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ORIGINAL ARTICLE

Device-detected nonsustained ventricular tachycardia in adult congenital heart disease without tetralogy of fallot

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Abstract

Objectives: To evaluate any association between non-sustained ventricular tachycardia (NSVT) detected by intra-cardiac device and clinical outcomes in repaired adult congenital heart disease (ACHD) without tetralogy of Fallot (TOF).

Background: NSVT portends a higher risk of serious ventricular tachyarrhythmia in TOF. However its clinical significance when incidentally detected by implantable cardiac device is not well elucidated in non-TOF ACHD cohort.

Methods: We performed a single center, retrospective, longitudinal follow-up study in repaired ACHD (≥18 years) patients without TOF who hosted a pacemaker or automatic implantable cardiac defibrillator (AICD). The cohort was divided based on presence/absence of device detected NSVT. The primary end-point was a composite of sustained ventricular tachycardia (VT), ventricular fibrillation (VF), or sudden cardiac death (SCD).

Results: One hundred fifty eight patients (male 56.3%, median [IQR] age of 35 [28–43] years at last follow-up] with longitudinal post-implant follow-up duration of 8 (5–12) years were included. NSVT was detected in 52 (33%) patients. The primary composite end-point was more frequent in NSVT group [11.5% vs. 2.8%; $p = .04$]. Patients with NSVT were (i) older at the time of initial implant (age 25 vs. 18 years, $p = .011$) and more frequently demonstrated (ii) systemic ventricular dysfunction (44% vs. 26%; $p = .015$), as well as (iii) history of ventriculotomy (38% vs. 21%; $p = .017$).

Conclusions: In our repaired ACHD cohort, we noted a significant association between device-detected-NSVT and the primary composite end-point of sustained VT/VF or SCD. Systemic ventricular dysfunction and history of ventriculotomy were more frequent in the NSVT group and likely constituted the clinical milieu.

KEYWORDS
adult congenital heart disease, implantable cardiac device, nonsustained ventricular tachycardia, sudden cardiac death

1 | INTRODUCTION

Ventricular tachyarrhythmia is a well-recognized, long term sequela in approximately 30% of adults with repaired congenital heart disease (ACHD).[1] It accounts for significant morbidity and mortality in this sub group.[2,3] The etiology is multifactorial. This includes ventriculotomy scar, residual disease resulting in ventricular dilatation or hypertrophy from pressure/volume overload, arrythmogenesis secondary to heart failure, hypoxic/ischemic injury to the myocardium, as well as congenitally malformed conducting system.[2]

Thus far, a risk stratification schema for primary prevention of sudden cardiac death (SCD) related to ventricular tachyarrhythmia is only adjudicated in adults with repaired tetralogy of Fallot (TOF).[3–6] In the later, nonsustained ventricular tachycardia (NSVT) is a retrospectively validated clinical risk arbitrator. Specifically, it is a surrogate marker for SCD and is associated with appropriate shocks delivered by the automated implantable cardioverter-defibrillator (AICD).[5,6] However, there is paucity of data regarding the incidence and clinical significance of NSVT in a non-TOF ACHD population. A previous study was confounded by enrichment of adults with repaired TOF and had limited longitudinal follow-up.[7]

Implanted cardiac devices (pacemakers, loop recorders, and AICD) can provide accurate and longitudinal data regarding NSVT episodes. However, incorporation of such data into clinical decision-making algorithms is not entirely transparent and this often poses a clinical dilemma. NSVT detected by the AICD portends an increased risk of appropriate shocks/interventions in adults with hypertrophic cardiomyopathy ($n = 51$) and those with left ventricular dysfunction ($n = 416$).[8,9] In the latter population, it is also correlated with increased cardiac mortality and hospitalizations for heart failure.[9] There is lack of such correlative data in patients with repaired ACHD other than those with repaired TOF. Further investigation into the role of NSVT in this patient population is warranted and presence of an implanted device provides a perfect opportunity to study this further.

The principal objective of our study was to evaluate any association between device-detected-NSVT and a priori specified composite endpoints during longitudinal follow-up in a non-TOF repaired ACHD population. The primary composite end point was the first episode of sustained ventricular tachycardia (VT), ventricular fibrillation (VF), or SCD. The key secondary composite end point was the first episode of hospitalization for heart failure, need for orthotropic heart transplant, or all-cause mortality. Additional pre-specified analysis included identification of clinical, echocardiographic, electrocardiographic, and surgical variables associated with device detected NSVT.

2 | METHODS

2.1 | Study population

We performed a retrospective study in patients with repaired ACHD and implanted cardiac devices with atrial and ventricular leads (Pacemaker/AICD) followed at our institution between January 2004 and December 2019. The patients were ≥18 years old at their most recent follow-up. Patients with TOF, single chambered atrial pacemakers, and those with incomplete data were excluded. This study protocol was approved by the Institutional Review Board of Wayne State University and Detroit Medical Center. Pertinent demographic and clinical data were collated from the electronic medical records. NSVT was adjudicated after review of the stored electrogram tracings obtained during device interrogation.

