General and Disease-Specific Psychosocial Adjustment in Patients With Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy With Implantable Cardioverter Defibrillators: A Large Cohort Study

Cynthia A. James, ScM, PhD; Crystal Tichnell, MGC; Brittney Murray, MS; Amy Daly, MS; Samuel F. Sears, PhD; Hugh Calkins, MD

Background—Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is characterized by frequent life-threatening ventricular arrhythmias, diagnosed on average in the teens to mid-50s and commonly treated by implantable cardioverter defibrillators (ICDs). As younger age and high frequency of ICD discharges are risk factors for difficulties in psychosocial adjustment, we developed a study to assess psychosocial adjustment among patients with ARVD/C and to determine risk factors for poor adjustment in this high-risk population.

Methods and Results—Eighty-six adults enrolled in the Johns Hopkins ARVD Registry (38 male; mean age, 45.4±12.9 years), with an ICD in place for a median 3.2 years (range, 0.2 to 20.1 years), completed a set of questionnaires measuring ICD-specific anxiety (Florida Shock Anxiety Scale), device acceptance (Florida Patient Acceptance Survey), anxiety and depression (Hospital Anxiety and Depression Scale), and functional capacity (Duke Activity Status Index). Although overall device acceptance (Florida Patient Acceptance Survey mean, 76.7±15.3) was normative, patients with ARVD/C had substantially elevated body image concerns (Florida Patient Acceptance Survey subscale mean, 17.9±23.5) and device-related distress (subscale mean, 26.5±19.2), particularly among younger patients (P<0.01). Patients with ARVD/C had elevated ICD-specific (Florida Shock Anxiety Scale mean, 22.9±7.8) and general clinical anxiety (Hospital Anxiety and Depression Scale anxiety subscale mean, 6.2±3.9). Device-specific anxiety (Florida Shock Anxiety Scale) was predicted by younger age (P<0.0001), poorer functional capacity (P=0.016), having an ICD shock (P=0.003), and shorter time since ICD implant (P=0.007). Participants with poor device adjustment had an increased likelihood of clinically significant anxiety (P=0.006) and depression (P=0.008).

Conclusions—Patients with ARVD/C are at elevated risk for anxiety, and young patients face challenges with device acceptance. Risk factors for poor device adjustment may be used clinically to identify patients at high-risk of psychological distress. (Circ Cardiovasc Genet. 2012;5:18-24.)

Key Words: cardiomyopathy ■ defibrillation ■ genetics

Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is a heritable cardiomyopathy characterized by fibro-fatty myocardial replacement of the right ventricle, which predisposes patients to life-threatening ventricular arrhythmias and right ventricular dysfunction.1,2 Patients with ARVD/C typically present in their mid-teens to mid-40s with symptomatic premature ventricular beats and/or ventricular arrhythmias of a left bundle branch block morphology.3 Sudden cardiac death may be the first manifestation.3-5 ARVD/C is frequently an inherited disease. Up to 60% of ARVD/C cases are associated with mutations in genes encoding the cardiac desmosome.6-15

Editorial see p 2
Clinical Perspective on p 24

Once a diagnosis of ARVD/C is established in a family, an important management decision is whether to place an implantable cardioverter-defibrillator (ICD) for treatment of sustained ventricular arrhythmias and prevention of sudden cardiac death in affected individuals and at-risk family members. This is a critical decision because these are often young patients with few or no symptoms, who are expected to have a nearly normal life expectancy should sudden cardiac death be prevented; however, these individuals are also likely to have a long course with their ICD, exposing them to repeated medical procedures, ICD
therapies, ICD-associated complications, and subsequent potential psychosocial challenges over decades.

