

Original Research Article

Profile of arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) patients presenting with sustained ventricular tachycardia in a tertiary care center

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ABSTRACT

Background: Arrhythmogenic right ventricular cardiomyopathy /dysplasia (ARVC/D) is a genetic form of cardiomyopathy and is one among the most common causes of sudden cardiac death (SCD). The aim of our study was to analyze the clinical profile of (ARVC/D) patients presenting with sustained Ventricular Tachycardia (VT).

Methods: This single center cohort study evaluated 107 patients who presented with sustained ventricular tachycardia (VT) in our hospital. After aetiological evaluation of all these patients, 15 patients were found to have ARVC/D as the cause of sustained ventricular tachycardia (VT) as per the Modified Task Force Criteria. The clinical profile of these patients was observed in detail to enhance our knowledge about this entity in our part of the world.

Results: Mean age at presentation was 30 years and 12 patients were males. Nine patients were haemodynamically stable at the time of sustained VT and the rest of patients were haemodynamically unstable. Left Bundle Branch Block (LBBB) was the most common ECG morphology present in 11 patients. Antiarrhythmic drugs terminated VT in 7 patients. All the 6 patients presenting in a state of haemodynamic instability received DC cardioversion. Mortality occurred in 2 patients during the hospital stay.

Conclusions: ARVC/D presenting with sustained VT is an important manifestation of the disease. Males are more commonly affected than females. Haemodynamic instability at the time of presentation carries a poor prognosis.

Keywords: Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D), Intracardiac defibrillator (ICD), Right ventricle (RV), Sustained ventricular tachycardia (VT), Sudden cardiac death (SCD)

INTRODUCTION

The arrhythmogenic right ventricular cardiomyopathy /dysplasia (ARVC/D) is a genetic form of cardiomyopathy usually transmitted by an autosomal dominant pattern. It is characterized by fibrofatty replacement, primarily of right ventricular (RV) musculature. Although it primarily affects right ventricle but can also affect left ventricular (LV) musculature and may culminate in biventricular heart failure (HF), life

threatening ventricular arrhythmias and sudden cardiac death (SCD).¹⁻⁵ It accounts for 11 to 22 percent of the cases of sudden cardiac death in the young athlete population.

ARVC/D was first described by the Pope's physician, Giovanni Maria Lancisi in his book *De Monty Cordis et Aneurysmatibus* published in 1736.⁶ However the first clinical profile of the disease was published in 1982.⁷

Pathologically it is characterized by the myocardial atrophy, fibrofatty replacement, fibrosis, thinning of the wall with aneurysm formation.⁸ A genetic background has been demonstrated in 30 to 50 percent cases of ARVC/D.⁹ Disease is typically inherited as autosomal dominant trait with variable penetration and incomplete expression. Most of the genes identified code for desmosome family of proteins. Acquired factors have also been suggested as the cause of ARVC/D. The strongest association has been made with the viral myocarditis including arrhythmogenic cardiomyopathy. It is possible that wide variation in the presentation of the ARVC/D patients could be explained by its genetic heterogeneity and modifying factors such as exercise and/or viral myocarditis.^{10,11}

The most common clinical presentation of ARVC/D is ventricular arrhythmia arising predominantly from the RV. These arrhythmias range from isolated premature ventricular beats to sustained ventricular tachycardia (VT) or ventricular fibrillation that may lead to sudden cardiac death. The most common presenting symptoms of the disease are palpitations, chest discomfort, near syncope or syncope. The most common arrhythmia is sustained monomorphic VT that originates in the RV and thus has a left bundle branch block (LBBB) morphology. Alternatively, in some cases where left ventricle is involved, right bundle branch block morphology (RBBB) can be present.

The diagnosis of the ARVC/D is often difficult because there is no single investigation to establish or to exclude the diagnosis. However, the results of history, physical examination, and a number of specific tests including electrocardiogram (ECG), echocardiography, cardiac magnetic resonance imaging (CMRI) and right ventriculography can be used to establish diagnosis. The Original International Task Force Criteria for the clinical diagnosis of ARVC/D were published in 1994 and were based on structural, histological, ECG, arrhythmic and familial features of the disease.¹² The 2010 updated Task Force guidelines incorporated advances in our understanding particularly in the genetics of ARVC/D and the technology to improve diagnostic sensitivity while maintaining specificity.