2.2 | Definitions

Device-detected NSVT was defined as ≥3 consecutive beats of ventricular ectopy at a rate ≥120 beats per minute lasting ≤30 s.[10] Sustained VT was defined as ≥3 consecutive beats of ventricular ectopy at a rate ≥120 beats per minute lasting either (i) >30 s or (ii) ≤30 s, but associated with hemodynamic instability, syncope, or terminated by an appropriate AICD therapy.[11] SCD was defined as unexpected death from a presumed cardiac cause within 1 h of symptom onset (witnessed) or within 24 h of last being observed in normal health (unwitnessed).[11] When death occurred as result of documented sustained VT/VF, it was adjudicated as SCD.

The primary composite end point was defined as the first episode of sustained VT/VF or SCD during follow-up after initial device implant. The secondary composite end point (hospitalization for heart failure or heart transplant or all-cause mortality) was defined similarly. The endpoints were to be met only once in order to avoid double counting of patients.

2.3 | Clinical characteristics

Demographic data included age, sex, ethnicity, age at device implant, as well as age at which end-points were met. Longitudinal clinical data that was collected included (i) traditional cardiovascular co-morbidities (diabetes mellitus, hypertension, obesity, smoking, cerebrovascular accidents, and chronic kidney disease), (ii) New York Heart Association (NYHA) functional heart failure classification (I-IV) at device placement and at last follow up,[12] (iii) American College of Cardiology (ACC) /American Heart Association (AHA) heart failure stage (A-D) at last follow-up,[13] (iv) number of admissions for heart failure, (vi) orthotropic heart transplant, (vi) sustained VT/VF, (vii) SCD, and (viii) overall mortality. The surgical data such as the original cardiac diagnosis, type of surgical repair, number of sternotomy, ventriculotomy, valve repair/replacement, and ventricular patch placement were also collated.

2.4 | Rhythm characteristics

The 12 lead electrocardiograms at the time of device placement and last follow up were analyzed. Electrogram recordings from device interrogations performed during clinic visits as well as through remote

TABLE 1 Demographics and clinical variables

Demographics/Clinical variablesMedian (IQR 25%–75%)Percent [%]	Device detected nonsustained VT		
	Yes ($n = 52$)	No ($n = 106$)	p value
Age at 1st device placement in years	25 (16–32)	18 (11–26)	.011
Age at last follow-up in years	35 (31–40)	34.5 (27.3–43.8)	.57
Total duration of follow-up in years	11.5 (9–12)	10 (7–13)	.459
Post device follow-up in years	7.5 (4–10.3)	8.5 (6–12)	.141
Male	28 [54%]	61 [57%]	.733
Caucasians	37 [71%]	68 [64%]	.474
Hypertension	5 [9.6%]	6 [5.7%]	.506
Diabetes mellitus	2 [3.8%]	5 [4.7%]	.86
Smoking	1 [2%]	6 [5.7%]	.427
Coronary artery disease	2 [3.8%]	1 [1%]	.252
Cerebrovascular accidents	5 [9.6%]	4 [3.8%]	.156
Obesity	3 [5.8%]	13 [12.3%]	.267
Chronic kidney disease	2 [3.8%]	1 [1%]	.252
PM	42 [81%]	97 [91%]	.068
BiV CRT-PM	3 [6%]	1 [1%]	.104
ICD for primary prevention	6 [11%]	3 [3%]	.061
ICD for secondary prevention	1 [2%]	5 [5%]	.664
Single ventricle with fontan palliation	7 [13.5%]	28 [26.4%]	.101

Abbreviations: AICD, automatic implantable cardioverter defibrillator; BiV CRT, biventricular cardiac resynchronization therapy; PM, pacemaker.

monitoring (e.g., Medtronic Carelink website) were scrutinized by the electrophysiologist. Data including episodes of NSVT/VT/VF as defined above as well as any atrial and/or junctional arrhythmias were recorded from the saved device electrograms. Interventions (overdrive pacing, appropriate, and inappropriate shocks) performed by the device were also analyzed. Detailed chart review was performed to record the clinical interventions pursuant to detection of NSVT and other findings mentioned above.

2.5 | Echocardiographic characteristics

Serial echocardiographic data was analyzed from the time of device placement to last follow up. Cardiac anatomy, systemic and subpulmonary ventricular dysfunction, atrio-ventricular (AV) valve stenosis/insufficiency, pulmonary and systemic outflow tract stenosis/insufficiency were assessed. Based on the presence of single functioning ventricle or two ventricles and the morphology of the systemic ventricle, patients were classified into four sub-groups: (a) single systemic left ventricle (LV), (b) single systemic right ventricle (RV), (c) biventricular repair with systemic LV and (d) biventricular repair with systemic RV. Systemic LV dysfunction was defined as an ejection fraction ≤40% based on established criteria.[14] The definition of ≥ moderate systemic RV dysfunction was predicated on qualitative assessment of wall motion and thickening of the ventricle in ≥2 views.[15] Significant AV/semilunar valve stenosis/ regurgitation were defined as ≥ moderate as per ASE criteria.[16]

2.6 | Study design and statistical analysis

Patients were categorized into two groups (NSVT and No NSVT) depending on the presence or absence of device-detected NSVT respectively. Various parameters as described above were compared between the two groups. Categorical data was expressed a number (percentage) and compared using two-tailed Chi-Squared ($X^{2)}$ or Fisher exact test ($n < 5$) as appropriate. Continuous numerical data was expressed as median (25th–75th centile inter quartile range or IQR) and compared using the nonparametric Wilcoxon rank-sum (Mann–Whitney U) test. Data were analyzed using SPSS software for PC version 21 (SPSS Inc., Chicago). Relative risk (RR) and 95% confidence interval (CI) were calculated for significant results. A p value of <.05 was considered statistically significant.

