RBSALA	50/25	X	X	Yes	Yes	Distal LPF
	VT2	333	RBRA	50/25	X	X	Yes	X	Distal LAF and a line connecting LPF
	VT1 after 8 years	353	RBSALA	60/not seen	?	No	Yes	No	DCCV
	VT2 after 8 years	305	RB normal axis	60/not seen	?	No	Yes	No	Midway LPF–LAF distal and LBB

§changes in fascicular potentials (FP-FP) drove changes in ventricular potentials (V-V)

N/A = data not available, LPF = left posterior fascicle, LAF = left anterior fascicular, ICRBBB = incomplete right bundle branch block, ECG = electrocardiogram, VT = ventricular tachycardia, RBLA = right bundle left axis, RBIA = right bundle, inferior axis, LBBB = left bundle branch block, RBSA = right bundle superior axis, RBSALA = right bundle superior axis left axis

recurrent DC cardioversion, but was slowed with the drugs [VT2, Figure 1A2].

After 5 days the patient was referred for a third procedure (retrograde approach). The diastolic Purkinje (P1) potentials were mapped during NSR using the CARTO 3D system. VT2 was easily induced. The distal left common fascicle (LBB) was ablated far from the His-bundle and then a proximal application of both fascicles, first the anterior then the posterior, terminated the VT just when ablating midway between them [Figure 1D2, Figure 1E2]. After termination of the tachycardia, the diastolic potential (P1) was noted to occur after the QRS complex during sinus rhythm [Figure 1F2]. We could not induce VT at the end of the procedure with PES from ventricle or atrium using various cycle lengths, nor could we induce PVCs with similar morphology to VT (i.e., ventricular echo beat). All medications were discontinued the same day with an early discharge.

A follow-up (clinical and holter recordings) of more than 1 year with the patient not taking medications was uneventful, with freedom from arrhythmia.

Case 3

A healthy 24 year old male presented with normal echo and recurrent episodes of stress-induced palpitations since the age of 17, lasting up to several hours and leading to multiple hospitalizations. The first episode was associated with fever and was mistakenly diagnosed as supra-ventricular tachycardia (SVT). Only one sustained episode required hospitalization and has been well documented: VT with RB-left axis (LA) morphology at 240 bpm, not responsive to adenosine but terminated with verapamil. The patient underwent RFCA of LPF. VT was ablated at a site where earliest activation was -40 ms. The procedure was acutely successful; however, recurrent VT occurred the following night. The frequency of the episodes was aggravated but they were relatively controlled by low doses of verapamil.

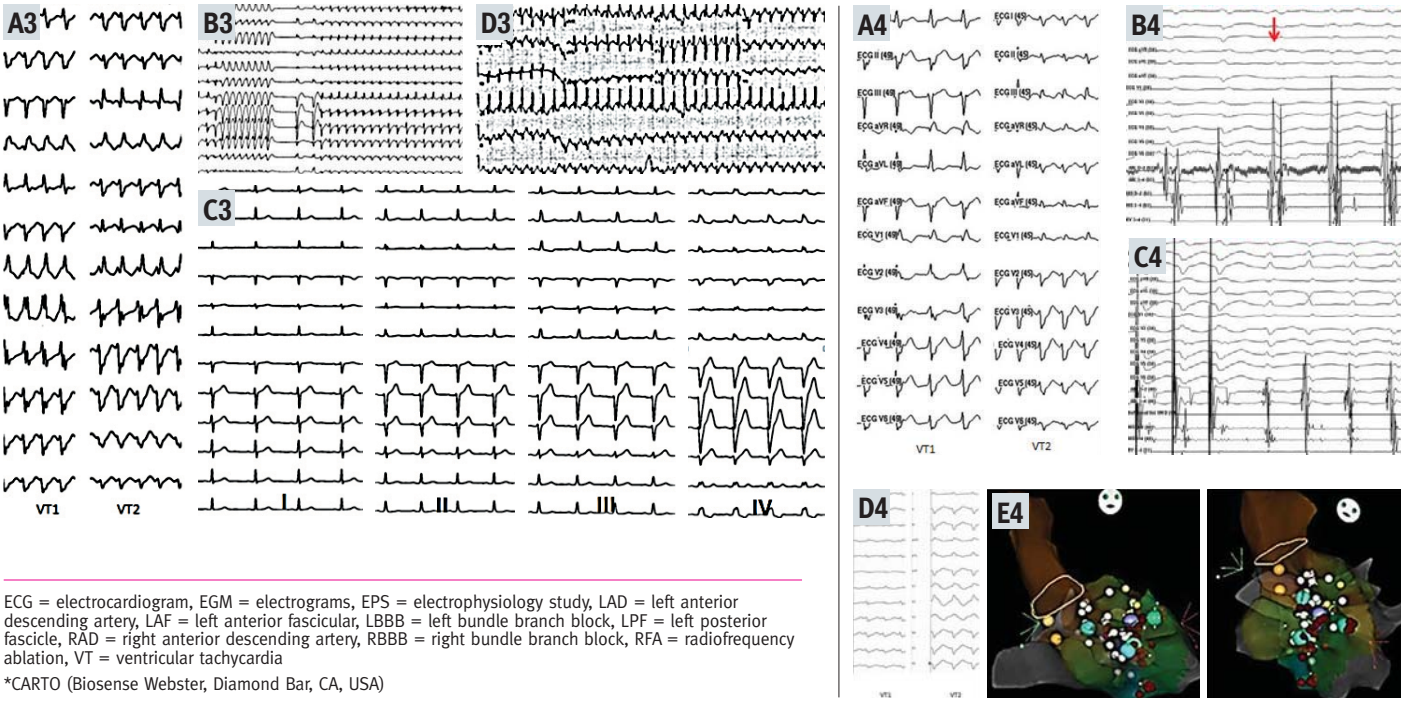
A redo procedure was conducted 4 months later at another hospital. EPS showed normal baseline measurements. The clinical VT could not be induced with rapid atrial or ventricular pacing, but was induced under the infusion of isoproterenol (VT1, RB-LA, 230 bpm) [Figure 2A3], although it was non-sustained. The LPF was mapped in NSR and ablated where a very early Purkinje potential of the LPF was recorded and a good pace-map was achieved. Transient rapid ectopic ventricular rhythm identical to clinical VT was observed during the RF pulse.