Living with arrhythmias and the threat of ICD shock represents a challenge for patients to prepare and recover. The survival benefits of the ICD may be tempered in patients who develop clinically significant symptoms of anxiety and depression. Patients with ARVD/C may be at particularly high risk for adverse outcomes for several reasons. First, those with ARVD/C present at a young age relative to others with ICDs. Studies have suggested that young age can be a risk factor for psychological maladjustment. Second, a high frequency of defibrillator discharge is often related to increased anxiety and poor adjustment. Individuals with ARVD/C have a high discharge rate, with several series showing a 50% to 80% appropriate ICD discharge rate for treatment of a sustained ventricular arrhythmia during a mean 3-to-5-year follow-up. Third, nearly half of patients with ARVD/C are women, a much higher proportion than in typical ICD populations. Women are considered to be at higher risk for poor ICD-related adjustment. Finally, patients with ARVD/C may be at particularly high risk because ARVD/C is a genetic disease. This disease etiology by itself raises well-established psychosocial burdens, including anxiety about risks to family members (particularly to children), guilt, blame, and stigmatization. How these risks combine in patients with patients with ARVD/C is uncertain, as is the optimal way to identify patients with ARVD/C at high risk for poor psychosocial adjustment and to provide care to maximize adjustment. Therefore, we developed a study with 2 objectives: (1) to assess psychosocial adjustment to life with an ICD among patients with ARVD/C; and (2) to determine risk factors for poor adjustment in this high-risk population.

Methods

Study Population

The Johns Hopkins ARVD Program (http://arvd.com) was established in 1995 to provide clinical care for patients and conduct research on this rare disease. Study participants in the Johns Hopkins ARVD Registry are recruited through 3 main sources: (1) patients referred to the program for an evaluation or treatment of ARVD/C; (2) individuals who contact the program through the Johns Hopkins-sponsored website arvd.com and indicate they are interested in joining research; and (3) participants in the annual ARVD/C Family Conference. Participants are offered re-enrollment in the ARVD Registry every 5 years.

Adults enrolling or re-enrolling in the ARVD Registry between February 2009 and November 2010 who (1) had an ICD in place for either primary or secondary prevention of ventricular tachycardia; (2) curried a clinical diagnosis of ARVD/C; and (3) could speak English were invited to participate in this study. All subjects gave written informed consent to participate. All aspects of the study were approved by the Johns Hopkins School of Medicine Institutional Review Board.

Study Design

This is a cross-sectional analysis of patients with ARVD/C with ICDs. After consenting to the study, participants were given the choice of completing paper questionnaires, providing responses over the telephone, or submitting responses online via Survey Monkey, Inc software (www.surveymonkey.com). Links to the electronic questionnaires are available on the Johns Hopkins ARVD Program website: http://www.arvd.com/icd_study.html. Although participants enrolling agreed to 3 years of prospective follow-up, the current paper reports baseline data.

Statistical Analyses

To determine univariate associations between 2 categorical variables, $\chi^2$ testing was used. The distribution of continuous variables was assessed graphically and using the Kolmogorov-Smirnov statistic. Associations between continuous dependent variables and categorical variables were tested using a 2-tailed t test (for binary independent variables) or an analysis of variance (for variables with more than 2 categories). Associations between categorical dependent variables and continuous independent variables were tested using binary logistic regression. Stepwise linear regression, using forward selection, assessed independent effects of predictor variables. Variables $P < 0.15$ were entered into the regression model. Analyses were performed using PASW statistics 18.0 (SPSS Inc). A probability value $\leq 0.05$ was considered significant.

Results

Study Population

The study population (Table 1) included 86 adults, aged 18 to 79 years (mean, 46 years), with a clinical diagnosis of...
Table 1. Demographic and Clinical Characteristics

<table>
<thead>
<tr>
<th>Measure</th>
<th>Range</th>
<th>N (%) or Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (no. male)</td>
<td>38 (44)</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>18.1 to 79.4</td>
<td>45.8 ± 12.9</td>
</tr>
<tr>
<td>Age at first ICD implant (y)</td>
<td>14.6 to 73.8</td>
<td>41.1 ± 13.0</td>
</tr>
<tr>
<td>Duration ICD has been in place (y)</td>
<td>0.15 to 20.1</td>
<td>4.90 ± 4.62</td>
</tr>
<tr>
<td>Indication for ICD implant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary prevention</td>
<td>46 (54)</td>
<td></td>
</tr>
<tr>
<td>Primary prevention</td>
<td>39 (45)</td>
<td></td>
</tr>
<tr>
<td>Syncope</td>
<td>16 (41)</td>
<td></td>
</tr>
<tr>
<td>Non-sustained VT</td>
<td>16 (41)</td>
<td></td>
</tr>
<tr>
<td>Family history ARVD/C (no. yes)</td>
<td>15 (38)</td>
<td></td>
</tr>
<tr>
<td>Unavailable</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>No. of ICD shocks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>39 (45)</td>
<td></td>
</tr>
<tr>
<td>1 to 5</td>
<td>26 (30)</td>
<td></td>
</tr>
<tr>
<td>&gt;5</td>
<td>21 (25)</td>
<td></td>
</tr>
<tr>
<td>Participants with at least 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appropriate shock</td>
<td>45 (52)</td>
<td></td>
</tr>
<tr>
<td>Inappropriate shock</td>
<td>12 (14)</td>
<td></td>
</tr>
<tr>
<td>Family history ARVD/C (no. yes)</td>
<td>34 (40)</td>
<td></td>
</tr>
<tr>
<td>Desmosomal mutation carrier (no. yes)</td>
<td>21 (24)</td>
<td></td>
</tr>
</tbody>
</table>