3 | RESULTS

The study enrolled a total of 158 patients (male 56.3%, median [IQR] age of 35 [28–43] years at last follow-up) with an accrued longitudinal follow-up duration of 10.5 (7.3–12.8) years. The majority (90.5%) underwent an initial pacemaker implant. The indications for initial

TABLE 2 Type of repaired congenital heart defects and ventricular morphology

Diagnosis	*N* = 158
Single ventricle, systemic LV	25 [16%]
Tricuspid atresia	9
PA, IVS	7
DILV	7
DORV	1
Complex heterotaxy syndrome	1
Single ventricle, systemic RV	10 [6%]
HLHS	4
L-TGA, PA	3
RV dominant AVC	2
Complex heterotaxy syndrome	2
Biventricular repair, systemic LV	65 [41%]
AVC	16
Coarctation of aorta	8
VSD	6
D-TGA	6
Truncus arteriosus	5
PA, VSD, MAPCAS	5
DORV	4
ASD	4
Ebstein anomaly	3
VSD, AS	3
TAPVR	1
DILV, L-TGA, VSD	1
Shone's complex	1
Biventricular repair, systemic RV	58 [37%]
D-TGA	47
L-TGA	9
DORV, D-TGA	2

Abbreviations: AS, aortic stenosis; ASD, atrial septal defect; AVC, atrioventricular canal; DILV, double inlet left ventricle; DORV, double outlet right ventricle; D-TGA, D-loop transposition of great arteries; HLHS, hypoplastic left heart syndrome; IVS, intact ventricular septum; L-TGA, L-loop transposition of great arteries; MAPCAS, major aorto-pulmonary collaterals; PA, pulmonary atresia; TAPVR, total anomalous pulmonary venous return; VSD, ventricular septal defect.

pacemaker implantation were either sinus or AV node dysfunction (n = 89), isolated high degree AV blocks (n = 41), supraventricular tachyarrhythmias (n = 9) or biventricular resynchronization for heart failure (n = 4). In nine patients with supraventricular tachyarrhythmias, pacemaker was implanted for anti-tachycardia pacing properties and optimization of antiarrhythmic medications. The rest were initially implanted with AICD for either primary (n = 9) or secondary prevention (n = 6) of VT/VF or SCD. Post device follow-up duration was 8 (5–12) years. One third of the patients had device-detected NSVT (n = 52, 32.9%) at a median age of 33 (28–37) years. A total of 132 episodes of NSVT were recorded (2.5 NSVT/patient).

3.1 | Demographics and clinical variables (Table 1)

At first implant, patients in the NSVT group (n = 52, male 54%, pacemaker 81%, single ventricle 13.5%, comorbidities <10%, median post device follow-up 7.5 years) were older (median age of 25 vs. 18 years, p = .011) than those without NSVT (n = 106, male 57%, pacemaker 91%, single ventricle 16.4%, comorbidities <10%, median post device follow-up 8.5 years). The other parameters including frequency of initial primary or secondary prevention AICD were not significantly different between the two groups.

3.2 | Surgical repair and ventricular morphology (Table 2)

Three fourths of our patients had biventricular repair with nearly equal distribution of systemic LV and RV (53 vs. 47%). Amongst the single ventricle/Fontan cohort (n = 35; 22%), systemic morphologic LV (71%) was predominantly seen.

3.3 | Primary and secondary endpoints (Table 3)

The primary composite end-point event defined as the first episode of sustained VT/VF or SCD was more frequent in the NSVT group [11.5% vs. 2.8%; RR, 4.08; 95% CI, 1.06–15.66; p = .04]. In the NSVT group, the first event was either sustained VT (n = 5) or SCD (n = 1). In those without NSVT, the first event was sustained VT (n = 3). SCD occurred as the second event in one of those three patients. The number of patients with sustained VT (9.6% vs. 2.8%) or SCD (1.9% vs. 0.9%) was not statistically different between the two groups.

The key secondary composite end point event (hospitalization for heart failure, heart transplantation, or all-cause mortality) was also similar between the two groups (26.9% vs. 25.5%). In the NSVT group, two patients died while two underwent orthotropic heart transplant. The cause of death in the two patients was SCD or refractory heart failure with rejection after heart transplant. In the No NSVT group, five patients died and none were transplanted. The cause of death was either SCD (n = 1) or refractory heart failure with cardiogenic shock (n = 4). Additional pre-specified analysis based on number of hospitalizations for heart failure, NYHA functional class or ACC/AHA heart failure stages were not different between the two groups.

The annual incidence of the (i) primary composite end-point (1.10% vs. 0.30%), (ii) hard end point of SCD (0.18% vs. 0.09%), and (iii) all-cause mortality (0.37% vs. 0.49%) was also calculated for NSVT (mean postimplant follow-up of 10.5 years) and No NSVT (mean post-implant follow-up of 9.7 years) groups respectively.