Pacing after ablation caused reproducible induction of non-sustained and then sustained VT of a different morphology at 230 bpm compatible with antegrade activation over the LAF (VT2) [Figure 2A3]; therefore, ablation of this fascicle was attempted. RF was delivered during VT at this presumed area where the Purkinje potential preceded the QRS by 30 ms. A very short proximal pulse at the LAF site close to the His-bundle region (7 seconds, 7 Watts, 52 degrees) was applied. Immediately afterward, complete left bundle branch block (LBBB) was seen on several sinus beats (with PR 140 ms, AH 84 ms, and HV 42 ms) associated with incessant VT2 [Figure 2B3, Figure 2C3] that partially responded to verapamil and selective beta blockers. Two hours later LBBB disappeared. Since the disappearance of the LBBB, no sustained VT has occurred. A few PVCs were still present intermittently. The next day, the patient underwent an exercise ECG test showing a few PVCs

Figure 2. Patient 3 (A3–D3) and patient 4 (first procedure [A4–C4] and second procedure [D4–E4])

Patient 3: [A3] ECG of VT1 and VT2 **[B3]** A very short pulse was given at the LAF site. Immediately afterward, complete LBBB was seen associated with incessant VT2. **[C3]** Baseline ECG (I), before RFA (II), post RFA of LPF (III) and post RFA of proximal LAF (showing LBBB) (IV), after which incessant VT occurred and stopped once the LBBB had resolved. **[D3]** ECG of VT3

Patient 4: [A4] ECG of VT1 (RBBB LAD) and VT2 (RBBB RAD). **[B4]** EGM of transformation from VT1 (LAD) to VT2 (RAD) during ablation at distal LPF site (arrow). **[C4]** Induction of VT2 (RBB RAD) with LPF pacing, showing a different QRS morphology versus that produced during LPF pacing. **[D4]** ECG of clinical VT (original VT2) and ECG of original VT1 induced during EPS with isuprel only. **[E4]** CARTO* images of ablation sites (His-bundle [yellow], fascicular potentials [white], ablation sites [red], pacing sites on top of fascicular potentials [large turquoise and purple], posterior fascicle [grey], anterior fascicle [blue])



ECG = electrocardiogram, EGM = electrograms, EPS = electrophysiology study, LAD = left anterior descending artery, LAF = left anterior fascicular, LBBB = left bundle branch block, LPF = left posterior fascicle, RAD = right anterior descending artery, RBBB = right bundle branch block, RFA = radiofrequency ablation, VT = ventricular tachycardia

*CARTO (Biosense Webster, Diamond Bar, CA, USA)

and couplets. No VT was induced during maximal exercise. The patient was discharged with beta blockers and verapamil.

