Arrhythmogenic Right Ventricular Cardiomyopathy: What Have We Learned from the Johns Hopkins ARVC Program and Genetic Screening

Presented at the 10th Annual Scientific Session of the Korean Heart Rhythm Society

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www.ARVD.com
Arrhythmogenic Right Ventricular Cardiomyopathy: What Have We Learned from the Johns Hopkins ARVC Program and Genetic Screening

- Overview of ARVD
- Genetic Basis of ARVD
- Clinical presentation and follow-up
- Management of ARVD and Risk Stratification
- Conclusion and Future Directions
Arrhythmogenic Right Ventricular Dysplasia

Overview

• Genetically determined cardiomyopathy

• Characterized by:

  • Progressive replacement of the right ventricular myocardium with fatty & fibrous tissue

  • Ventricular arrhythmias of right ventricular origin

  • A left dominant form of ARVD has been described leading to some to refer to the disease as “arrhythmogenic cardiomyopathy”.
ARVD Overview: Epidemiology

• Prevalence: 1 per 2000 in Italy & 1 per 5000 in the US

• Slightly more common in men than women

• 20% of sudden deaths in young individuals in Italy

• 5% of sudden deaths in young individuals in the US
Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia

Proposed Modification of the Task Force Criteria

Frank I. Marcus* Chair, William J. McKenna Co-Chair, Duane Sherrill, Cristina Basso, Barbara Bauce, David A. Bluemke, Hugh Calkins, Domenico Corrado, Moniek G.P.J. Cox, James P. Daubert, Guy Fontaine, Kathleen Gear, Richard Hauer, Andrea Nava, Michael H. Picard, Nikos Protonotarios, Jeffrey E. Saffitz, Danita M. Yoerger, Jonathan S. Steinberg, Harikrishna Tandri, Gaetano Thiene, Jeffrey A. Towbin, Adalena Tsatsopoulou, Thomas Wichter, and Wojciech Zareba

European Heart J 2010; 31: 806-814.
Circ 2010; 121; 1533-41
<table>
<thead>
<tr>
<th>Parameter</th>
<th>1994 Criteria</th>
<th>2010 Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV Size and Function</td>
<td>Non quantitative</td>
<td>Quantitative</td>
</tr>
<tr>
<td>Biopsy (major)</td>
<td>Fibrofatty replacement</td>
<td>&lt; 60% nl myocytes &amp; fibrous replacement +/- fat</td>
</tr>
<tr>
<td>T wave inversion v2 and V3</td>
<td>Minor criteria in absence RBBB</td>
<td>Major criteria in absence of RBBB QRS &gt; 120 msec</td>
</tr>
<tr>
<td>Epsilon waves (major)</td>
<td>Epsilon or localized prolongation &gt; 110 ms V1-V3</td>
<td>Epsilon waves</td>
</tr>
<tr>
<td>SAECG (minor)</td>
<td>Late potentials</td>
<td>Quantitative, 1 of 3 parameters</td>
</tr>
<tr>
<td>TAD</td>
<td>NA</td>
<td>&gt;= 55 msec in V1-v3</td>
</tr>
<tr>
<td>LBBB VT (minor)</td>
<td>Minor criteria</td>
<td>Major criteria if LB sup axis VT, minor criteria if not</td>
</tr>
<tr>
<td>Frequent PVCs (minor)</td>
<td>&gt; 1000/ 24 hrs</td>
<td>&gt; 500 / 24 hrs</td>
</tr>
<tr>
<td>Family History (Major)</td>
<td>Familial disease confirmed by autopsy or surgery</td>
<td>ARVD in first degree relative OR pathogenic mutation in patient</td>
</tr>
<tr>
<td>Family History (Minor)</td>
<td>FH of premature SCD &lt; 35 yrs or family hx of ARVD</td>
<td>FH of ARVD where task force criteria unclear or premature SD &lt; 35 yrs</td>
</tr>
</tbody>
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## 2010 ARVD Diagnostic Criteria

