Inappropriate implantable cardioverter-defibrillator shocks in repaired tetralogy of fallot patients: Prevalence and electrophysiological mechanisms

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Abstract

Background: Patients with Tetralogy of Fallot (TOF) are at increased risk for sudden cardiac death, often undergo implantable cardioverter defibrillator (ICD) implantation at younger ages, and are at greater risk of experiencing inappropriate shocks. We investigated occurrences of ICD shocks in TOF patients to identify prevalence, characteristics associated with inappropriate shocks, and therapeutic interventions after inappropriate shocks.

Methods: Records of patients with repaired TOF and ICD implantation who were followed at Columbia University Irving Medical Center between 1/1/2000 and 5/1/2019 were analyzed.

Results: 44 patients with repaired TOF and ICD implantation were reviewed. Mean age at implantation was 39 ± 13 years. Eight (18%) patients received both appropriate and inappropriate shocks, 6 (14%) received only appropriate shocks, and 3 (7%) received only inappropriate shocks. Three patients received inappropriate shocks for sinus tachycardia, 7 for atrial arrhythmias, and 1 for noise artifact. Inappropriately shocked patients had lower beat per minute (bpm) cutoff values for ICD therapy (mean = 162 ± 24 bpm vs. 182 ± 16 bpm, p = 0.007). After inappropriate shocks, 1 patient underwent lead replacement, 1 had the VT cutoff increased, and 6 were treated with medications.

Conclusions: One quarter of TOF patients with ICDs experienced inappropriate shock therapy, the timing of which was most often clustered within the first two years after implant or years later. Lower shock therapy zones were associated with increased risk for inappropriate shocks, and the majority of inappropriate shocks resulted from atrial arrhythmias with rapid ventricular response. Treatments for inappropriate shocks included increasing VT therapy bpm and rhythm and/or rate control medications.

1. Introduction

Patients with repaired Tetralogy of Fallot (TOF) are one of the most commonly seen adult congenital heart diseases (CHD) groups due to the relatively high prevalence and success of corrective surgeries for TOF [1]. Nevertheless, patients with TOF have a high prevalence of arrhythmias, including ventricular arrhythmias [2], and are at increased risk for sudden cardiac death (SCD) [1]. Many of these deaths are attributable to ventricular arrhythmias [3], and American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines recommend implantable cardioverter defibrillator (ICD) implantation as a Class I recommendation if the initial presentation of ventricular arrhythmia is sustained ventricular tachycardia (VT) or ventricular fibrillation (VF), and as a Class IIa recommendation for patients who have inducible sustained VT and/or VF during an EP study [4].

While ICD implantation is effective for prevention of sudden cardiac death, inappropriate shocks can have a negative impact on quality of life and may even be associated with increased mortality [5–7]. In the general adult and pediatric ICD population, inappropriate shocks are often caused by supraventricular tachyarrhythmias, oversensing of far-field potentials, or artifacts caused by faulty electrodes [8–10]. Adult patients with CHD, including TOF patients, have a high rate of ICD implantation [11], a high prevalence of atrial tachyarrhythmia [2], and often undergo...
ICD implantation at younger ages than most adult ICD patients (average implant age = 63–67 years for all ICD patients [8,12–14] versus 24–37 years for CHD patients [15–17]). Similarly, adult patients with TOF are at increased risk for inappropriate ICD therapy over time [16].

While prior reports have documented the presence of increased rates of inappropriate ICD therapy in TOF patients, there are fewer data regarding: (i) the particular clinical characteristics associated with inappropriate ICD shocks in TOF patients, (ii) reasons for inappropriate shocks, and (iii) treatments and interventions after inappropriate shocks. Therefore, we reviewed our population of TOF patients with ICDs to identify the prevalence and characteristics associated with inappropriate shocks, and the therapeutic interventions after inappropriate shocks in order to add to the existing literature by providing a more detailed description for why such shocks occur and steps taken to address them. We hypothesized that inappropriate shocks in TOF patients with ICDs would not only have high rates of inappropriate shocks, but also that they would be associated both with younger age at implant and lower programmed VT detection rates for therapy.