On follow-up 2 years later the patient had several short-lasting episodes of palpitations after the last ablation. He also had documented sustained VT 2 years post-ablation, which was terminated with verapamil. Surprisingly, the ECG during that VT showed another type of VT (VT3) that was not seen during ablation. It showed RB with LA of -30 degrees; that is, an axis that was much less negative than VT1 (VT3) [Figure 2D3]. QRS during sinus rhythm was perfectly normal, without LBBB or fascicular block.

Case 4

A 57 year old healthy male was hospitalized for a first documented episode of sustained VT lasting 1 hour. He had a normal baseline ECG in sinus, normal echo, and a history of frequent episodes of palpitations lasting a few minutes during the month preceding his hospitalization. On admission, VT at 160 bpm (RB SA LA morphology) was converted to sinus with IV lidocaine. QRS alternans was noted during VT (VT1) [Figure 2A4]. He was discharged on beta blockers and referred for ablation 2 weeks later.

RADIOFREQUENCY ABLATION #1

Clinical VT1 was induced and remained sustained, mainly during infusion of isoproterenol. When variations in the tachycardia CL were observed, changes in fascicular potentials (FP-FP) drove changes in ventricular potentials (V-V). In addition, the FP preceded the ventricular electrogram and the HV interval was very short during FT. These observations served to exclude bundle branch reentry (BBR) and myocardial VT. During radiofrequency ablation (RFA) at the distal LPF site there was a transformation of that VT to another type with RB RA deviation [Figure 2B4]. The latter VT (VT2) [Figure 2A4] could be induced with LPF pacing [Figure 2C4] and was successfully ablated with RFA delivered at the LAF site and then a continuation of that line, thereby connecting LPF and LAF distally. No VT could be induced at the end of the procedure with ventricular pacing and IV isoproterenol.

RADIOFREQUENCY ABLATION #2

The patient was arrhythmia-free and doing well for the next 8 years, when he felt four episodes of palpitations lasting 10 minutes each. Six months later he had a long-lasting episode and presented to the emergency department with wide-complex tachycardia 165 bpm and QRS morphology resembling VT2 [Figure 2D4] that was observed during the previous procedure. IV adenosine did not affect the VT. This VT terminated spontaneously after a few minutes. Baseline ECG in sinus was normal with no LPF or LAF block. The patient was treated with flecainide and beta blockers until 24 hours prior to a redo-procedure, using retrograde aortic approach and CARTO 3D mapping.

There was no induction of any arrhythmia using rapid atrial, RV, or LV pacing. Under isoproterenol infusion, LV pacing induced VT1 (RB LA morphology) [Figure 2D4] 170 bpm that lasted 8 seconds and transformed spontaneously to VT2 (apparently the clinical VT observed a few weeks before) that had smaller and narrower QRS with RB and normal axis morphology and a distal to proximal direction of activation according to propagation map in CARTO 3D mapping. The latter was sustained and less hemodynamically stable, necessitating DC cardioversion.

Ablation was based on earliest activation and pace-mapping data and recording of fascicular potentials in sinus rhythm. It was a distal line of ablation connecting LPF and LAF, crossing the mid-septum, presumably the septal fascicle area [Figure 2E4], but catheter trauma to the LBB (with HV prolongation to 76 ms) was observed and resolved after 30 minutes. At the end of the procedure there was no inducible arrhythmia despite multiple attempts of LV pacing with and without isoproterenol. Final ECG showed HV of 60 ms with LPF block. The patient was discharged on beta blocker treatment.

DISCUSSION

Nogami et al. [3,4] and Sung et al. [9] described the complex interplay between the anatomy of the three left fascicles (posterior, anterior, septal/auxiliary). These fascicles create different morphologies of fascicular VTs that can either exist exclusively or can interchange in the same patient, spontaneously or sometimes following ablation of one fascicle [9]. The explanations given for underlying mechanisms of LV VT are not well known and their fascicular origin is still debated.

Our case series shows that the interchange between the fascicles might cause a change in clinical course when shifting from one route to another and sometimes might aggravate symptoms (no response to medications or DC cardioversion), necessitating ablation at the other hemifascicle or at the basal septal areas, and aimed at either the upper septal fascicle (the retrograde final common pathway of all tachycardias) or close to the confluence of the posterior and the anterior hemifascicles, thus affecting both. Ablation in basal septum carries a particular risk of bundle/AV nodal block. Fortunately these complications were transient in our patients.