ICD indicates implantable cardioverter defibrillators; VT, ventricular tachycardia; SCD, sudden cardiac death; ARVD/C, Arrhythmogenic right ventricular dysplasia/cardiomyopathy; DASI, Duke Activity Status Index.

ARVD/C. Slightly more women (56%) participated. Participants had an ICD in place for a mean 4.9 years (median, 3.2 years). More than half (54%) of participants received an ICD for secondary prevention of sustained ventricular tachycardia or ventricular fibrillation. Among the 39 implanted for primary prevention, all had cardiac testing consistent with the diagnosis of ARVD/C, 16 had experienced syncope, 16 had documented nonsustained ventricular tachycardia, and 15 had a family history of ARVD/C and/or of premature sudden cardiac death. Slightly more than half of the whole population had experienced at least 1 appropriate or inappropriate ICD shock, with one quarter experiencing 6 or more shocks. Twelve participants had a documented history of at least 1 inappropriate shock; 2 had only inappropriate discharges. Forty percent of participants had a family history of ARVD/C, although one quarter knew they carried an ARVD/C-associated desmosomal mutation at the time of questionnaire completion. The functional capacity of the population was reasonably good, with a mean DASI activity status index of 48.1, equivalent to peak oxygen uptake of 30.3 mL/min.

Device Acceptance (FPAS)

Psychometric scale and subscale scores are presented in Table 2. Mean FPAS total scale score was 76.7 ± 15.3; median score was 80.0, reflecting a long leftward (low score) tail in the distribution. In bivariate analysis, older age ($\beta=0.34$, SE=0.12, $P=0.007$), longer duration since device implant ($\beta=0.85$, SE=0.36, $P=0.021$), and better functional capacity (DASI) ($\beta=0.38$, SE=0.14, $P=0.008$) were significant predictors of better device adjustment (higher FPAS scores). Older age at first ICD implant had a borderline association with device acceptance ($\beta=0.24$, SE=0.13, $P=0.065$). There was no significant association between FPAS score and sex (male mean, 76.6 [SE 2.6]; female mean, 76.8 [SE 2.1], $P=0.94$), history of at least 1 appropriate or inappropriate ICD shock (no shock mean, 78.3 [SE 2.5]; shock mean, 75.4 [SE 2.4]; $P=0.37$), or family history (positive family history mean, 77.5 [SE 2.4] versus no family history mean, 76.2 [SE 2.2], $P=0.72$). In multivariate linear regression (Table 3), current age, age at first ICD implant, functional capacity, and duration since device implant were entered into the model, as we expected confounding of current age, age at first implant, and duration since first implant. Confounding of functional capacity and the age variables was also expected because of disease progression over time. Age and functional capacity alone remained significant independent predictors of device acceptance in the final model (Table 3).

