

## Characterization of Anatomic Ventricular Tachycardia Isthmus Pathology After Surgical Repair of Tetralogy of Fallot

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**Background**—Although catheter ablation has been used to target the critical isthmuses for re-entrant monomorphic ventricular tachycardia in tetralogy of Fallot, the anatomy and histology of these regions have not been fully characterized. Autopsy hearts with tetralogy of Fallot were evaluated to clarify the pathological substrate.

**Methods and Results**—Twenty-seven hearts with the diagnosis of tetralogy of Fallot were examined. Anatomically defined isthmuses included (1A) ventriculotomy-to-tricuspid annulus, (1B) ventriculotomy-to-ventricular septal defect patch, (2) ventriculotomy-to-pulmonary annulus, (3) pulmonary annulus-to-ventricular septal defect patch, and (4) ventricular septal defect patch-to-tricuspid annulus. Length and wall thickness were measured for all specimens, and light microscopy was performed for those surviving surgery. For subjects  $\geq 5$  years at death, isthmuses 1A and 1B were present in 88%, isthmus 2 in 25%, isthmus 3 in 94%, and isthmus 4 in 13%. Isthmus 1A had the greatest dimensions (mean length,  $3.9 \pm 1.08$ ; thickness,  $1.5 \pm 0.3$  cm), isthmus 1B intermediate dimensions (mean length,  $2.4 \pm 0.8$ ; thickness,  $1.1 \pm 0.4$  cm), and isthmuses 2, 3, and 4 the smallest dimensions (mean length,  $1.5 \pm 0.5$ ,  $1.4 \pm 0.8$ , and  $0.6 \pm 0.4$  cm; thickness,  $0.5 \pm 0.2$ ,  $0.6 \pm 0.2$ , and  $0.3 \pm 0.04$  cm, respectively). Histological examination ( $n=7$ ) revealed increased fibrosis in anatomic isthmuses relative to nonisthmus controls.

**Conclusions**—Consistencies in isthmus dimensions and histology are found among patients with repaired tetralogy of Fallot. Isthmus 1A is associated with the largest morphological dimensions, whereas the nearby newly described isthmus 1B is significantly smaller. Of isthmuses with the smallest dimensions, isthmus 3 is the most common. (*Circ Arrhythm Electrophysiol.* 2013;6:905-911.)

**Key Words:** catheter ablation ■ congenital heart disease ■ isthmus ■ tachycardia, ventricular ■ tetralogy of Fallot

Ventricular tachycardia (VT) is a major source of morbidity and mortality for patients with repaired tetralogy of Fallot (TOF). Risk factors predictive of sudden cardiac death closely linked to ventricular arrhythmia in this population include palpitations and syncope,<sup>1,2</sup> QRS duration,<sup>3,4</sup> prior palliative repair,<sup>2,4,5</sup> the presence of a discrete ventriculotomy,<sup>4,6</sup> and right ventricular (RV) dilation.<sup>7,8</sup> More recently, left ventricular dysfunction has also been implicated in cases of sudden cardiac death.<sup>4,9</sup> Catheter ablation for VT has been used with increasing success but reasons for failure include nonsustained episodes of induced VT, poor hemodynamic tolerance of VT, or inadequate modification of the arrhythmia substrate. In addition, recurrences have been noted, suggesting the possibility of incomplete conduction block.<sup>10,11</sup>

The pathological substrate responsible for the re-entrant monomorphic VT circuit has been shown to involve discrete isthmuses between both anatomic and surgically induced barriers that are critical to successful repair of TOF.<sup>12</sup> Although commonly targeted for ablation, detailed pathological and

anatomic analyses of these isthmuses have not been performed. We sought to examine the morphological characteristics of these ventricular isthmuses in a large group of archival hearts with a history of surgically repaired TOF, hypothesizing that significant differences in substrate pathology exist. We also considered a previously undescribed isthmus between the ventriculotomy incision and the ventricular septal defect (VSD) patch as a potential alternative for catheter ablation.