2. Methods

This study was approved by the Columbia Human Research Protection Office (IRB- AAAB3432). Medical records of consecutive CHD patients with a history of repaired TOF and ICD implantation who were followed at Columbia University Irving Medical Center between 1/1/2000 and 5/1/2019 were reviewed. ICD parameters were abstracted from device interrogations. Inappropriate therapy was defined as any device shock when the underlying rhythm was not VT or VF. Episodes of antitachycardia pacing (ATP) were not considered to be ICD shock therapy for this study.

2.1. Statistical analysis

Demographic and clinical data are reported as means and standard deviations for continuous variables and as frequencies for categorical variables. Univariate Cox proportional hazard models were used to determine the relationship between the time to inappropriate shock and potential predictors (age, gender, clinical history, cardiovascular risk factors, medications, and echocardiographic assessments, as well as appropriate shocks and VT ablation). The joint effects of any significant variables by univariate analysis were assessed in a multivariable Cox model (that also included age and gender). For these analyses, appropriate shocks and VT ablation were treated as time-dependent covariates. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC). A critical p-value of 0.05 was used for significance in all analyses.

3. Results

3.1. Patient population and prevalence

We reviewed the charts of 44 patients at Columbia University Irving Medical Center with surgical repair of TOF who had undergone ICD implantation for a history of either reduced EF, sustained VT, cardiac arrest, or syncope with positive EP study, or of unexplained etiology. Clinical characteristics of patients are shown in Table 1. Mean age at implantation was 39 ± 13 years; 27 (61.4%) were male. Median follow-up time was 15 years post-ICD implant, with a range of 1 to 34 years. Eleven (25%) of the 44 TOF patients received inappropriate shocks. Total follow-up time was greater among patients with inappropriate shocks than those without inappropriate shocks (mean 19.1 years vs 12.8 years, p = .0098).

| Table 1 Characteristics of the study population. |
|-----------------------------------------------|
| Number of Subjects | 44 |
| **Age at ICD implantation (mean ± SD)** | 39 ± 13 |
| Males | 27 (61.4%) |
| Body Mass Index (mean ± SD) | 25.8 ± 5.1 |
| ICD for primary prevention | 14 (31.8%) |
| Dual Chamber ICD | 28 (63.6%) |
| Pre-implant/concurrent VT Ablation | 4 (9.1%) |
| Post-implant VT Ablation | 8 (18.2%) |
| Cardiovascular Risk Factors |
| Hypertension | 21 (47.7%) |
| Diabetes | 7 (15.9%) |
| Hyperlipidemia | 14 (31.8%) |
| Coronary Artery Disease | 10 (22.7%) |
| Echocardiography |
| Left Atrial Dimension > 4.0 cm | 18 (40.9%) |
| Left Ventricular Ejection Fraction < 50% | 14 (31.8%) |
| Left Ventricular Diastolic Diameter > 5.9 cm male, > 5.3 cm female | 2 (4.5%) |
| Left Ventricular Systolic Diameter > 3.9 cm male, > 3.5 cm female | 10 (22.7%) |
| Left Ventricular Posterior Wall Thickness > 1 cm male, > 0.9 cm female | 21 (48.8%) |
| Interventricular Septum Thickness > 1 cm male, > 0.9 cm female | 23 (53.5%) |
| Medications |
| Antiarrhythmic | 14 (31.8%) |
| Beta Blocker | 30 (68.2%) |
| Calcium Channel Blockers | 6 (13.6%) |