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</tr>
<tr>
<td></td>
<td></td>
<td>Minor: T wave inv V1, V2 or in V4, V5, and V6 or T in V1-v4 w RBBB</td>
</tr>
<tr>
<td>Epsilon waves (major)</td>
<td>Epsilon or localized prolongation &gt; 110 ms V1-V3</td>
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<td>FH of ARVD where task force criteria unclear or premature SD &lt; 35 yrs</td>
</tr>
</tbody>
</table>
ECG Features of ARVD
MRI Features of ARVD

Tandri, et al  JACC 2005;45:98-103
Please Remember:

1. MRI Imaging is not the “gold standard” for diagnosis of ARVD

2. MRI imaging is the most common reason for “over diagnosis” of ARVD

3. The most common reasons for over diagnosis of ARVD include:
   - Lack of awareness of the diagnostic criteria for ARVD
   - Failed recognition that presence of myocardial fat and wall thinning are not diagnostic for ARVD.
   - Failed recognition that RV wall motion abnormalities may result from a RV free wall tether between RV and sternum, pectus excavatum, and a RV moderator band.
   - Overdiagnosis of an apical aneurysm. ARVD spares the apex which is only impacted in very severe disease.
Outline

• Overview of ARVD
• Genetic Basis of ARVD
• Clinical presentation and follow-up
• Management of ARVD
• Cases from the Clinic
• Conclusion
Cardiac abnormalities in familial palmoplantar keratosis

N PROTONOTARIO, A TSATSOPLOU, P PATSOURAKOS,
D ALEXOPOULOS, P GEZERLIS, S SIMITSIS, G SCAMPARDOHIS

From the Department of Cardiology, 401 Army General Hospital, Athens, Greece

SUMMARY Cardiac abnormalities were identified in patients with familial palmoplantar keratosis. All of them were descended from families on the Greek island of Naxos. Four families were studied and nine cases of palmoplantar keratosis were identified; seven of them showed symptoms and signs of heart disease. Cardiomegaly on chest x ray and electrocardiographic abnormalities were common findings. Three cases had episodes of ventricular tachycardia and a fourth patient died suddenly. All patients with cardiac signs and symptoms showed echocardiographic enlargement of the right ventricle and a right ventricular band; in three the left ventricle was also affected.
Identification of a deletion in plakoglobin in arrhythmogenic right ventricular cardiomyopathy with palmoplantar keratoderma and woolly hair (Naxos disease)

Godfrina McKoy, Nikos Protonotarios, Andrew Crosby, Adalena Tsatsopoulou, Aris Anastasakis, Aman Coonar, Mark Norman, Christina Baboonian, Steve Jeffery, William J McKenna

Lancet 2000
Mutation in Human Desmoplakin Domain Binding to Plakoglobin Causes a Dominant Form of Arrhythmogenic Right Ventricular Cardiomyopathy

Alessandra Rampazzo, Andrea Nava, Sandro Malacrida, Giorgia Beffagna, Barbara Bauce, Valeria Rossi, Rosanna Zimbello, Barbara Simionati, Cristina Basso, Gaetano Thiene, Jeffrey A. Towbin, and Gian A. Danieli

Departments of 1Biology, 2Cardiology, and 3Pathology, and 4CRIBI, University of Padua, Italy; and 5Department of Pediatrics, Pediatric Cardiology, Baylor College of Medicine, Houston

Am. J. Hum. Genet. 2002

Mutations in the desmosomal protein plakophilin-2 are common in arrhythmogenic right ventricular cardiomyopathy

Brenda Gerull, Arnd Heuser, Thomas Wichter, Matthias Paul, Craig T Basson, Deborah A McDermott, Bruce B Lerman, Steve M Markowitz, Patrick T Ellinor, Calum A MacRae, Stefan Peters, Katja S Grossmann, Beate Michely, Sabine Sasse-Klaassen, Walter Birchmeier, Rainer Dietz, Günter Breithardt, Eric Schulze-Bahr & Ludwig Thierfelder