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### Methods

The autopsy and surgical pathology databases at UCLA were searched for cases of TOF and its major variants (including TOF with pulmonary atresia and TOF with absent pulmonary valve). Baseline demographic and clinical data were obtained from the medical records. All specimens were evaluated for the presence of naturally or surgically related anatomic isthmuses corresponding to those that have been previously described. In addition, isthmus 1 was redesignated as 1A,<sup>12</sup> and

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the previously undescribed but adjacent isthmus between the ventriculotomy incision and the VSD patch was classified as 1B. Using this new classification, anatomic isthmuses included (1A) ventriculotomy-to-tricuspid annulus, (1B) ventriculotomy-to-VSD patch, (2) ventriculotomy-to-pulmonary annulus, (3) pulmonary annulus-to-VSD patch, and (4) VSD patch-to-tricuspid annulus (Figure 1). For all subjects (n=27), isthmus dimensions were recorded, which included both isthmus length, the shortest distance between 2 nonconducting barriers (along the presumptive path of targeted catheter ablation lesions), and isthmus thickness corresponding to the minimum and maximum ventricular wall thickness in this area measured from the endocardium to the epicardium. Care was taken to exclude epicardial fat in the measurement of the latter isthmus, and this was manually removed if necessary from the coronary vessels and the atrioventricular groove to visualize the myocardium.<sup>13</sup> For subjects surviving surgical repair (n=7), tissue from the previously defined isthmuses was excised, processed routinely, and sectioned. Slides were stained with hematoxylin-eosin and trichrome/elastic-Van Gieson. Several sections were prepared to confirm whether a complete isthmus of myocardium was present. In some cases, as many as 15 serial sections, 4- $\mu$ m thick, were evaluated from a single paraffin block. Morphological examination included measurement of the degree of secondary endocardial fibroelastosis as described previously,<sup>14</sup> as well as a quantitative assessment of the combination of interstitial myocardial fibrosis and replacement myocardial fibrosis. The quantitative assessment was performed after microscopic evaluation of the entire length and depth of the ventricular isthmus, with the percentage of total isthmus determined by visual inspection. Percentage of fibrosis per isthmus was evaluated by microscopic examination on the trichrome-stained/elastic-Van Gieson-stained slides. Fibrosis grading was by consensus of 2 cardiac pathologists (A.S. and M.C.F.). In addition, sections were taken from the RV and left ventricular apical free wall (1 cm from the apex) in each of these specimens to serve as nonisthmus controls.

Results are presented as mean $\pm$ SD, with the exception of non-normal distributions, where medians and interquartile range are reported. Differences in isthmus length and wall thickness were analyzed with a linear mixed effects model after checking model assumptions of normality and homogeneity of variance. Significant outliers related to marked deviation from standard surgical technique were removed before analysis. In this model, isthmus category is a fixed effect, and heart specimen is a random effect. The random effect component allows multiple observations on the same individual to be correlated and is an acceptable method of dealing with data that are missing at random. Tukey honestly significant difference test was used for multiple comparisons after application of the model. McNemar test was used to evaluate differences in paired proportions between isthmus categories, using the Bonferonni-Holm method for

multiplicity of tests. Adjusted *P* values of  $\leq 0.05$  established statistical significance. Statistical analysis was performed with JMP software (SAS Inc, Cary, NC)

## Results

### Clinical Data

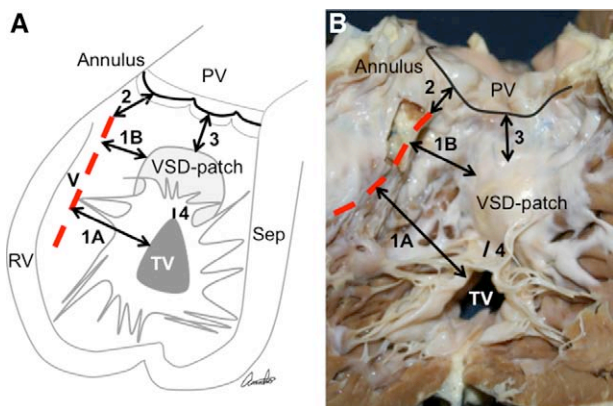
A total of 43 hearts with the diagnosis of TOF were identified, of which 27 had a history of prior surgical repair and were included in the analysis. The diagnosis was predominantly the usual morphology of TOF (n=24), whereas TOF with pulmonary atresia (n=2) and TOF with absent pulmonary valve (n=1) were also identified. A discrete ventriculotomy or patch in the RV outflow tract (RVOT; noncontiguous with the pulmonary annulus) was present in 7 specimens (26%), a transannular patch or ventriculotomy extending across the pulmonary annulus was present in 16 (59%), and a prosthetic conduit was present in 2 (7%). Two specimens had no identifiable RV incision (7%). Two patients, both with a prior transannular patch, had a bioprosthetic valve in the pulmonary position. The median age was 7.0 years (range, 35 days to 66 years), with 7 subjects surviving the surgical repair—all by  $\geq 1$  year. Two subjects surviving surgical repair had a history of implantable cardioverter-defibrillator placement with appropriate therapy for VT, and 1 patient died suddenly. Baseline demographic data and details of surgical intervention are presented in Table 1.