POSSIBLE MECHANISMS OF OUR CASE SERIES

Case 1

The original VT (VT1) was an LPF VT that changed its exit site by ablation of the LPF, probably distal to the circuit, blocking antegrade activation of the LV down the septum (without abolishing the actual VT circle). Thus, the exit activated the proximal LPF retrogradely and then the anterior (or septal) fascicle antegrade to the rest of the ventricle [Figure 1C1]. Therefore during VT there was a change in ventricular activation pattern into LAF VT pattern (VT2 – RB RA pattern). Ablation at the LAF area again changed the tachycardia circuit into VT3, a narrow complex variant that was finally ablated at the second procedure at a high septal location [Figure 1C1].

The morphology of VT3 that was very similar to the sinus QRS can be explained by one of two previously described pathways [4,9]. One is that VT3 used the remaining LAF as an antegrade limb and the septum as the retrograde limb with simultaneous conduction to the right ventricle over the RB branch (RBB), creating a balanced narrow QRS [9]. This tachycardia was abolished by ablating its retrograde limb (the septal fascicle) at the high septum. The other potential explanation is that VT3 used the remaining fibers of both the LPF and LAF as simultaneous antegrade limbs (thus forming a balanced narrow QRS) and the septal fascicle as retrograde limb that was successfully ablated [Figure 1C1] [4,10,11].

Cases 2 and 4

Both left anterior and posterior fascicles are the antegrade limbs of the reentrant circuit in VT, and the specialized Purkinje tissue at the left ventricular upper septum or a proximal intermediate fascicle is the common retrograde limb of the circuit in VT and is the ablation target.

Another mechanism assumes persistent LPF VT with an aberrant exit and a very proximal (high septal) circuit [12]. In a fascicular VT, arising in the proximal conduction system (such as bifurcation, LPF, or LAF), when we ablate at a more distal site, there is essentially an antegrade exit block through that fascicle. The same focus/micro-reentrant circuit will then have to exit either through the LAF, intermediate fascicles, or RBB with an LBBB morphology VT (e.g., when LAF is bumped).

The circuit of the proximal type of the LAF VT is as follows: During VT, the antegrade limb is the proximal portion of the specialized Purkinje tissue with decremental properties and the retrograde limb is the Purkinje fibers near the LAF.

Initially the reentrant circuit revolves around the LPF and septal fascicles. After ablation of LPF (with either antegrade block or with significant conduction delay), the tachycardia

circuit switches to revolve around the LAF and septal fascicles, resulting in RA IA morphology VT.

Kottkamp and colleagues [8] reported one patient who had two left VT configurations with RA deviation and LA deviation. In the patient, RF catheter ablation delivered to the single site between the LAF and LPF successfully eliminated both VTs. This outcome suggests a septal common pathway for both tachycardias [4,10,11].

Sung and co-authors [9] showed that only by ablating the auxiliary fascicle did they terminate all VT forms. Ablation of only the antegrade limbs (LPF and LAF) resulted in BBRT due to persistent retrograde limb. Ablation of the auxiliary fascicle was based on concealed entrainment mapping, localizing concealed entrainment to the region just apical to the LBB, or an attempted line of ablation just distal to the LBB extending from a region close to the LAF to a region close to the LPF in an attempt to transect the auxiliary fascicle.

Other theoretical explanations cannot be ruled out from our EP studies. For example, we cannot rule out from the ECG a new-onset upper septal fascicular VT (FVT) [13] or a focal Purkinje VT (propranolol-sensitive automatic VT) that started after the ablation of the first reentrant VT [14,15], perhaps from a more proximal portion of the fascicle. Those patients exhibit RB-LA morphology and an HV interval during VT that is shorter than during sinus, similar to the reentrant fascicular type. This automatic/trigger-based VT [16] can be induced by exercise and catecholamines, and cannot be induced or terminated by PES from ventricles. It is responsive to lidocaine and beta blockers and usually does not respond to verapamil. It may be transiently suppressed by adenosine and overdrive pacing. They respond poorly to catheter ablation. Some of our patients were responsive to verapamil before their first ablation but were responsive to beta blockers alone after the first ablation, suggesting a theoretical change in the underlying mechanism.