Nature Genetics 2004
**REPORT**

**DSG2 Mutations Contribute to Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy**

Mark M. Awad, Darshan Dalal, Eunpi Cho, Nuria Amat-Alarcon, Cynthia James, Crystal Tichnell, April Tucker, Stuart D. Russell, David A. Bluemke, Harry C. Dietz, Hugh Calkins, and Daniel P. Judge

Arrhythmogenic right ventricular dysplasia/cardiac myopathy (ARVD/C) is a disorder characterized by fibrofatty replacement of cardiac myocytes that typically manifests in the right ventricle. It is inherited as an autosomal dominant disease with reduced penetrance, although autosomal recessive forms of the disease also occur. We identified four probands with ARVD/C caused by mutations in *DSG2*, which encodes desmoglein-2, a component of the cardiac desmosome. No association between mutations in this gene and human disease has been reported elsewhere. One of these probands has compound-heterozygous mutations in *DSG2*, and the remaining three have isolated heterozygous missense mutations, each disrupting known functional components of desmoglein-2. We report that mutations in *DSG2* contribute to the development of ARVD/C.

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**Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy Associated with Mutations in the Desmosomal Gene Desmocollin-2**

Petros Syrris, Deirdre Ward, Alison Evans, Angeliki Asimaki, Estelle Gandjbakhch, Srijita Sen-Chowdhry, and William J. McKenna

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Am J Hum Genetics 2006
ARVD: A Disease of the Desmosome

5 desmosomal genes:
PKP2, DSP, JUP, DSG2, DSC2
ARVD Genetic Mutations: 2018

**Up to Two Thirds Harbor Mutations in Desmosomal Genes**

- **PKP2** (plakophilin-2) - 25% of cases
- **DSG2** (desmoglein-2) - 10% of cases
- **DSP** (desmoplakin) - 10% of cases
- **DSC2** (desmocollin-2) - 3% of cases
- **JUP** (plakoglobin) Naxos syndrome – rare, recessive

**Extra Desmosomal Genes Are Found in a Small Subset of Pts**

- **TMEM43**\* Newfoundland, highly penetrant, lethal, nuclear pore
- **Ryr2**\* (ryanodine receptor) - atypical disease – catech PMVT
- Others include desmin TGFB3, (DES), titin (TTN), lamin A/C (LMNA), Phospholaban (PLN), Na 1.5 (SCNA), Filamin C (FLNC), Cadherin 2 (CDH2)
ARVD Genetic Mutations: 2018

• Inheritance of desmosomal mutations predominantly follows an autosomal dominant pattern with age related incomplete penetrance, and variable expressivity.

• ARVC patients with multiple mutations (compound heterozygosity - two mutations one gene, and/or digenic heterozygosity - mutations in more than one gene ) is not uncommon with a prevalence ranging from 4% to 20%.

• No pathogenic mutation found in approximately one third of patients
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ARVD/C: A Transatlantic experience in 1001 index patients (N=439) and (N = 562) at risk family members

Aditya Bhonsale, Cindy James, Anneline te Riele, Dennis Dooijes, Crystal Tichnell, Abhishek Sawant, Brittney Murray, Jeroen van der Heijden, Harikrishna Tandri, Pieter Doevendans, Daniel Judge, Arthur Wilde, Peter van Tintelen, Richard Hauer, and Hugh Calkins

Results- Index patients

With pathogenic mutations n=264, 63%

vs

Without identified mutations n=152, 37%

• Mean age at presentation 34 in mutation carriers vs. 38 years in those without mutations, p<0.001
Impact of genotype on clinical course in arrhythmogenic right ventricular dysplasia/cardio-myopathy-associated mutation carriers