**Table 1. Population Characteristics**

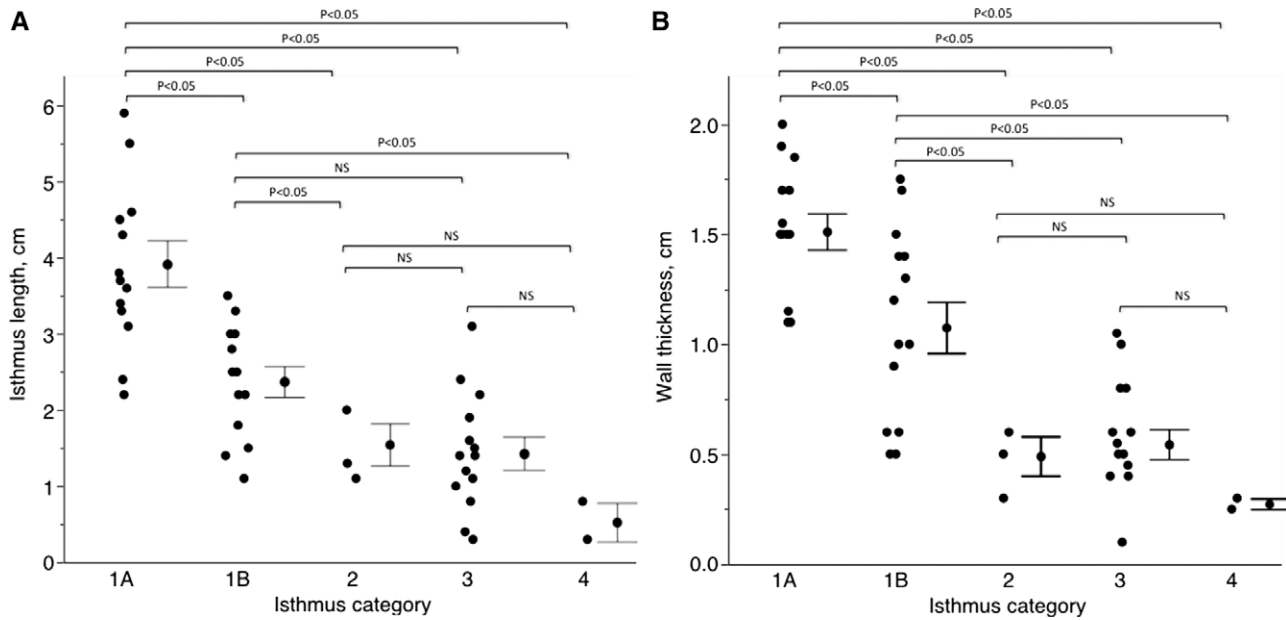
Subject Characteristic	All Subjects (N=27)	Subjects $\geq 5$ y (n=16)
Age, y	7 (2.5–12)	10 (7.3–40)
Age category, n		
<1	4	...
1–5	7	0
6–10	8	8
11–20	3	3
21–30	0	0
>30	5	5
Sex, men (%)	12 (44)	6 (38)
Heart weight, g	135 (78–240)	217 (127–585)
LV length, cm	5.4 (4.6–6.6)	6.0 (5.3–8.5)
Diagnosis (%)		
TOF	24 (89)	16 (100)
TOF/PA	2 (7)	0
TOF/absent PV	1 (4)	0
Type of RVOT surgery (%)		
Ventriculotomy	7 (26)	4 (25)
Isolated conduit	2 (7)	0
Transannular incision/patch*	16 (59)	10 (63)
None	2 (7)	2 (13)
Year of surgery	1973 (1964–1998)	1972 (1963–2002)
Postsurgical survival, y	0.003 (0.001–1.08)	0.006 (0.001–11.0)
Postsurgical survival >1 y (%)	7 (26)	6 (38)

IQR indicates interquartile range; LV, left ventricle; PA, pulmonary atresia; PV, pulmonary valve; RVOT, right ventricular outflow tract; and TOF, tetralogy of Fallot.

\*Group includes subjects with a bioprosthetic pulmonary valve (n=2). Values in parenthesis represent IQR unless specified otherwise.