3.4 | Electrophysiological characteristics (Table 4)

During follow up, a total of five patients with a pacemaker (four in NSVT and one in No NSVT group) were upgraded to an AICD, for either

TABLE 3 Primary and secondary endpoints

Clinical variablesMedian (IQR 25%–75%)Percent [%]	Device detected nonsustained VT		
	Yes ($n = 52$)	No ($n = 106$)	*p* value
Primary composite endpoint	6 [11.5%]	3 [2.8%]	**.040**
i) Sustained VT/VF	5 [9.6%]	3 [2.8%]	.085
ii) SCD	1 [1.9%]	1 [0.9%]	.612
Secondary composite endpoint	14 [26.9%]	27 [25.5%]	.611
i) Hospitalization for heart failure	14 [26.9%]	26 [24.5%]	.522
ii) Heart transplantation	2 [3.8%]	0 [0%]	.133
iii) All-cause mortality	2 [3.8%]	5 [4.7%]	.803
Total number of hospitalizations	28	55	
Per patient	0.53	0.51	
NYHA at device placement: Class 1 & 2	41 [79%]	95 [90%]	.086
NYHA at device placement: Class 3 & 4	11 [21%]	11 [10%]	.086
NYHA at last follow up: Class 1 & 2	48 [92%]	100 [94%]	.730
NYHA at last follow up: Class 3 & 4	4 [8%]	6 [6%]	.731
HF stage B at last follow up	24 [46%]	59 [55%]	.438
HF stage C at last follow up	23 [44%]	41 [39%]	.438
HF stage D at last follow up	5 [10%]	6 [6%]	.438

Abbreviations: HF, heart failure; NYHA, New York Heart Association; SCD, sudden cardiac death; VF, ventricular fibrillation; VT, ventricular tachycardia.

TABLE 4 Electrophysiological characteristics

Electrophysiological characteristicsMedian (IQR 25%–75%)Percent [%]	Device detected nonsustained VT		
	Yes ($n = 52$)	No ($n = 106$)	*p* value
Device upgrade during follow up period			
PM→AICD for primary prevention	2 [5%]	1 [1%]	.216
PM→AICD for secondary prevention	2 [5%]	0	.089
PM→BiV CRT PM	1 [2%]	5 [5%]	.667
AICD→BiV CRT D	1 [14%]	1 [12%]	1
Electrocardiogram findings at device placement			
Conducted QRS duration in msec	115 (92.5–145.75)	106 (94–133.5)	.317
Conducted QTc duration in msec	451.5 (424.75–481)	442 (422.5–461)	.11
Other arrhythmias			
Atrial tachyarrhythmias	32 [61%]	58 [55%]	.494
Antiarrhythmic medications			
Beta blocker	32 [61%]	29 [27%]	**.0001**
Calcium channel blocker	3 [6%]	6 [6%]	1
Amiodarone	3 [6%]	5 [5%}	.718
Sotalol	9 [17%]	26 [25%]	.415
Flecainide	8 [15%]	20 [19%]	.662
Digoxin	10 [19%]	36 [34%]	.063

Abbreviations as mentioned in Table 1 and 2.

TABLE 5 Echocardiographic parameters

Echocardiographic findings	Device detected NSVT percent [%]		*p* value
	Yes ($n = 52$)	No ($n = 106$)	
Systemic LV (Single ventricle)	5 [10%]	20 [19%]	.167
Systemic RV (Single ventricle)	2 [4%]	8 [8%]	.499
Systemic LV (Biv Repair)	25 [48%]	40 [38%]	.232
Systemic RV (Biv Repair)	20 [38%]	38 [35%]	.861
Any systemic ventricular dysfunction	23 [44%]	27 [26%]	**.015**
Systemic RV or LV dysfunction (Biv Repair)	22 [42%]	22 [21%]	**.004**
Systemic LV dysfunction	9 [17%]	4 [4%]	**.008**
Systemic RV dysfunction	13 [25%]	18 [17%]	.327
Systemic RV or LV dysfunction (Single ventricle)	1 [2%]	5 [5%]	.659
Systemic LV dysfunction	1 [2%]	4 [4%]	1
Systemic RV dysfunction	0 [0%]	1 [1%]	1
≥Moderate AI (Biv Repair)	5 [10%]	4 [4%]	.156
≥Moderate PI (Biv Repair)	3 [6%]	5 [5%]	.712
≥ Moderate MR (Biv Repair)	3 [6%]	1 [1%]	.105
≥Moderate TR (Biv Repair)	10 [19%]	14 [13%]	.638
≥Moderate AI (Single ventricle)	2 [4%]	3 [3%]	.664
≥ Moderate AV regurgitation (Single ventricle)	2 [4%]	4 [4%]	1
Progression of AI	0	2 [2%]	1
Progression of PI (Biv Repair)	1 [2%]	0	.329
Progression of systemic AV valve regurgitation	0	1 [1%]	1
Progression of pulmonary ventricular AV valve regurgitation (Biv Repair)	0	2 [2%]	1

Abbreviations: AI, aortic insufficiency; AV, atrio-ventricular valve; Biv, biventricular; LV, left ventricle; MR, mitral regurgitation; PI, pulmonary insufficiency; RV, right ventricle; TR, tricuspid regurgitation.

primary ($n = 3$) or secondary prevention ($n = 2$) indication. An upgrade to a primary prevention AICD ensued in two patients upon detection of NSVT by the pacemaker. In addition, pacemaker was upgraded to a biventricular cardiac resynchronization therapy (BiV CRT) device in six patients and AICD was upgraded to BiV CRT-Defibrillator in one patient. The indication was symptomatic heart failure in presence of severely reduced systemic ventricular function despite guideline directed medical treatment.