Aditya Bhonsale1, Judith A. Groeneweg2,3, Cynthia A. James1, Dennis Dooijes4, Crystal Tichnell1, Jan D. H. Jongbloed5, Brittnay Murray1, Anneline S. J. M. te Riele1,2, Maarten P. van den Berg6, Hennie Bikker7, Douwe E. Atsma8, Natasja M. de Groot9, Arjan C. Houweling10, Jeroen F. van der Heijden2, Stuart D. Russell1, Pieter A. Doevendans2, Toon A. van Veen11, Harikrishna Tandri1, Arthur A. Wilde12, Daniel P. Judge1, J. Peter van Tintelen5,3,13, Hugh Calkins1, and Richard N. Hauer2,3,*

1Division of Cardiology, Johns Hopkins University School of Medicine, Baltimore, USA; 2Department of Cardiology, University Medical Center Utrecht, Utrecht, The Netherlands; 3Interuniversity Cardiology Institute of the Netherlands (ICIN), PO Box 19258, 3501 DG Utrecht, The Netherlands; 4Department of Genetics, University Medical Center Utrecht, Utrecht, The Netherlands; 5Department of Genetics, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; 6Department of Cardiology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; 7Department of Clinical Genetics, Academic Medical Center, Amsterdam, The Netherlands; 8Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands; 9Department of Cardiology, Erasmus Medical Center, Rotterdam, The Netherlands; 10Department of Genetics, VU Medical Center, Amsterdam, The Netherlands; 11Department of Medical Physiology, University Medical Center Utrecht, Utrecht, The Netherlands; 12Department of Cardiology, Academic Medical Center, Amsterdam, The Netherlands; and 13Durrer Center for Cardiogenetic Research, Utrecht, The Netherlands

doi:10.1093/eurheartj/ehu509
Genotype of 577 Subjects

- Premature Truncating (60%)
- Splice Site (23%)
- Missense Mutation (14%)
Main Finding #1: Patients Presenting with Sudden Death Were Younger Than Those Presenting with Sustained VT and Asymptomatic Patients
Main Finding #2: Patients with more than one mutation had an earlier onset of symptoms (median age 23) and an earlier occurrence of sustained VT (median age 25) as compared with those with only one mutation.
Main Finding #3: LV dysfunction is related with genotype, and is more common in patients with DSP and nondesmosomal mutations.
Main Finding #4: Gender Impacts Phenotype

1. Presentation with SCD mainly in men (78%)
2. Men more likely to be probands (68%) and symptomatic at presentation (50% vs 37%)
3. Among those presenting alive, arrhythmia free survival lower in men
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ARVD Management

Accurate Diagnosis

Cascade Family Screening

Risk Stratify For SCD

Minimize Symptoms And ICD Shocks

Prevent Progression
ARVD Management

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Important Variables for Risk Stratification in ARVC

- History of sudden cardiac death
- History of sustained ventricular tachycardia
- Proband status
- Male gender
- Extent of disease
- PVC frequency on 24 hour Holter
- Cardiac syncope
- Exercise Plans
- Results of EP Testing
- Patient values and preferences
Incidence and Predictors of Implantable Cardioverter-Defibrillator Therapy in Patients With Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy Undergoing Implantable Cardioverter-Defibrillator Implantation for Primary Prevention

Aditya Bhonsale, MD, Cynthia A. James, PhD, Crystal Tichnell, MS, Brittney Murray, MS, Dmitri Gagarin, MD, Binu Philips, MD, Darshan Dalal, MD, Ryan Tedford, MD, Stuart D. Russell, MD, Theodore Abraham, MD, Harikrishna Tandri, MD, Daniel P. Judge, MD, Hugh Calkins, MD

JACC 2011

Baltimore, Maryland

- 84 patients
- 31.9 ± 11.9 yrs
- 39 men (46%)
- 4.73 ± 3.39 years

- Palpitations: 40 pts (48%)
- Syncope: 23 (27%)
- Chest pain: 14 (17%)
- Asx: 20 (24%)
Incidence and Predictors of ICD Therapy in Primary Prevention ARVD Patients