**Figure 1.** **A**, Diagram of the ventricular isthmuses in modified left anterior oblique view and **B** representative gross specimen displayed in an identical view. (1A) ventriculotomy (V; dotted line)-to-tricuspid annulus, (1B) ventriculotomy-to-ventricular septal defect (VSD) patch, (2) ventriculotomy-to-pulmonary annulus (solid black line), (3) pulmonary annulus-to-VSD patch, and (4) VSD patch-to-tricuspid annulus. PV indicates pulmonary valve; RV, right ventricle; Sep, septum; and TV, tricuspid valve.



**Figure 2.** Scatter plots of length (A) and ventricular wall thickness (B) by isthmus category. The isthmus mean (center circle) and SEM (vertical bars) are displayed to the right of each sample population. Ventricular isthmus length and wall thickness both varied significantly by isthmus category.

**Gross Examination**

The presence of various isthmuses differed significantly among categories. Isthmuses 1A, 1B, and 3 were encountered more frequently than isthmuses 2 and 4 ( $P<0.001$ ). Both isthmuses 1A and 1B were present in 25 cases (93%). Isthmus 2 was present in 7 cases (26%) and was related to a discrete ventriculotomy or patch in all specimens. Isthmus 3 was present in 24 cases (89%) while being absent in the single case of TOF with absent pulmonary valve and in the 2 cases with bioprosthetic pulmonary valves that had been sewn to the region of the VSD patch in the RVOT. Isthmus 4 was least commonly seen (19%) and was identified in 3 subjects who had died in the immediate perioperative period and in only 2 surgical survivors.

Isthmus dimensions also varied significantly by category. Length of isthmus 1A was greater than the length of isthmuses 1B, 3, and 4 ( $P<0.05$ ). Maximum ventricular wall thickness also varied among categories, whereas there was no significant difference in minimum wall thickness. Mean maximum thickness was greatest for isthmus 1A relative to isthmuses 1B, 2, and 3 ( $P<0.05$ ).

There were 2 outliers related to substantial deviation in standard surgical technique. The first was a 61-year-old woman who underwent intracardiac repair in 1965. Gross evaluation revealed a circular ventriculotomy in the inferolateral RV free wall remote from both the pulmonary and the tricuspid annuli. The second was an 11-year-old girl who had undergone repair in 1972 and whose cardiac evaluation demonstrated an unusual ventriculotomy measuring 11.5 cm that extended inferiorly from the pulmonary annulus to the midportion of the RV free wall and then transversely to within 0.15 cm of the tricuspid annulus. Isthmus 1A and 2 dimensions for these subjects were significant outliers and were therefore not used in the statistical analysis.

**Subgroup Analysis**

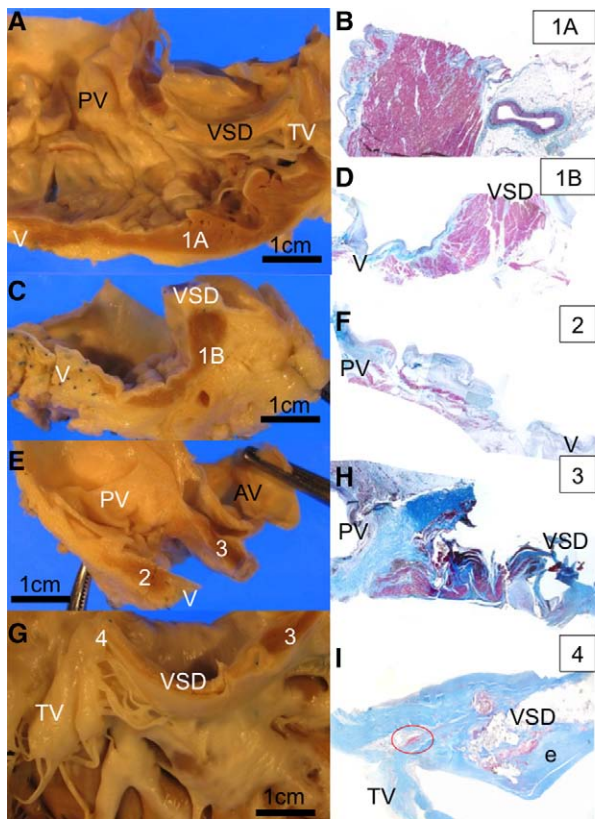
Subjects  $\geq 5$  years at the time of death ( $n=16$ ) were analyzed separately. The frequency of ventricular isthmuses again varied by category, with isthmuses 1A and 1B present in 13 cases (88%), isthmus 2 in 3 cases (25%), isthmus 3 in 14 cases (94%),