3.2. Electrophysiological mechanisms

Eight (18%) patients received both appropriate and inappropriate shocks, 3 (7%) received only inappropriate shocks, and 6 (14%) received only appropriate shocks. Ventricular rates during appropriately shocked VT episodes ranged from 142 bpm to 300 bpm. Characteristics of the inappropriately shocked patients are shown in Table 2. Of the 11 (25%) inappropriately shocked patients, 3 received shocks for sinus tachycardia, 7 patients for atrial arrhythmias with rapid ventricular response (5 AF, 1 AFL, 1 unspecified atrial arrhythmia), and 1 patient was shocked due to noise artifact inappropriately sensed as VF. Among patients who were inappropriately shocked for atrial arrhythmias, 8 patients were treated with intravenous antiarrhythmic medication (5 AF, 2 AFL, 1 unspecified atrial arrhythmia), and 1 patient was shocked due to noise artifact and a p-value of 0.05 was used for significance in all analyses.
Inappropriate Shocks.

3.3. Treatments and follow up

After experiencing inappropriate shocks, 1 patient underwent epicardial rate sensing lead implant (patient anatomy precluded endocardial placement), 1 had the VT therapy zone cut-off rate increased, 3 were treated with antiarrhythmics, 3 were treated with beta blockers, and 3 did not have follow-up information available. Four of the patients who were inappropriately shocked for atrial arrhythmias later underwent ablation for atrial tachycardia. ATP had been programmed in 6 (66%) of the 9 inappropriately shocked patients for whom this data was available, and none of these patients had available data. None of the patients for whom follow-up data was available continued to experience inappropriate shocks after ablation or once their therapy cutoff was raised, rate or rhythm control drugs were added, or their device or lead was replaced.

4. Discussion

4.1. Prevalence, timing, and causes of inappropriate shocks

We report several conclusions regarding inappropriate shocks in adult TOF patients. First, approximately 1 in 4 patients with a history of repaired TOF and ICDs are at risk of experiencing inappropriate shock therapy from their ICDs. These findings are similar to other previous studies regarding the rates of inappropriate shocks among patients with CHD. Various prospective and retrospective studies have found lifetime inappropriate shock rates of 21–41% in patients with CHD [15–19]. Second, the major reasons for inappropriate shocks included supraventricular tachycardia and lead malfunction. Third, with regard to the timing of these inappropriate shocks, analysis of Fig. 2A indicates that they tended to cluster either within the first 2 years after device implant or generator change, or at least 8 years afterward. These data suggest that inappropriate therapy may be related either to suboptimal programming at implant/generator change, or to atrial arrhythmia or device malfunction as the patient and ICD system age. Fourth, lower VT therapy zone was associated with more inappropriate shocks in repaired TOF patients with ICDs. In cases where inappropriate shocks were for sinus tachycardia or atrial arrhythmias, most physicians opted for a rate or rhythm control medication strategy, rather than increasing the VT detection rate, likely due to a history of slow VT. In addition, four of the patients who were inappropriately shocked for atrial arrhythmias later underwent atrial ablation, though these were often several years after patients were shocked, likely after medical therapy was deemed insufficient. If VT detection rates are to be lowered to treat VTs occurring at relatively low rates, strategies that include effective atrioventricular nodal blocking agents for rate control, antiarrhythmic medications, and/or catheter ablation are effective tools to prevent inappropriate ICD shock therapy.

4.2. Primary and secondary prevention of inappropriate shocks

As Fig. 2B illustrates, inappropriate shock therapy can occur even a decade after patients have undergone initial implantation. These findings reinforce the need for thoughtful consideration of tachycardia parameter settings at each device check/interrogation, as well as at each generator change. They also reinforce the need for remote monitoring of patients to assess potential development of device/lead malfunction, as well as the early identification of supraventricular arrhythmias such as atrial flutter or tachycardia with rapid ventricular response, that can lead to inappropriate shock therapy. In addition, as patients age, healthcare providers must remain vigilant to the fact that such patients may be at higher risk for development of atrial tachycardia that can be mis-interpreted by their devices as VT/VF, leading to inappropriate shock therapy, with consequent adjustments to detection and treatment algorithms as patients age.