Appropriate ICD Therapy

ICD interventions for VFL/VF

Cumulative Event (Appropriate ICD therapy) free survival vs. Follow up (years)

Cumulative Event (ICD therapy for VF/VF) free survival vs. Follow up (years)
A

Cumulative Event (Appropriate ICD therapy) free survival

Log Rank (Mantel-Cox) p = 0.003

Non Inducible

Inducible

B

Cumulative Event (Appropriate ICD therapy) free survival

Log Rank (Mantel-Cox) p < 0.001

C

Cumulative Event (Appropriate ICD therapy) free survival

PVC >1000/24 hrs

Log Rank (Mantel-Cox) p = 0.017

D

Cumulative Event (Appropriate ICD therapy) free survival

Log Rank (Mantel-Cox) p < 0.001

PVCs > 1000

Proband Status
A Model Risk Prediction in Primary Prevention Arrhythmogenic right ventricular Cardiomyopathy

Inclusion Criteria

1. Patients with a definite ARVC diagnosis according to the 2010 TFC¹

2. No history of sustained ventricular arrhythmia at the time of diagnosis (primary prevention)

Patient Population: 5 Registries (14 centers) in North America and Europe (Largest primary prevention ARVC cohort)

Marcus, Eur H J. 2010
<table>
<thead>
<tr>
<th>Predictors</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td>Male Sex</td>
<td>Sustained Ventricular Arrhythmia</td>
</tr>
<tr>
<td>Age</td>
<td>1-Sustained Ventricular tachycardia (VT)/Ventricular fibrillation</td>
</tr>
<tr>
<td>Recent Cardiac Syncope</td>
<td>2-Sudden cardiac arrest or death</td>
</tr>
<tr>
<td>Non Sustained Ventricular Tachycardia</td>
<td>3- Sustained Ventricular tachycardia (VT)/Ventricular fibrillation treated by a defibrillator</td>
</tr>
<tr>
<td>24h Monitoring:</td>
<td></td>
</tr>
<tr>
<td>Number of ventricular extrasystoles</td>
<td></td>
</tr>
<tr>
<td>ECG:</td>
<td></td>
</tr>
<tr>
<td>Number of leads with T-wave inversion</td>
<td></td>
</tr>
<tr>
<td>Right Ventricular Ejection Fraction</td>
<td></td>
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<tr>
<td>Left Ventricular Ejection Fraction</td>
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## Baseline Characteristics

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<tr>
<th></th>
<th>Total</th>
<th>Johns Hopkins</th>
<th>Canada</th>
<th>Netherlands</th>
<th>Swiss</th>
<th>Nordic</th>
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<tbody>
<tr>
<td>n</td>
<td>528</td>
<td>226 (42.8)</td>
<td>33 (6.3)</td>
<td>147 (27.8)</td>
<td>46 (8.7)</td>
<td>76 (14.4)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>236 (44.7)</td>
</tr>
<tr>
<td>Age at diagnosis (years)</td>
<td>38.16 ± 15.47</td>
</tr>
<tr>
<td>Proband status</td>
<td>263 (49.8)</td>
</tr>
<tr>
<td>Pathogenic mutation</td>
<td>340 (64.4)</td>
</tr>
<tr>
<td>PKP2</td>
<td>258 (48.9)</td>
</tr>
<tr>
<td>Recent syncope</td>
<td>48 (9.1)</td>
</tr>
<tr>
<td>RVEF (%)</td>
<td>43.80 ± 10.40</td>
</tr>
<tr>
<td>LVEF &lt;50%</td>
<td>67 (12.7)</td>
</tr>
<tr>
<td>ICD</td>
<td>218 (41.3)</td>
</tr>
</tbody>
</table>
Event-Free Survival

Follow-up (years)  
4.83 [2.44, 9.33]

Primary outcome (sustained VA)  
146 (27.5)