**Table 2. Summary of Anatomic Ventricular Isthmus Characteristics in the Subgroups of Patients  $\geq 5$  Years and Surgical Survivors**

Isthmus	Overall Frequency, % (n=16)	Mean Length, cm (n=16)	Mean Wall Thickness, cm (n=16)	Median Fibrosis, % (n=7)	Median EFE, mm (n=7)
1A	88	3.9 (1.08)	1.5 (0.29)	20 (10–40)	1.0 (0.9–1.0)
1B	88	2.4 (0.75)	1.1 (0.43)	35 (35–65)	2.2 (1.0–2.25)
2	25	1.5 (0.47)	0.5 (0.15)	60 (55–65)	1.8 (1.4–2.2)
3	94	1.4 (0.77)	0.6 (0.25)	50 (35–75)	1.4 (1.3–1.6)
4	13	0.6 (0.35)	0.3 (0.04)	60 (50–70)	0.9 (0.5–1.2)

Mean (SD) is reported for subgroup aged  $\geq 5$  y ( $n=16$ ) and median (IQR) for those surviving surgery that were evaluated histologically ( $n=7$ ). Wall thickness values are the maximum values observed across the isthmus. EFE indicates endocardial fibroelastosis; and IQR, interquartile range.





**Figure 3.** Representative macroscopic and microscopic anatomic isthmuses for case 3 (isthmuses 1–3) and case 5 (isthmus 4) who had a history of appropriate implantable cardioverter-defibrillator therapy for ventricular tachycardia and who died suddenly, respectively (equivalent magnification for all gross specimens). **A**, Isthmus 1A is both longer and associated with a greater wall thickness than other isthmuses. The maximum wall thickness (yellow arrowhead) is shown in **B**, where microscopic evaluation with trichrome/elastic-Van Gieson stain shows minimal replacement/interstitial fibrosis. **C**, Isthmus 1B is of a shorter dimension and lesser wall thickness, as well as noticeable fibrosis (**D**). **E**, Isthmuses 2 and 3 are shown. These isthmuses were shorter and thinner and associated with a greater degree of fibrosis (**F** and **H**). **G**, Isthmus 4 was least frequently observed but was associated with the smallest dimensions and most prominent fibrosis. **I**, Red circle highlights surviving myocyte bundles in isthmus 4 from case 5 although serial microscopic sections revealed that the isthmus was not continuous. AV indicates aortic valve; E, endocardial fibroelastosis; IF, interstitial myocardial fibrosis; p, VSD patch; PV, pulmonary valve; RF, replacement myocardial fibrosis; TV, tricuspid valve; V, outflow tract patch; and VSD, ventricular septal defect.

and isthmus 4 in 2 cases (13%). Isthmuses 1A, 1B, and 3 were more common than isthmuses 2 and 4 ( $P < 0.05$ ), similar to that of the overall population. Isthmus dimensions were likewise different among categories, with greater length for isthmus 1A compared with all other isthmus categories, including isthmus 1B (Figure 2A). Likewise, maximum ventricular wall thickness varied by category, with greater thickness for isthmus 1A versus all other isthmus categories and greater thickness for isthmus 1B versus all other categories with the exception of 1A. No significant differences in length or wall thickness were seen among isthmuses 2, 3, and 4 (Figure 2A and 2B). Subgroup characteristics are summarized in Table 2.

Gross evaluation of hearts revealed consistent anatomic findings pertinent to the ventricular wall thickness. For

isthmus 1A, minimum wall thickness was typically related to surgical thinning near the site of the prior ventriculotomy or patch. This thinning extended for a variable distance toward the tricuspid annulus where wall thickness tended to increase substantially (Figure 3). Wall thickness of isthmus 1B was more uniform than that of isthmus 1A, with the exception of occasional specimens in which a prominent parietal band coursed superiorly and laterally to the VSD patch. Isthmus 2 showed little variation in thickness dimension and was thin-walled in those specimens in which it was present. Isthmus 3 was also notable for minimal wall thickness that was related to surgical resection of the anteriorly malaligned conal septum. For isthmus 4, ventricular wall thickness was minimal for all specimens in which it was observed.