METHODS

Aims of the study to evaluate the demography, presentation, management, intervention and final outcome of patients of arrhythmogenic right Ventricular cardiomyopathy/dysplasia ARVC /D who presented with sustained ventricular tachycardia in our hospital.

Study design

This single center based prospective study was conducted at Sher-i-Kashmir Institute of Medical Sciences, a tertiary care center in Srinagar, Jammu and Kashmir, India, between August 2012 and May 2016.

Study population

Inclusion criterion: All cases with definite sustained ventricular tachycardia (VT) (lasting more than 30 s or terminated by intervention) already admitted in the hospital or presenting in accident emergency department were evaluated for the aetiology of sustained ventricular tachycardia (VT) and those having ARVC/D as per the proposed modification of task force criteria, were included.

Exclusion criterion: Following patients were excluded

- Patients who were found to have other aetiologies of sustained VT, other aetiologies being in the form of coronary artery disease (CAD), Non-ischemic idiopathic dilated cardiomyopathy (DCMP) and idiopathic among others.
- Patients who died early after hospitalization thereby precluding further evaluation.
- Patients who refused for further evaluation.
- Patients with recurrent episodes of sustained ventricular tachycardia (VT), only the first episode was considered as an index event and evaluated.

Consent

An informed consent was obtained from each subject after explaining the study in detail.

Initial Evaluation

Every patient of sustained VT (ECG diagnosis was made by applying “Brugada algorithm” and /or “The Avr Verecke Alogrithm”) was subjected to battery of tests after aborting acute attack of VT.^{13,14} We defined two groups of patients based on their haemodynamic status on presentation: Haemodynamically stable and Haemodynamically unstable. Haemodynamic instability was defined as need for immediate cardioversion due to loss of consciousness, hypotension, shock or occurrence of congestive heart failure. Otherwise the patients were defined as hemodynamically stable. The aetiological evaluation was done in all the patients. ECG characteristics during VT and in resting stage were observed. 2-D echocardiography was done in all the patients. Exercise test and 24 hours Holter monitoring was done in selective cases. Patients in whom ARVC/D was suspected on the basis of family history, ECG characteristics, echocardiography, stress test or 24 hours Holter monitoring were subjected to cardiac MRI. Only those patients who qualified the Modified Task Force criterion of ARVC/D were included in ARVC/ D group.¹⁵

Other relevant investigations

Standard Chest radiography in standing position was done in all the cases.

Serum electrolytes: Potassium levels were seen in all the patients. Hypokalemia was defined as serum potassium levels of less than 3.5mg/dl. Hypomagnesemia was defined as serum magnesium levels less than 1.5mg/dl. Coronary angiography was done in patients with definitive or suspected myocardial infarction and those patients with intermediate to high risk of coronary artery disease derived from Framingham risk calculator.

VT termination and follow up

The therapy for termination of VT followed a well-established protocol as per latest ACLS guidelines. Patients who were hemodynamically unstable were administered DC cardioversion. Pulseless VT patients were administered cardiopulmonary resuscitation (CPR) till the time defibrillator was made ready for delivery of DC shock. Intravenous antiarrhythmic drugs in recommended doses were given to haemodynamically stable patients. The choice of antiarrhythmic drug was on attending physicians discretion. Electrical cardioversion was given to those patients who became secondarily unstable or in whom antiarrhythmic drugs failed to terminate VT.

RESULTS

In our study a total of 107 patients of sustained VT were enrolled. Out of these, 15 patients fulfilled the criterion of ARVC/D as proposed by modified task force criteria. Following are the important characteristics of these fifteen patients (Figure 1).