There was no difference between the groups with respect to frequency of device upgrade, duration of the conducted QRS or QTc interval, and the prevalence of atrial tachyarrhythmias (61% vs. 55%). The overall use of calcium channel blocker, digoxin, and class I or III antiarrhythmic drugs (Flecainide, Amiodarone, and Sotalol) was also not different between the two groups.

However, patients in the NSVT group were more frequently treated with a beta-blocker [61% vs. 29%; RR, 2.25; 95% CI, 1.54–3.28; $p = .0001$]. This was driven predominantly by a new prescription of the drug (15/52 or 29% of patients) pursuant to detection of NSVT. Only a minority (15.4%) of patients were prescribed a new class I or III anti-arrhythmic medication (Flecainide [$n = 3$], Amiodarone [$n = 1$], or Sotalol [$n = 4$]) following detection of NSVT.

3.5 | Echocardiographic parameters (Table 5)

Systemic ventricular dysfunction was more prevalent in those with biventricular repair compared to single ventricle repair. Patients in the NSVT group demonstrated a higher prevalence of systemic ventricular dysfunction [44% vs. 26%; RR, 1.74; 95% CI, 1.11–2.71; $p = .015$]. This was driven by systemic ventricular dysfunction in those with biventricular repair [42% vs. 21%; RR, 2.04; 95% CI, 1.25–3.32; $p = .004$] who had LV dysfunction [17% vs. 4%; RR, 4.59; 95% CI, 1.48–14.20; $p = .008$]. No such correlation was noted in patients with a functional single ventricle. In terms of semilunar or AV valve regurgitation or its progression, the two groups were not significantly different. Semilunar or AV valve stenosis was not documented in our cohort.

3.6 | Surgical variables (Table 6)

Upon review of surgical records, a higher frequency of ventriculotomy was documented in the NSVT group [38% vs. 21%; RR, 2.39; 95% CI, 1.12–3.08; $p = .017$]. There was no difference in other variables such as number of sternotomy, surgical valve replacements, or presence of VSD patch.

TABLE 6 Surgical Variables

Surgical variables	Device detected NSVT: Yes ($n = 52$)	Device detected NSVT: No ($n = 106$)	p value
Total number of sternotomies	91	169	-
Number of sternotomies/patient	1.75	1.59	.36
Presence of VSD patch	14 [27%]	18 [17%]	.201
Ventriculotomies	20 [38%]	22 [21%]	**.017**

Abbreviations as mentioned in Table 2

3.7 | Clinical characteristics: Patients who met primary composite endpoint (Table 7 and 8)

Overall, nine patients (male 67%, biventricular repair in 89%, initial pacemaker implant in 33%, median age [IQR] at device implant of 23 [14–32.5] years) met the primary composite endpoint at a median (IQR) age of 33 (19–36) years and over a follow-up of 9 (7.5–12.5) years. None of the nine patients had a secondary prevention AICD. Four patients (44%) experienced recurrent events due to sustained VT with AICD shock ($n = 2$) or SCD due to VT storm ($n = 2$). The clinical characteristics of the individual patients are elaborated in Table 7 and 8.

4 | DISCUSSION

In this sentinel study of patients with repaired ACHD other than TOF, we noted an association between device-detected NSVT and the primary composite endpoint of sustained VT/VF or SCD over a total accrued long term follow-up of 1569 person-years (Figure 1). The key secondary composite endpoint of hospitalization for heart failure, heart transplant, or all-cause mortality was similar between the two groups (Figure 1). The results of this exploratory study should be cautiously interpreted in the context of the findings enumerated below. Patients in the NSVT group were slightly older at the time of initial implant (Figure 2). They also demonstrated a higher prevalence of systemic ventricular dysfunction and a history of ventriculotomy (Figure 1). In this milieu, they met the primary end point more frequently.

Our data can be referenced in the background of a previous retrospective, multicenter study performed by Teuwen et al. This was a heterogeneous ACHD population ($n = 145$, mean age at presentation 40 ± 14 years, repaired ACHD 92%, TOF 29%) enriched by TOF and included patients with/without a cardiac device.[7] There was no age difference between patients with NSVT (n = 103, 40 ± 14 years), sustained VT ($n = 25$, 36 ± 13 years), or VF ($n = 17$, 44 ± 16 years) at first presentation. Sustained VT/VF frequently recurred in their patients after its initial presentation, but it was rare in those with isolated NSVT at presentation. A minority of their patients with NSVT (16%) were implanted with a primary prevention AICD. Over an intermediate median follow-up duration of 5 years, sustained VT/VF occurred in 5 (5%) patients with NSVT, of whom only 1 (1%) hosted a primary prevention AICD. Decreased ventricular function was reported in 9% of patients with NSVT. However, additional detailed correlation with echocardiographic/surgical variables, medications, or heart failure (stage/functional class/hospitalizations) was not furnished. A conservative strategy of "wait and watch" was recommended for most patients with isolated NSVT.[7]

In comparison, our study population comprised of younger adults. Our objective and inclusion criteria were also different. We only included patients with a pacemaker/AICD to specifically evaluate the clinical significance of device detected NSVT in a repaired ACHD cohort unskewed by TOF. The latter group was strategically excluded as they represent a better-studied population in whom NSVT may herald a higher risk of serious ventricular tachyarrhythmia.