Annual event rate  
5.6%
## Predictors included in the model

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Complete cohort analysis (multiple imputation)</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Sex</td>
<td>HR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td></td>
<td>1.61 (1.14-2.27)</td>
<td>0.006</td>
</tr>
<tr>
<td>Age (per year increase)</td>
<td>0.98 (0.97-0.99)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Recent cardiac syncope (within 6 months)</td>
<td>1.95 (1.20-3.15)</td>
<td>0.007</td>
</tr>
<tr>
<td>Prior NSVT</td>
<td>2.27 (1.48-3.48)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>24 h. PVC count (ln)*</td>
<td>1.17 (1.03-1.33)</td>
<td>0.013</td>
</tr>
<tr>
<td>Leads with TWI anterior + inferior (per lead increase)</td>
<td>1.12 (1.03-1.22)</td>
<td>0.010</td>
</tr>
<tr>
<td>RVEF (per % decrease)</td>
<td>1.03 (1.01-1.04)</td>
<td>0.001</td>
</tr>
<tr>
<td>LVEF (per % decrease)</td>
<td>(Not included in the final model)</td>
<td></td>
</tr>
</tbody>
</table>

\[ P_{VA \text{ at 5 years}} = 1 - 0.800^{\exp(\text{Prognostic index})} \]
Online calculator

http://149.212.159.125:8838/acm2/
ARVD Management

Accurate Diagnosis

Cascade Family Screening

Prevent Progression

Risk Stratify For SCD

Minimize Symptoms And ICD Shocks
Methods for Minimizing Symptoms and ICD Shocks

- Stop exercising – especially stop competitive and endurance sports. Take beta blockers.
- Take ACE inhibitors, especially if significant disease.
- Consider taking antiarrhythmic medications if recurrent sustained VT or symptomatic nonsustained VT (sotolol, flecainide, tikosyn, amiodarone)
- Consider catheter ablation if AA drugs do not work or have side effects.
What Data Exists to Support The Recommendation to Stop Exercising?

• ARVD is a disease of desmosomal dysfunction.

• Desmosomes are structures that connect cells together.

• During exercise pressures in the RV increase three fold and the RV dilates increasing wall stress.

• Most ARVD patients, especially those that present at young ages are high level athletes.

• Exercise is a common trigger of arrhythmias and sudden death in ARVD patients.

• One mouse study demonstrates the provocative role of exercise.

• Two clinical studies from Johns Hopkins demonstrate that exercise is bad in patients at risk for developing ARVD.

• These findings have been confirmed in the Nordic Registry
To test whether in ARVD/C-associated desmosomal mutation carriers exercise influences: Penetrance, Arrhythmic risk, Progression to heart failure

<table>
<thead>
<tr>
<th></th>
<th>Overall (N = 87)</th>
<th>Endurance Athlete (n = 56)</th>
<th>Not Endurance Athlete (n = 31)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>46 (53)</td>
<td>32 (57)</td>
<td>14 (45)</td>
<td>NS</td>
</tr>
<tr>
<td>Probands</td>
<td>36 (41)</td>
<td>28 (50)</td>
<td>8 (26)</td>
<td>0.028</td>
</tr>
<tr>
<td>Age at interview, yrs</td>
<td>44 ± 18</td>
<td>42 ± 15</td>
<td>45 ± 22</td>
<td>NS</td>
</tr>
<tr>
<td>Presentation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at clinical presentation, yrs</td>
<td>35 ± 17</td>
<td>32 ± 14</td>
<td>38 ± 20</td>
<td>NS</td>
</tr>
<tr>
<td>Type of presentation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic presentation</td>
<td>44 (51)</td>
<td>36 (64)</td>
<td>8 (26)</td>
<td>0.002</td>
</tr>
<tr>
<td>Resuscitated SCD</td>
<td>3 (3)</td>
<td>2 (4)</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>40 (46)</td>
<td>18 (45)</td>
<td>22 (71)</td>
<td></td>
</tr>
<tr>
<td>Sustained VT/VF at presentation</td>
<td>26 (30)</td>
<td>18 (32)</td>
<td>8 (26)</td>
<td>NS</td>
</tr>
</tbody>
</table>
Likelihood of ARVD/C Diagnosis Is Associated With Exercise History