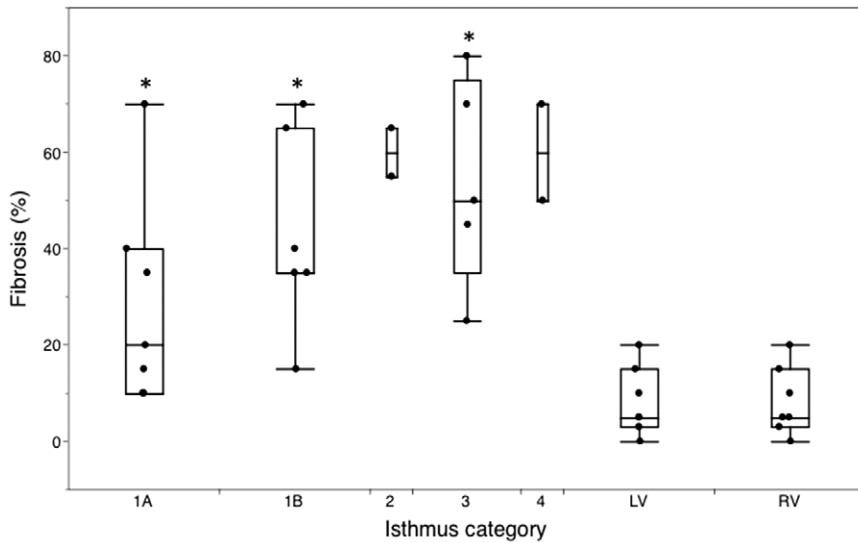
### Histological Examination

Histological examination for all cases surviving surgical repair ( $n=7$ ) revealed maximum endocardial fibroelastosis that was particularly prominent at sites of prior surgery, including the VSD patch and the RV free wall incision. The median maximal endocardial fibroelastosis for all isthmuses was 1.03 mm, ranging from 0.12 to 4.0 mm. The degree of interstitial fibrosis and replacement fibrosis was significantly greater than the nonisthmus apical control sections for isthmuses 1A, 1B, and 3 ( $P < 0.05$ ; Figure 4). The mean ratio of maximal endocardial fibroelastosis to wall thickness was 48% for isthmus 2, 35% for isthmus 4, 29% for isthmus 3, 19% for isthmus 1B, and 8% isthmus 1A ( $P=ns$ ). For case 5, surviving myocyte bundles were encountered at an initial section of isthmus 4 but not in remaining sections, indicating the absence of a true isthmus for this case (Figure 3G). In addition, clinical correlation for case 7 revealed the presence of isthmus 4 in a prior surgical report (VSD patch closure), whereas no evidence of this isthmus was present at microscopic analysis. Details of the histological examination for the 7 surgical survivor cases are given in Table 3.

### Discussion

We report the first detailed analysis of the gross anatomic and histological characteristics of the known potential VT isthmuses in patients with surgically repaired TOF. The 3 major findings in this study are that (1) the various ventricular isthmus categories are significantly different in terms of their overall geometric size, with isthmus 1A larger than the remaining isthmuses, (2) the presence of the various VT isthmuses is highly variable (in particular, isthmuses 1A, 1B, and 3 are most frequently observed), and (3) a substantial amount of fibrosis is observed in all of these anatomic regions after surgical repair when compared with nonisthmus sites, with implications for their role in arrhythmogenesis.

This first finding has potential value for catheter ablation for interruption of re-entrant VT after repair of TOF because inadequate modification of the isthmus substrate may be more likely to occur in regions of lengthier or thicker ventricular tissue. Longer isthmus targets may yield unsatisfactory results because gaps in linear ablation and recurrences are typically more common as the length of the targeted isthmus increases.<sup>15</sup>



**Figure 4.** Box-plots of percentage of fibrosis by isthmus category. Upper and lower margins of boxes correspond to the interquartile range, whereas center horizontal line corresponds to the median for each group. The box width is proportional to the number of observations in each isthmus category. \*Isthmuses 1A, 1B, and 3 contained significantly greater degrees of fibrosis than the control sections taken from the right ventricular (RV) apex and left ventricular (LV) apex.

In addition, the creation of lesions with deep tissue penetration seems to be a requirement for transection of the ventricular isthmus in the setting of TOF<sup>16</sup> similar to the situation for other VT circuits.<sup>17-19</sup> Although the now mainstream use of irrigated catheter technology can increase the size of lesions produced by radiofrequency energy, maximum tissue depths of only ≈1 cm are observed when both catheter tip cooling and contact pressure are optimized.<sup>20</sup> Although creation of a bidirectional block is the optimal end point after linear ablation, the inability to achieve this goal with ablation of lengthier and thicker isthmuses, such as 1A, may account for clinical recurrences. The present study suggests that prominent myocardial hypertrophy commonly exists near the tricuspid annulus, and this may create difficulty for effective catheter ablation of this isthmus. Knowledge of the typical morphology derived from this study may be useful when considering catheter ablation for VT in the setting of TOF.