In our study, NSVT was first detected at a median age of 33 (28–37) years. During follow-up, a total of nine patients (5.7%) met the prespecified primary end point of sustained VT/SCD at 33 (19–36) years of age with a higher frequency (11.5%) in the NSVT group. This can be likely explained on the basis of longer duration of follow-up when compared to study reported by Teuwen and colleagues.[7]

In our study, systemic ventricular dysfunction was correlated with NSVT. This was driven by systemic LV dysfunction in patients with biventricular repair. No such correlation was noted in patients with a repaired functional single ventricle, although small numbers may have precluded a meaningful analysis. In two previous larger studies, systemic and/or subpulmonary ventricular dysfunction was associated with SCD.[3,17] In another study of patients with repaired TOF ($n = 413$, median follow-up of 2.9 years), LV global longitudinal dysfunction was correlated with an increased risk of SCD or serious ventricular tachyarrhythmias.[18]

History of ventriculotomy scar was a significant predictor of device detected NSVT in our cohort. Other surgical variables such as type of surgical repair, presence of a VSD patch did not track the occurrence of NSVT. In prior studies of patients with repaired TOF, ventricular incision, patch and scar burden were associated with ventricular tachyarrhythmias.[19–22]

Detection of ventricular tachyarrhythmias by intracardiac devices has an impact on the management of patients with ACHD, especially those with repaired TOF.[6,19,23,24] Symptomatic NSVT in patients with ACHD is a risk predictor for appropriate AICD shocks.[6,23] Therefore, current guidelines recommend a primary prevention AICD for patients with NSVT in certain high-risk subgroups, such as repaired TOF with additional risk factors.[19]

However, there is paucity of data driven guidelines directing clinical decision-making process pursuant to detection of NSVT in ACHD patients other than TOF. Clinical management thus remains discretionary and dilemmatic. Amongst our patients in the NSVT group ($n = 52$, initial pacemaker in 87%), only two (3.8%) were subsequently upgraded from pacemaker to a primary prevention AICD. This was in the setting of NSVT associated with ventricular dysfunction and heart failure. The primary endpoint occurred in a total of six patients out of whom four patients were already implanted with an AICD. The singular occurrence of SCD was due to an unsuccessful primary prevention

TABLE 7 Clinical characteristics of patients with NSVT detected by the device who met the primary composite endpoint

Patients	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Sex	Male	Female	Female	Male	Male	Male
Ethnicity	Caucasian	Caucasian	Caucasian	Non-Caucasian	Noncaucasian	Caucasian
Heart defect	d-TGA	AVC	VSD + AS	PA+VSD	d-TGA	d-TGA
Surgical repair	Mustard	Biventricular repair	VSD repair, Ross/Konno	Unifocalization, RV-PA conduit	Mustard	Mustard
Initial device	AICD	PM	PM	AICD	AICD	PM
Age in years at 1st device	35	32	8	17	33	23
Follow up in years	5	13	12	8	7	12
Systemic RV/LV dysfunction	Yes	Yes	Yes	No	Yes	Yes
Valve dysfunction	TR	MR	No	No	No	TR
NYHA Class at device placement	3	2	2	1	4	4
NYHA Class at last follow up	2	1	1	1	3	1
HF stage at last follow up	C	C	C	B	D	C
HF admissions	1	1	0	0	2	5
Device upgrade prior to primary endpoint event	No	No	No	No	No	Yes; 1 prevention AICD
First primary endpoint event	AICD shock for sustained VT	External shock for sustained VT	Sustained VT treated with IV Amiodarone	AICD shock for sustained VT	SCD due to VT storm	AICD shock for sustained VT
Time to first primary endpoint event in years	1	4	12	8	7	12
Oral antiarrhythmic drug used after VT	Amiodarone	Amiodarone	Sotalol	Nadolol	-	Atenolol
Device upgrade after sustained VT	No	Yes; 2 prevention AICD	Yes; 2 prevention BiV CRT- D	No	No	No
Recurrence of sustained VT	Yes (1 episode)	Yes (1 episode)	No	No	No	No
OHT	No	No	No	No	No	Yes
Subsequent mortality	No	No	No	No	SCD	No

Abbreviations as mentioned in Table 1, 2, and 3.

AICD shock in a patient with Mustard palliation and depressed systemic RV function.

Thus, recommendation for primary prevention AICD in a special population as studied here (repaired ACHD without TOF) is contingent upon a shared decision-making process. The important pre requisites are emphasized below. The net benefit of a primary prevention AICD is most aptly conceptualized in a competing risk framework model. This construct balances the absolute risk of SCD relative to all-cause mortality attributable to other comorbidities. When viewed from the vantage point of net life-span gain, the maximum benefit is derived in those who are (i) younger, (ii) have a higher absolute risk of SCD, and (iii) a higher ratio SCD/all-cause mortality.[25] Previously, a ≥3% absolute annual risk of SCD has been suggested as an appropriate cut off for implanting a primary prevention AICD in a patient with ACHD.[26] There are still lacunae in existing literature regarding such parameters in the population reported here. In this context, the results of our preliminary study should be interpreted as hypothesis generating.