Case 3

In this case, another mechanism was probably responsible for the incessant VT that started after the last proximal RFA. The incessant VT started only after the LBB was damaged but not eliminated [Figure 2B3]. The VT stopped after the LBBB resolved. Thus, the mechanism of the VT was iatrogenic; that is, it was caused by slowing the conduction over the LBB, enabling a slow and stable incessant VT cycle to occur. Once the conduction over the LBB was recovered, the VT stopped. This result was a clear example of the iatrogenic origin of this multiform VT concept; only by damaging some fascicles could other routes be formed and cause sustained tachycardia.

The pro-arrhythmic effect of the ablation that caused LBBB can be explained in few ways:

- A change in the conduction of the reentry cycle due to damage of the tissue that is part of the circuit, thus when the conduction is slower the arrhythmia becomes incessant
- A mechanism of concealment that is changed after the RFA, thereby parts of the reentry cycle are no longer refractory when the electrical activity comes from a different direction

LIMITATIONS

The most significant limitation of our study was the sample size; however, previous studies had also described the rarity of upper-septal VT [10,13], septal fascicle in human hearts [11], and multiform fascicular VT [9].

Another limitation relates to the possible mechanism. Similar cases were first described by Sung et al. [9] and then by Nogami et al. [3,4]. It is difficult to be sure whether the varied arrhythmias were related to mechanical damage as posited by Nogami or whether the original FT actually involved the mid-septal fascicle initially. In addition, extensive entrainment mapping could not be performed in all cases, thus we could not rule out in all cases the presence of a proximal triggered focus that had changed its VT morphology by ablating different exits. Furthermore, previous studies of FT have used 3D or multipolar catheters to clearly delineate the circuit and demonstrate antegrade vs. retrograde conduction along the fascicles [4,5]. Without these catheters, it may be difficult to distinguish between inter-fascicular VT and intra-fascicular VT (verapamil-sensitive LAF VT) by the surface ECG. Intracardiac recordings of LPF can show whether this is the retrograde limb (in inter-fascicular VT) or a bystander (as in LAF VT) [4,17]. Since these catheters were not used, we could not rule out that the true origin of the tachycardia may actually be in the atrio-ventricular junction or His-bundle, given the remarkable similarity to sinus rhythm in QRS duration and axis in Case 1. Thus when we mapped the exit site or the distal fascicles, they were the earliest that we saw, but they could have been passively activated by an upstream source. To prove this, we needed to prove that the His-bundle activation was retrograde. However, we think that the combination of 3D EAM to define spatial location and multipoint fascicular activation mapping with the ablation catheter was sufficient to determine the direction of fascicular conduction.

CONCLUSIONS

We present four cases of FT with changing morphologies related to ablation that caused a change and even aggravation in clinical course when shifting from one reentry circuit to another. Septal fibers play a key role in maintaining changing VT patterns; thus, targeting the septal proximal conduction system (areas such as bifurcation, LPF, LAF, high septal/auxiliary pathway) is very useful in terminating and preventing all types of tachycardias. In summary, some FVT patients may have multiple pathways/mechanisms. In these cases careful mapping looking for fascicular potentials and ablating as proximally as possible yields success.

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Capsule

Progress for pulmonary arterial hypertension (PAH)

In pulmonary arterial hypertension (PAH), pulmonary arteries are thickened and occluded, and mitochondrial respiration is suppressed. **Michelakis** and colleagues treated lungs from PAH patients with dichloroacetate, a drug that inhibits the mitochondrial enzyme pyruvate dehydrogenase kinase. Dichloroacetate increased mitochondrial function, but the response was variable. This variable response was mirrored in a phase 1 trial, with some patients showing improved hemodynamics and functional capacity. Interestingly, patients with inactivating mutations in two genes encoding mitochondrial proteins were less responsive to dichloroacetate.

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Capsule

Varus thrust and incident and progressive knee osteoarthritis

To determine if varus thrust, a bowing out of the knee during gait (i.e., the first appearance or worsening of varus alignment during stance), is associated with incident and progressive knee osteoarthritis, **Sharma** et al. undertook an osteoarthritis initiative ancillary study. The incident osteoarthritis sample included 4187 knees (2610 persons); the progression sample included 3421 knees (2284 persons). In knees with osteoarthritis, thrust was associated with progression as assessed by each outcome measure, with adjustment for age, sex, body mass index, and pain on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale. In knees without osteoarthritis, varus thrust was not associated with incident osteoarthritis or other outcomes. After adjustment for alignment, the thrust–progression association was attenuated, but an independent association persisted for partial-grade JSN and JSW loss outcome models. WOMAC pain and alignment were consistently associated with all outcome measures. Within the stratum of varus knees, thrust was associated with an increased risk of progression.

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