Interestingly, the previously undescribed isthmus between the RVOT incision and the VSD patch (isthmus 1B) was evaluated in this study, and this may serve as an alternate

strategy for creation of a conduction block between the ventriculotomy incision and the tricuspid annulus in many cases. This isthmus is adjacent to isthmus 1A but traverses an area that is typically excised to a greater extent by the surgeon at the time of repair, that is, RV infundibulum, resulting in shorter length and reduced wall thickness along its path. These observations suggest that isthmus 1B can serve as a superior target for catheter ablation when electrophysiological evaluation suggests that the region between the ventriculotomy and the tricuspid annulus is a critical part of the re-entrant circuit. Overall, the combination of block in isthmuses 1B and 4 can produce the same electric sequelae as block across isthmus 1A. In the absence of a muscular connection between the VSD patch and the tricuspid annulus, transection of isthmus 1B can be a useful and technically more straightforward alternative to ablation of isthmus 1A. Because there is a low prevalence of muscular tissue in the region of isthmus 4, conduction through this site may rarely pose a problem. However, if myocardial tissue at this site is encountered, ablation of this additional isthmus can

**Table 3. Detailed Characteristics of Subjects Surviving Intracardiac Repair**

Case No.	Age, y	Cause of Death	Postsurgical Survival, y	Isthmus 1A			Isthmus 1B			Isthmus 2			Isthmus 3			Isthmus 4		
				Length	Thick	% IF/RF	Length	Thick	% IF/RF	Length	Thick	% IF/RF	Length	Thick	% IF/RF	Length	Thick	% IF/RF
1	9	Intraop*	1.1	4.4	2	35	2.7	1.6	40	...	...	...	1	0.7	45	0.8	0.3	70
2	19	Sepsis	5.0	2.7	0.6	70	1.3	1.3	70	...	...	...	1	1.1	50	...	...	...
3	66	OHT**	11.0	5.5	1.2	20	2.5	0.6	35	1.1	0.3	65	1.6	0.4	70	...	...	...
4	42	OHT	35.0	4.5	1.2	10	2.7	0.7	15	...	...	...	1.1	1	25	...	...	...
5	61	SCD	43.0	3.3	1.8	40	3.1	1.4	35	4.0†	1	55	...	...	...	‡	‡	‡
6	1.1	Periop*	1.0	2.2	1.3	10	1.9	1.5	35	...	...	...	...	...	...	0.4	0.2	50
7	34	OHT**	31.0	4.2	1.9	15	1.8	1	65	...	...	...	0.6	0.3	80	§	§	§

IF indicates intersittal fibrosis, OHT, orthotopic heart transplant; RF, replacement fibrosis; SCD, sudden cardiac death; VSD, ventricular septal defect; and VT, ventricular tachycardia.

\*Two subjects died perioperatively during surgical revision, >1 y after initial intracardiac repair.

\*\*Two subjects with prior implantable cardioverter-defibrillator placement had appropriate therapy for VT prior to transplantation.

†Significant outlier.

‡Surviving myocytes were found in isthmus 4 but were noncontiguous by serial section.

§Surgical report described a muscular rim around the VSD, but this was not found during histological section.

be performed to interrupt reentry completely through the entire region (Figure 1). Because the VSD patch in TOF may extend to the superior aspect of the TA in many cases after repair, it is possible that catheter ablation intended to target isthmus 1A may even inadvertently create conduction block between the RV incision and the VSD patch at times (isthmus 1B). This may, in part, explain reports of successful ablation of the classically described isthmus 1A, despite seemingly unfavorable characteristics in this region.<sup>12</sup>

Although not specifically addressed in the present study, AV conduction tissue is known to run along the posteroinferior border of the VSD in the setting of TOF, so that lesions placed as laterally as possible in isthmus 4 will be most remote from the conduction system and are expected to be of greatest safety. Nevertheless, given its inherent proximity to the conduction system, we think that ablation of isthmus 4 should always be conducted with great care.