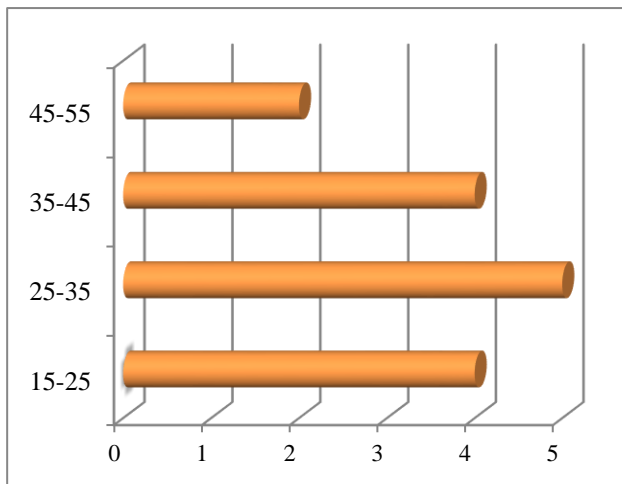


Figure 1: Showing age distribution in years.

Majority of patients were males (12 patients, 80 %). Age of the patients ranged from 15 to 55 years whereas mean age at presentation was 30 years. A positive family history of premature sudden cardiac death (SCD) in a first degree relative was found in 5 patients (Figure 2).

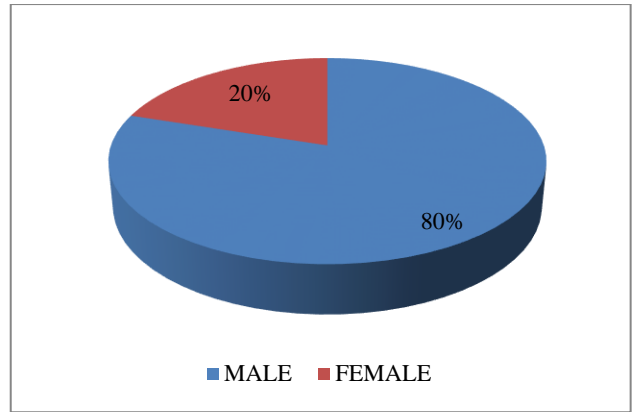


Figure 2: Showing sex distribution of patients.

Haemodynamic instability was found in 6 patients (40 %). Monomorphic VT was the most common pattern (13 patients, 87 %). Polymorphic VT was found in 2 patients. Left Bundle Branch Block (LBBB) morphology was the most common morphology seen in 11 patients (73%) followed by Right Bundle Branch Block (RBBB) morphology in 2 patients (Figure 4).

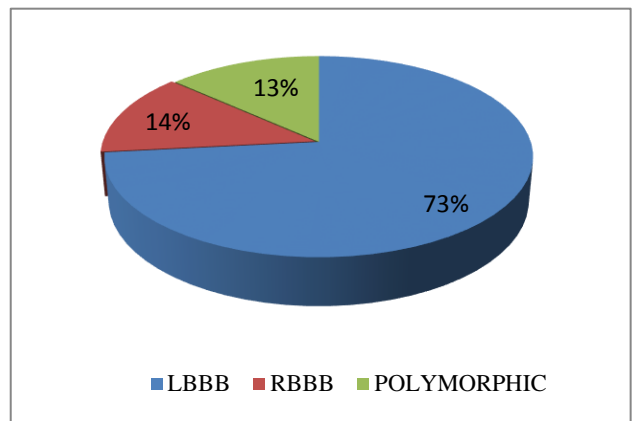


Figure 3: Showing patterns of ECG morphology seen in patients.

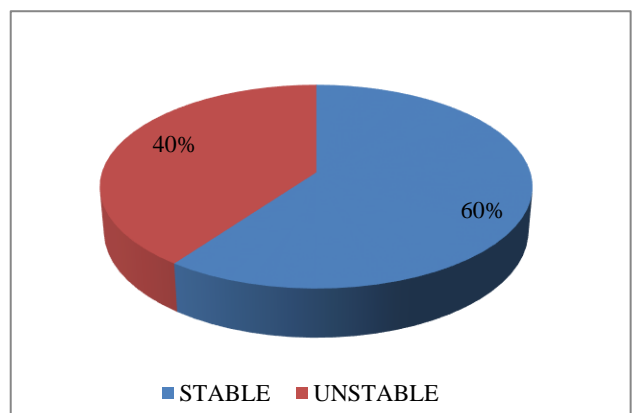


Figure 4: Showing haemodynamic status of patients.