With regard to specific treatment strategies to decrease inappropriate shock rates in TOF patients, our data are in agreement with studies in the non-congenital ICD population in general, which note that using higher therapy cutoff rates (as well longer detection times) result in better health outcomes in ICD patients. In MADIT-RIT [20], a faster VT cutoff was associated with fewer inappropriate therapies and lower mortality, and delayed therapy was associated with fewer inappropriate therapies. In ADVANCE III [21], fewer therapies, fewer inappropriate shocks, and fewer hospitalizations were observed in the longer detection window group [22]. In PROVIDE [23], a longer detection interval was asso-
associated with lower all cause shock and a reduction in mortality. Initially, programmed “factory” ICD settings vary between ICD manufacturers and models [24]. It is important that physicians are familiar with the recommendations for the specific model with which a patient is equipped, and that the patient’s full history is taken into consideration when programming ICD parameters. Various strategies exist for determining a rate cutoff sensitive enough to protect against VT but selective enough to prevent inappropriate shocks [25–27]. These include supraventricular tachycardia (SVT) discriminators, ventricular morphology discriminators, and sudden onset discriminators.

ATP can also be an effective method of interrupting both slow and fast VT, as well as SVTs, although a small risk of accelerating ventricular arrhythmias exists [28]. Incorporating ATP when programming an ICD likely can prevent inappropriate shock therapy [26–28]. Receiving ATP may be associated with higher quality of life.

Fig. 1. (A) Age at first ICD implant. (B) VT therapy rate at time of shock for patients who experienced shocks, or lowest recorded rate for patients who did not experience shocks. Patients who experienced inappropriate shocks were more likely to have lower VT detection rates than those who did not experience inappropriate shocks.
than shock therapy [29]. ATP has been shown to be effective in TOF patients [30], but further research into the effect of ATP therapy on inappropriate shock therapy in TOF patients is warranted.

Finally, the high rate of inappropriate shocks due to atrial arrhythmias also stresses the importance of atrial/ventricular arrhythmia discrimination. In patients with TOF, who are at increased risk for atrial arrhythmias, a strategy of implanting dual chamber devices with atrial sensing to identify atrial/ventricular dissociation may protect against inappropriate shocks, recognizing that such algorithms are imperfect and that inappropriate shocks still occur in dual chamber sensing devices [31]. Given that only four of the inappropriately shocked patients had available data on SVT discriminators, the role of atrial leads as SVT discriminators in CHD patients requires further analysis.

5. Limitations

This study was a retrospective review of electronic health record of surgically repaired TOF patients with ICDs at Columbia University Irving Medical Center, and therefore is limited by a single center study with a small sample size. Given the fact that there were only 11 patients with inappropriate shocks, there was little power to detect significant predictors. As this is a select population, indications were not uniform, especially as some ICDs were implanted elsewhere. Several patients had their devices implanted at other hospitals, and experienced shocks before they were followed at this institution. As such, some information regarding shocks was self-reported. Finally, full data regarding ATP frequency and settings, dual chamber discrimination algorithms, and antiarrhythmic drug dosing was also not fully available for review.

6. Conclusions

In patients with repaired TOF and ICDs, inappropriate shock therapy is relatively common. The majority of inappropriate shocks occurred in the presence of atrial arrhythmias or sinus tachycardia. Lower VT detection rate was associated with increased risk for inappropriate shock therapy. These data point out the importance of considering the risks of inappropriate shocks when setting tachycardia therapy parameters in TOF patients with ICDs. Conservative programming with maximum use of atrial/ventricular discrimination algorithms, atrial lead discrimination, ATP therapy prior to shock therapy, concurrent use of medical and/or ablation therapy for atrial arrhythmias should be considered.
Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jichi.2020.100543.

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