Examined from those perspectives, our study yielded an overall low actuarial annual incidence of sustained VT/SCD in patients with NSVT (1.10%). However, this was still 3.5 times higher when compared to those without NSVT (0.30%). The annual incidence of the hard endpoint of SCD was low (0.18% vs. 0.09%) in both groups and our study

TABLE 8 Clinical characteristics of patients without NSVT detected by the device who met the primary composite endpoint

Patients	Patient 1	Patient 2	Patient 3
Sex	Female	Male	Male
Ethnicity	Caucasian	Noncaucasian	Caucasian
Heart defect	Truncus arteriosus	HLHS	VSD
Surgical repair	RV-PA conduit, AV valve repair	Norwood, Glenn, Fontan	Surgical patch repair
Initial device	AICD	AICD	AICD
Age in years at 1st device	17	11	32
Follow up in years	14	8	9
Systemic ventricle dysfunction	No	Yes	No
Valve dysfunction	No	No	TR
NYHA at device	1	2	1
NYHA at last follow up	1	2	1
HF stage at last follow	B	C	B
HF admissions	0	0	0
Device upgrade prior to primary endpoint event	No	No	No
First primary endpoint event	AICD shock for sustained VT	Multiple AICD shocks for sustained VT	AICD shock for sustained VT
Time to first primary endpoint event in years	1	1	1
Oral antiarrhythmic drug used after VT	Sotalol	Sotalol	Sotalol
Device upgrade after sustained VT	No	No	No
Post VT ablation	No	No	No
Recurrence of sustained VT	Yes (1 episode)	See below	No
Subsequent mortality	No	SCD due to VT storm	No

Abbreviations as mentioned in Table 1, 2, and 3.

was underpowered to detect a significant difference. The previously reported annual incidence of SCD in patients with congenital heart disease is similarly low (0.09%), albeit still higher than age-matched controls.[27] The annual incidence of all-cause mortality was also low (0.37% vs. 0.49%) in our study for patients with or without NSVT respectively.

Patients with a functional single ventricle often require a thoracotomy for surgical placement of a defibrillator lead. This poses a clinical dilemma when recommending primary prevention AICD in such patients after detection of NSVT. Our study cohort was enriched (22%) by patients with functional single ventricle/Fontan palliation. They were not over represented among patients with NSVT. Only one patient (1/35 or 2.8%) with a functional single ventricle and heart failure who hosted a primary prevention AICD met the primary endpoint. This patient was not detected to have NSVT prior to the first episode of sustained VT. Thus, a conservative approach in patients with single ventricle in the absence of heart failure may be justifiable after detection of NSVT. In this context, it is reassuring that in a 30-year long term follow up study of patients with single ventricle/Fontan palliation, the prevalence of SCD was around 5%, yielding an overall low annual risk.[28]

Finally, the high prevalence (57%) of atrial tachyarrhythmias in our cohort led to initiation of antiarrhythmic medications in some patients. Initiation of beta-blocker was the most common medical intervention after detection of NSVT (29%). This was followed by a new prescription of class I/III anti-arrhythmic medication in approximately 15% of patients with NSVT. Thus, our clinical management after detection of NSVT was essentially conservative with selective upgrade to an AICD (7.6%). In retrospect, we did not incur an excess mortality with this approach in those with NSVT when both groups were compared.

5 | STUDY LIMITATIONS

This single center study is limited by its retrospective design and smaller sample size. It is likely underpowered to detect a significant difference between hard end-points such as SCD and all-cause mortality between the two groups. Our study, like other published research in patients with ACHD, is encumbered by "immortal time bias." This is explicated on the basis of low background rate of SCD (<1%) and all-cause mortality in a relatively younger cohort of patients with repaired ACHD. The primary composite endpoint was driven by sustained VT which is at best a "loose" surrogate for SCD. Sustained VT was treated with an AICD/external shock in 7/8 (88%) patients. Appropriate AICD shock is a previously validated outcome measure in patients with TOF.[6]