ECG abnormalities were found in 12 patients (80%). Repolarization abnormalities were found in 10 patients (66%) and depolarization abnormalities (Epsilon waves) were found in 5 patients (33%). Echocardiography was done in all the patients (Figure 3). Typical ARVC/D changes meeting major diagnostic criterion were found in 11 patients (73%) and changes meeting minor diagnostic criterion were found in 3 patients (20%). Cardiac MRI was done in all the patients and showed changes compatible with the major diagnostic criterion in 9 patients (60%). Invasive tests like right ventriculography and endomyocardial biopsy was not done in any of our patient.

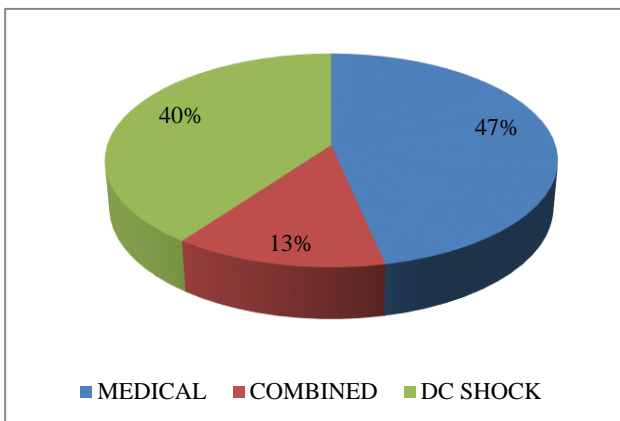


Figure 5: Showing treatment modality received by patients.

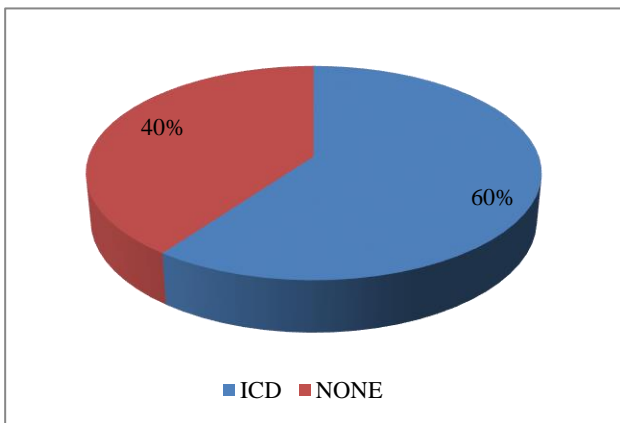


Figure 6: Showing percentage of patients implanted with ICD.

Antiarrhythmic drugs were given to 9 hemodynamically stable patients. 7 of these patients reverted with drugs alone and 2 patients needed additional electric cardioversion because of failure to restore sinus rhythm. Thus, the success rate of restoring the sinus rhythm by intravenous drugs was 78 %. So, a combination therapy (both medical and electric cardioversion) was given to 2 patients (13%) who did not respond to initial i/v drugs alone. All the 6 patients presenting with haemodynamic instability were reverted with DC cardioversion. VT was terminated successfully in all these 6 patients initially. Of

total 9 patients who received antiarrhythmic drugs, 5 patients (56%) received amiodarone, followed by sotalol in 2 patients (Figure 5). The remaining 2 patients received a combination of various drugs like amiodarone, sotalol and lignocaine among others. Intracardiac defibrillator (ICD) implantation was done in 9 patients. Mortality was seen in 2 patients and both of these patients were having haemodynamic instability at the time of presentation (Figure 6).

DISCUSSION

While observing the patients of ARVC/D presenting as sustained VT, the following important conclusions were drawn. Males are affected more commonly than the females. It is a disease of adolescent to adult population. LBBB is the most common morphology on ECG. Haemodynamic instability is present in a number of such cases and wherever present, it carries a poor prognosis.

