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Noninvasive Predictors of Ventricular Arrhythmias in Patients With Tetralogy of Fallot Undergoing Pulmonary Valve Replacement

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ABSTRACT

OBJECTIVES This study sought to test the hypothesis that a vectorcardiographic parameter, the QRS vector magnitude (QRSVm), can risk stratify those patients at risk for sustained spontaneous ventricular arrhythmias (VAs) or ventricular arrhythmia inducibility (VAI) in a large cohort of patients with tetralogy of Fallot (TOF).

BACKGROUND Patients with TOF have an increased risk of VAs, but predicting those at risk can often be challenging.

METHODS Blinded retrospective analyses of 177 TOF patients undergoing pulmonary valve replacement (PVR) between 1997 and 2015 were performed. VAI was evaluated by programmed electrical stimulation in 48 patients. QRS intervals and QRSVm voltage measurements were assessed from resting 12-lead electrocardiograms, and risk of VA was determined. Clinical characteristics, including imaging and cardiac catheterizations, were used for other modality comparisons.

RESULTS Sustained spontaneous VA occurred in 12 patients and inducible VA in 18 patients. Age and QRSVm were significant univariate predictors of VA. QRSVm was the only independent predictor of VAI ($p < 0.001$). Using a root mean square QRS value of 1.24 mV, the positive and negative predictive values were 47.9% and 97.8%, respectively, for spontaneous sustained VA. For VAI, using a QRSVm cutoff of 1.31 mV, positive and negative predictive values were 63.0% and 95.3%, respectively.

CONCLUSIONS In TOF patients undergoing PVR, older age was associated with increased spontaneous VA risk. Lower QRSVm predicted spontaneous VA or VAI risk with high negative predictive values. QRSVm is the only independent predictor of VAI. These clinical features may help further risk stratify TOF patients requiring therapies to prevent sudden death. (J Am Coll Cardiol EP 2016;■:■–■) © 2016 by the American College of Cardiology Foundation.

Patients with tetralogy of Fallot (TOF) have a significant burden of arrhythmias post-operatively, reported to be as high as 43.3% in some series (1). The clinical history remains important but may be insufficient for predicting the risk of ventricular arrhythmias (VAs). Invasive risk stratification via programmed electrical stimulation (PES) in TOF patients has been shown to have diagnostic and prognostic value (2). Noninvasive measures of the right ventricle (RV), such as QRS duration (QRSd), QRS fragmentation, increased RV volumes, as well as right ventricular ejection fraction (RVEF) and left ventricular ejection fraction (LVEF), have demonstrated association with increased risk of arrhythmias (3–7).

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

ECG = electrocardiogram

EP = electrophysiology

IQR = interquartile range

LVEDP = left ventricular end-diastolic pressure

LVEDV = left ventricular end-diastolic volume

LVEF = left ventricular ejection fraction

MRI = magnetic resonance imaging

OR = odds ratio

PES = programmed electrical stimulation

PVR = pulmonary valve replacement

QRSd = QRS duration

QRSVm = QRS vector magnitude

ROC = receiver-operating characteristic

RV = right ventricle

RVEDP = right ventricular end-diastolic pressure

RVEDV = right ventricular end-diastolic volume

RVEF = right ventricular ejection fraction

TOF = tetralogy of Fallot

VA = ventricular arrhythmia

VAI = ventricular arrhythmia inducibility

VF = ventricular fibrillation

VT = ventricular tachycardia

Vectorcardiographic principles provide additional clinical information to the 12-lead electrocardiogram (ECG) and have yielded further diagnostic (8-10) and prognostic (10-15) value to the ECG in the traditional 12-lead configuration. In a small cohort of adult TOF patients, increased risk of sustained spontaneous VA and inducible ventricular arrhythmia has been demonstrated by a measure of QRS dispersion called the QRS vector magnitude (QRSVm, or magnitude of the 3-dimensional QRS vector), with improved predictive value over QRSd or spatial QRS-T angle. The predictive value of QRSVm was independent of magnetic resonance imaging (MRI) RV volume, gadolinium enhancement, or hemodynamics measured via cardiac catheterization (16).

QRSVm denotes the magnitude of the maximum 3-dimensional QRS vector and is calculated as the root mean square of the QRS wave in 3-dimentional space. It is calculated from the equation:

$$\sqrt{\left\{(QRS maximum\ lead\ II)^2 + (QRS maximum\ lead\ V6)^2 + (-0.5 \cdot QRS maximum\ lead\ V2)^2\right\}}$$

We hypothesized that QRSVm, based on a sinus rhythm ECG recorded just before a TOF patient undergoes pulmonary valve replacement (PVR), will predict risk of spontaneous VA as well as risk of inducible VA during PES in a large cohort of TOF patients. We chose to evaluate QRSVm on ECGs at the time of PVR because of several clinical considerations: 1) the risk of VA and ventricular arrhythmia inducibility (VAI) is high during this time; 2) other clinical parameters (cardiac catheterizations and MRIs) are usually measured during this period so that correlations can be made; and 3) predicting VA or VAI risks before PVR may allow for changes in management at the time of PVR, such as cryoablation during open surgery or consideration of further risk stratification such as electrophysiological (EP) studies around the time of PVR.

PATIENTS AND METHODS

STUDY POPULATION. This study was approved by the institutional review board at the University of Colorado.

A blinded retrospective analysis was performed on available electrocardiograms and associated imaging data from 362 TOF patients from 1977 to 2015 at the University of Colorado Hospital systems (including the Children's Hospital of Colorado). This group included 177 TOF patients who were undergoing PVR via transcatheter insertion utilizing Melody valves (Medtronic, Minneapolis, Minnesota) or via cardiac surgery. Patients were excluded if they did not undergo a procedure for PVR or if they did not have an interpretable ECG with adequate baseline measurement recorded within the 6 months before PVR. Patients also were excluded if a diagnosis of TOF or TOF-like physiology was not certain or if they had left-sided obstruction at the time of PVR. ECG assessment near the time of PVR was chosen because cryoablation during this period might be able to prevent recurrence of arrhythmia (7).

Patients who had sustained spontaneous VA burden (seen by ECG, Holter, exercise stress test, pacemaker, or telemetry monitoring) were identified. Sustained spontaneous VA was defined as ≥30 s of VA or a VA that was associated with hemodynamic instability. For these patients, the arrhythmia had to have occurred within the 6 months before or 6 months after PVR, and their last sinus rhythm ECG before arrhythmia identification/treatment and before PVR was used for evaluation. Thus, at the time of ECG assessment, no patients were taking ion-channel inhibiting medications, had not undergone ablations, and had no new medical devices placed.

Comparisons were made between those patients with spontaneous sustained VA versus all patients without VA, including those undergoing PES (N = 177); for those with either VA or induced sustained VA (VAI) versus no VA or VAI; and for only those undergoing PES (n = 48), comparisons were made between those who had inducible sustained VA (VAI) versus those without VAI.

EP STUDIES AND ECGs. Some patients had undergone EP studies before PVR. Inducibility was evaluated from EP studies using PES, as previously described (2). Briefly, PES was performed at 2 drive trains and at 2 sites, with up to triple extrastimuli and decrementing to ventricular effective refractory period or 180 ms. If a patient was noninducible, the protocol was repeated on isoproterenol. Inducibility was defined as any VA (monomorphic VA, polymorphic VA, or ventricular fibrillation [VF]) that lasted ≥30 seconds or was hemodynamically unstable requiring pace termination or defibrillation.