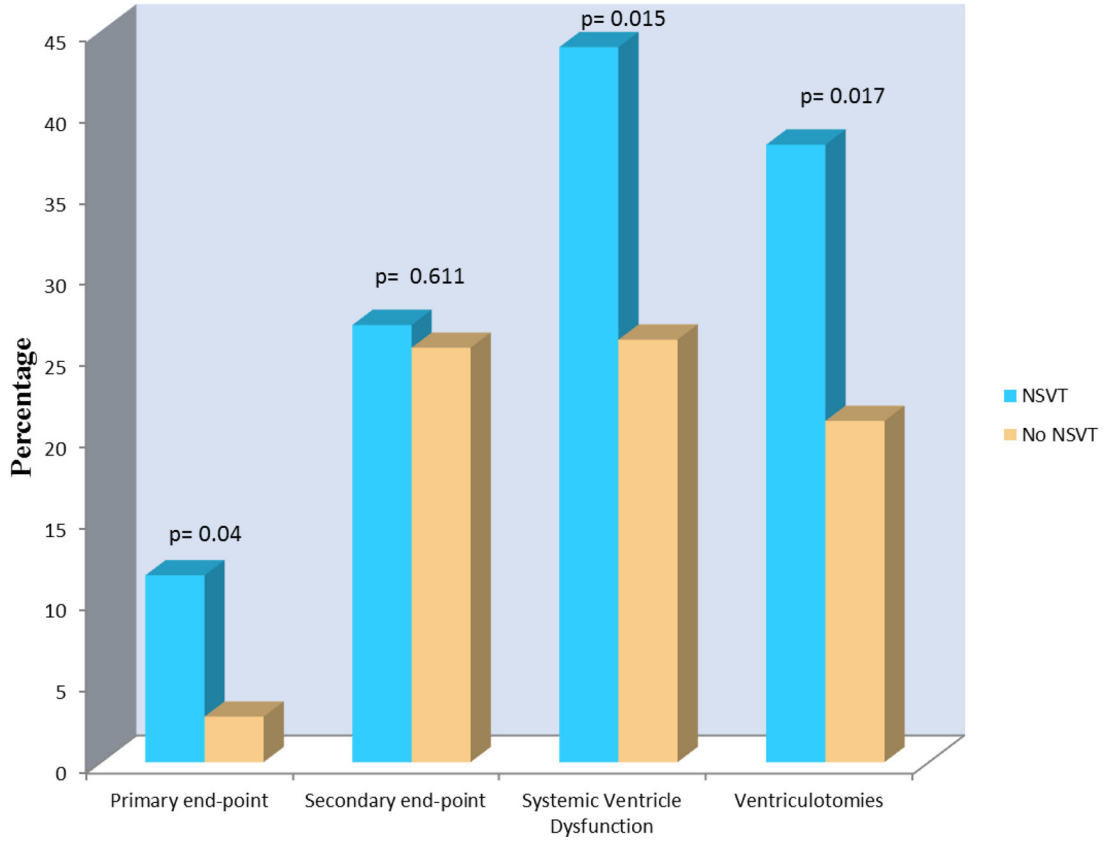

FIGURE 1 Percentage of end points, systemic ventricle dysfunction and ventriculotomies in patients with and without NSVT detection. The primary composite end points (sustained ventricular tachycardia, ventricular fibrillation or sudden cardiac death) (11.5% vs. 2.8%; $p = .04$), systemic ventricular dysfunction (44% vs. 26%; $p = .015$) and ventriculotomies (38% vs. 21%;$p = .017$) were significantly associated with device detected nonsustained ventricular tachycardia (NSVT) compared to those without as shown in the bar diagram. The occurrences of secondary composite endpoints such as heart failure admissions, heart transplantation or all cause mortality were similar between the two groups 26.9% vs. 25.5%; $p = .61$ [Color figure can be viewed at wileyonlinelibrary.com]

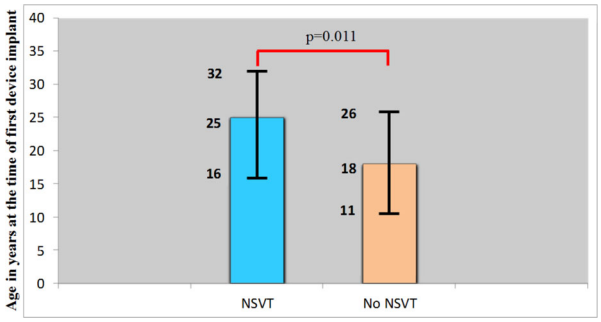

FIGURE 2 Bar diagram depicting median age and interquartile range of initial device placement between NSVT and No NSVT group. The age at initial device placement was significantly higher in patients with device detected nonsustained ventricular tachycardia (NSVT) compared to those without NSVT (median age of 25 vs. 18 years, $p = .011$) [Color figure can be viewed at wileyonlinelibrary.com]

Data from implantable loop recorders were not included as they were not frequently utilized at our institution during the study time line. The absence of any furnished data correlating NSVT with clinical symptoms is another limitation. There may be clinical bias towards prescribing treatment in symptomatic patients which is not captured here. Despite strategic exclusion of patients with TOF, the heterogeneous nature of our cohort precludes any lesion specific conclusions. The results derived from this study performed on a younger cohort with an implanted cardiac device are not generalizable to a larger ACHD population. However, the study design is deliberate and it seeks to specifically address existing lacunae in our knowledge. Any empirical data extricated on this specific topic is expected to facilitate a refined and informed clinical decision-making process.

6 | CONCLUSIONS

NSVT was detected in 1/3rd of this non-TOF repaired ACHD population with a pacemaker/AICD. On long term follow-up, NSVT was associated with the primary composite endpoint of sustained VT or SCD and was driven primarily by the former. The correlation between NSVT and variables such as slightly older age at device implant, systemic ventricular dysfunction, and history of ventriculotomy contextualize the clinical milieu in which the primary end-point occurred. Thus NSVT should not be viewed as an independent risk factor, but rather a co-dependent risk arbitrator. The hard end-points of SCD and all-cause

mortality were demonstrably low. The results of this exploratory study although hypothesis generating, warrant prospective validation in a larger cohort of patients.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

AUTHORS CONTRIBUTION

The first author, Pezad Doctor collated, analyzed the data, as well as drafted the manuscript. Chenni Sriram designed the study, analyzed the data and contributed in drafting the manuscript. The rest of the authors at our institution Doctors Sanjeev Aggarwal, David K. Lawrence, Pooja Gupta, and Gautam K. Singh who are my colleagues provided significant intellectual contributions to the manuscript and helped with critical review of the manuscript. Dr. Malini Madhavan is an Adult Electrophysiologist at Mayo Clinic who specializes in ACHD. She also provided significant intellectual contributions to the manuscript as well help in drafting it.

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