All of our patients were diagnosed on the basis of noninvasive diagnostic tests without a need for invasive testing like endomyocardial biopsy and right ventriculography. Majority of our patients (12 patients, 80%) were males which is consistent with the previous studies which showed a higher prevalence of ARVC/D in men.^{16,17} The age at presentation in our patients was in the range of 15 to 55 years. The incidence of ARVC/D is highest in 5 to 40 years as per existing data.¹⁸ The marked variability in the age of presentation suggests that ARVC/D remains concealed for a varying period of time in different individuals.¹⁹

Our study observed and evaluated patients of ARVC/D presenting as sustained VT which forms one of the most important presenting symptom of ARVC/D.²⁰

A family history of premature sudden cardiac death (SCD) in the first-degree relatives was present in 5 patients which constitutes a minor diagnostic criterion as per modified task force criteria.

The ECG characteristics of our cohort showed that LBBB morphology was the most common morphology of the sustained VT seen in 11 patients. This is consistent with the previous data published on the same topic.²¹ LBBB morphology was followed by RBBB and polymorphic morphology of sustained VT. It is important to mention here that both the patients of polymorphic VT were haemodynamically unstable on presentation. Domanovitis et al, studied clinical profile of VT patients presenting in emergency department and observed that only ECG characteristic that correlated with the haemodynamic instability was the polymorphic pattern of VT.²²

Another very helpful and useful method of diagnosing ARVC/D is echocardiography. This technique which is noninvasive, widely available and cost effective has played a crucial role in imaging the structural and

functional abnormalities of the right ventricle. Right ventricular function should be measured at several points, including the inflow and outflow tracts because of the focal nature of the disease.^{23,24} Echocardiography was done in all the patients in our study. The echocardiographic findings most suggestive of ARVC/D include dilation of the right ventricle (RV) with localized aneurysms and dyskinesia in the inferobasal region. Several studies have found that 2-D echocardiography has a high specificity and predictive value for ARVC/D. In our study typical ARVC/D changes meeting the major diagnostic criterion were seen in 11 patients (73%) and ARVC/D changes meeting the minor criterion were seen in 3 patients.

Cardiac MRI was done in all our 15 patients. Quantitative analysis shows that right ventricular (RV) end diastolic diameter and outflow tract area are significantly higher and RV ejection fraction is lower in ARVC/D patients as compared to controls.^{25,26} In our study cardiac MRI showed changes compatible with the major diagnostic criterion in 9 patients.

Various drugs have been investigated to suppress the life threatening arrhythmias of ARVC/D including beta blockers, lignocaine, sotalol and amiodarone.²⁷ In our study we used only amiodarone, sotalol, lignocaine and I/V betablockers as rest of the antiarrhythmic drugs were not available. These drugs were used in solo or in combination. 5 patients received amiodarone only and 2 patients received sotalol only. The remaining 2 patients received a combination of various drugs like amiodarone, sotalol, lignocaine and i/v beta blockers. DC shock remains a very crucial treatment modality in patients presenting in a state of haemodynamic instability or in conditions where VT cannot be reverted with medications alone. In our study, all the 6 patients presenting in haemodynamic instability received DC cardioversion.

The implantation of ICD device can effectively terminate life threatening arrhythmias in patients of ARVC/D and it is considered a standard therapy. Accepted indications for ICD therapy are the prevention of sudden cardiac death (SCD) in ARVC/D patients with documented sustained VT or ventricular fibrillation (Class 1 recommendation) and in patients with features such as extensive disease, a positive family history or undiagnosed syncope (Class 2a recommendation).²⁸ In our study, ARVC/D patients presenting with sustained VT were evaluated. So, ICD was indicated in all these patients, but ICD was implanted in 9 patients only due to various reasons.

Death in hospital occurred in 2 patients only. Both of these patients were in a state of haemodynamic instability at the time of presentation. The major limitations of our study are as follows:

- Total number of patients in this study seem to be far less than disease burden in our population. Not all potential patients of ARVC/D have been included.

Only the patients presenting with sustained VT were included.

- Invasive diagnostic modalities like endomyocardial biopsy and right ventriculography were not done in this study.
- Antiarrhythmic drugs were used on the discretion of the attending physician.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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