The second major finding in this study was that the ventricular isthmuses exist with variable frequency after surgical repair. Certain isthmuses, such as 1A, 1B, and 3, were commonly present in this study, whereas others, such as 2 and 4, were more often absent. Isthmus 2, between the ventriculotomy and pulmonary annulus, was frequently described in the literature as a target for catheter ablation.<sup>21–24</sup> However, this isthmus was often absent secondary to a transannular incision or avoidance of RVOT incision altogether, and it is likely that with changes in surgical technique this isthmus will be encountered even less frequently with time.<sup>4,6</sup> Likewise, isthmus 4 was seen only occasionally and was noticeably uncommon in the older surgical survivors in the present series. Because isthmus 4 is congenitally absent in most patients with TOF (existing a priori in only ≈20%), this finding is not surprising.<sup>25</sup> The results of the present study also suggest that the small rim of myocardium between the VSD patch and the tricuspid annulus may be easily disrupted at the time of surgical manipulation because of inflammatory and reparative processes. This finding was evident in ≥1 subject from the present series in whom a prior surgical report described this isthmus, whereas it was not detectable by our histological examination. The same phenomenon was possible in a second case with a few surviving myocyte bundles in 1 segment but not an intact isthmus, suggesting that loss of myocardium had occurred with progressive fibrosis after surgery.

The third finding in this study was the abundant evidence of fibrosis among the previously reported VT isthmuses.<sup>12</sup> Postrepair VT in the setting of TOF was originally classified as arising from both the OT and from the septal-inflow area of the RV where fractionated electrograms were commonly observed with their induction.<sup>21,26,27</sup> Follow-up studies based on excision of ventricular tissue at the time of arrhythmia surgery also demonstrated prominent fibrosis with subendocardial islets of surviving myocytes in the region of the RVOT.<sup>21</sup> The inclusion of a group of cases surviving surgical repair in the present analysis afforded an opportunity to evaluate these findings and confirm their consistent presence in the ventricular conduction isthmuses that have been more recently described in TOF.<sup>12</sup> Histological examination of these more recently described isthmuses revealed increased levels of both interstitial and replacement fibrosis in these regions,

supporting their pathogenic role in the maintenance of re-entrant VT after repair of TOF.

### Limitations

In addition to the aforementioned limited number of surgical survivors in the present study, the major limitation was the absence of clinical VT in the majority of the cases examined. Patients presenting with sustained monomorphic VT may possess a dissimilar ventricular substrate than the general population of patients with TOF in whom VT has not previously occurred. In particular, isthmus 1A has been reported to be successfully targeted for catheter ablation in patients with TOF with recurrent VT,<sup>12,16</sup> suggesting that this isthmus may possess alternate characteristics in such patients, possibly related to progressive RV volume overload and aneurysmal dilation over time. Alternatively, regional differences in surgical technique may have resulted in a different anatomic substrate in our series relative to that of other centers, contributing to the findings.

### Conclusions

There is significant variation both in the frequency and in the anatomic characteristics of VT isthmuses in patients with surgically repaired TOF. In general, isthmus 1A is of the greatest overall dimensions in terms of length and wall thickness, whereas the adjacent and previously undescribed isthmus 1B (from the ventriculotomy to the VSD patch) is significantly smaller and may serve as a superior ablation site. Although isthmuses 2, 3, and 4 are all of generally small morphological dimensions, isthmuses 2 and 4 are uncommon, whereas isthmus 3 is much more frequently observed. Knowledge of these differences may be useful when contemplating catheter ablation for treatment of monomorphic VT in the surgically repaired TOF population.

### Disclosures

None.

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### CLINICAL PERSPECTIVE

Anatomic ventricular tachycardia isthmuses in the postoperative setting of tetralogy of Fallot demonstrate region-specific morphological characteristics. The isthmus between the ventriculotomy incision and the tricuspid annulus is of the greatest size, and it may therefore be difficult to achieve complete conduction block with catheter ablation across this region. The nearby isthmus between the ventriculotomy incision and the ventricular septal defect patch is both of shorter length and of lesser wall thickness and can therefore be targeted in lieu of the aforementioned isthmus if necessary. This is because with frequent absence of intact myocardium between the ventricular septal defect patch and the tricuspid annulus after surgical repair, conduction block through this alternate isthmus achieves the same electrophysiological goal. The remaining isthmuses are generally favorable for catheter ablation, but of these, only the isthmus between the pulmonary valve and the ventricular septal defect patch is commonly found. Knowledge of these characteristics may facilitate successful therapy in patients with tetralogy of Fallot and recurrent monomorphic ventricular tachycardia by allowing the operator to target sites that are most favorable for catheter ablation. In addition, histological examination of these isthmuses provides compelling evidence that myocardial tissue disruption with interstitial and replacement fibrosis after surgery serves as the important substrate for re-entry.

## Characterization of Anatomic Ventricular Tachycardia Isthmus Pathology After Surgical Repair of Tetralogy of Fallot

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