![Graph showing the relationship between exercise history and the likelihood of ARVD/C diagnosis. The x-axis represents hours per year prior to presentation, divided into quartiles, and the y-axis represents the percentage meeting TFC. The graph compares exercise history (endurance athletics) and non-endurance athletics.](image-url)
Cumulative Lifetime Survival Free from Sustained Ventricular Arrhythmia and Class C Heart Failure
What is the Role of Catheter Ablation?

• EP testing and a limited endocardial ablation procedure is appropriate at the time of evaluation and / or diagnosis.

• Catheter ablation (endo +/- epi) is recommended for patients receiving frequent ICD therapies despite antiarrhythmic drug therapy.

• Catheter ablation is appropriate prior to antiarrhythmic drug therapy when performed in experienced centers.
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Prevent Progression

Cascade Family Screening
Remember: ARVD is a Progressive Disease

**MEDIAN PROGRESSION:**

- **RV-FAC (%)**
  - Baseline: 39.2 [12.1] %
  - Last follow-up: 34.0 [16.8] %
  - P<.001

- **LVEF (%)**
  - Baseline: 55.0 [8.0] %
  - Last follow-up: 54.0 [8.3] %
  - P=.001

- **RVOT-PLAX (mm)**
  - Baseline: 35.0 [8.0] mm
  - Last follow-up: 37.0 [8.3] mm
  - P<.001

- **RVOT-PSAX (mm)**
  - Baseline: 35.0 [7.8] mm
  - Last follow-up: 37.0 [7.0] mm
  - P<.001
Heart Failure Is Common and Under-Recognized in Patients With Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia

- 289 patients with ARVC
- Clinical heart failure – one heart failure sign or symptom
- 142 patients (49%) had HF
- 113 had isolated RV involvement
- 29 had evidence of LV dysfunction
- Average age of HF onset was 40 + 14 years
- Patients with HF were more likely to undergo cardiac transplantation (15/142 vs 1/147) or die (7 vs 0) during study follow-up.

Gilotra et al; Heart Failure in ARVC/D
Circ Heart Fail. 2017;10:e003819. DOI: 10.1161/CIRCHEARTFAILURE.116.003819
Heart Failure Is Common and Under-Recognized in Patients With Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia

A

Transplant/Death free survival

Log rank p = 0.0025

Follow up (years)

Number at risk
No heart failure 147
Heart failure 142

Transplant/Death free survival

Log rank p = 0.05

Follow up (years)

Number at risk
No heart failure 147
Heart failure 142

A

B

Gilotra et al; Heart Failure in ARVC/D

Circ Heart Fail. 2017;10:e003819. DOI: 10.1161/CIRCHEARTFAILURE.116.003819
Methods for Preventing Progression of ARVD/C

- Stop exercising – especially stop competitive and endurance sports.
- Take beta blockers.
- Take ACE inhibitors, especially if significant disease.
Conclusions

• ARVD is a rare but important cause of sudden cardiac death.
• ARVD is a disease of desmososomal dysfunction.
• Diagnosis of ARVD is challenging and requires a comprehensive evaluation with both noninvasive and invasive testing. Be slow to make a diagnosis of ARVD.
• Identification of genetic and clinical risk factors for sudden death has improved with a risk calculator.
• Catheter ablation of VT plays an important role in management.
• ARVC results in progressive cardiac dysfunction.
• Nearly 50% of ARVC patients will develop HF during follow-up.
• Vigorous exercise increases the chance of developing ARVD and results in a greater chance of ventricular arrhythmias and heart failure. Because of this, we advise against exercise.
THANK YOU!