To further explore what aspects of device acceptance were particularly problematic for younger individuals, we designated the youngest quartile of the population (those 35 and younger) as the “younger” group. We then assessed which FPAS subscale scores were particularly sensitive to differences in age. As shown in Figure, age most significantly affects the body image concerns subscale score, with younger individuals having a significantly worse mean score on this measure (30.1 versus 13.7) than the older population. (Body image subscale items include “I feel less attractive because of my device” and “I feel that others see me as disfigured by my
In bivariate analysis, FSAS scores representing greater ICD-related anxiety were associated with younger age at first implant ($\beta = -0.20$, SE $= 0.063$, $P = 0.002$), younger current age ($\beta = -0.24$, SE $= 0.061$, $P < 0.001$), and poorer functional capacity ($\beta = -0.16$, SE $= 0.075$, $P = 0.03$). History of at least 1 appropriate or inappropriate ICD shock (mean, no shock group, 21.1 [SE 1.3] versus shock group, 24.3 [SE 1.1], $P = 0.06$) and shorter duration of having an ICD in place ($\beta = -0.29$, SE $= 0.18$, $P = 0.12$) had a trend toward association with elevated FSAS scores. Neither sex (mean, males, 21.7 [SE 1.27] versus females, 23.7 [SE 1.13], $P = 0.23$) nor family history (mean, positive family history, 23.1 [SE 1.6] versus no family history, 22.7 [SE 1.0], $P = 0.84$) were associated with device-related anxiety.

Similarly, higher HADS anxiety subscale scores were associated with younger age ($\beta = -0.11$, SE $= 0.032$, $P = 0.001$), poorer functional capacity ($\beta = -0.085$, SE $= 0.038$, $P = 0.03$), younger age at first ICD implant ($\beta = -0.082$, SE $= 0.033$, $P = 0.02$), and having experienced an ICD shock (mean, no shock group, 5.2 [SE 0.59] versus shock group, 7.0 [SE 0.59], $P = 0.03$). A trend toward an association with a shorter duration of time since ICD implant was present ($\beta = -0.17$, SE $= 0.093$, $P = 0.07$). There was no association between sex and HADSa scores (mean, males 5.9 [SE 0.65] versus females, 6.4 [SE 0.58], $P = 0.63$). All variables except for sex were entered into the FSAS and HADSa linear regression models. In multivariate linear regression (Table 3), younger age, poorer functional capacity (DASI), having experienced at least 1 appropriate or inappropriate ICD shock, and a shorter duration of time since first ICD implant were significant independent predictors of both device-specific and generalized anxiety.

### Clinically Significant Anxiety and Depression

We defined clinically significant anxiety as a HADSa subscale score $\geq 8$ and clinically significant depression as a HADSd subscale score $\geq 8$. Twenty-seven participants (31%) had HADSa scores that classified them as having clinically significant anxiety, while eight (9%) had HADSd scores indicative of clinically significant depression. We investigated whether device acceptance (FPAS scale score) and device-specific anxiety (FSAS scale score) influenced the likelihood a participant would have scores indicative of clinically significant anxiety and depression. In univariate analysis, the odds a participant had clinically significant anxiety was significantly associated with poorer device ac-
Device Acceptance

Although overall mean device acceptance (FPAS) scores were consistent with those in other studies using this scale (76.7 in our analysis versus 76.0,28 78.3,29 76.6,34), our study reported the worst (highest) scores on the body image (17.9 versus 10.1,28 14.3,29 15.7,22) and device-related distress (26.5 versus 20.5,28 19.3,29) subscales. It is notable that our population had worse body image subscale scores than a study reporting ICD experiences of an exclusively female ICD population.22 As these are the same FPAS subscales in which our youngest cohort had particularly elevated scores, this pattern may reflect the fact that those with ARVD/C require ICD implantation at a younger age than the typical individual with an ICD, since body image concerns have been shown to be associated with younger age.22 Furthermore, both body image and device-related distress measure concepts thought to be associated with perception of stigma, which can be associated with having an inherited disease. Hence, the worse body image and device-related distress subscale scores may be caused, in part, by the genetic etiology of ARVD/C, rather than actual worse cosmetic or device related problems. We found no sex difference in either the overall scale (males, 76.6; females, 76.8) or subscale scores, including the body image subscale.

Anxiety

Device-related anxiety (FSAS) scores were worse in our population than others reported (22.9 versus 15.4,31 14.8,35 19.9,30 16.4,22). Furthermore, nearly one third had scores consistent with clinically significant anxiety. Women with ARVD/C appear to have no more anxiety than men, contrary to most other studies,17,35 while shock history, younger age, and poorer function were associated with elevated anxiety, consistent with other findings. It may be that anxiety levels are higher in our ARVD/C population merely because it is enriched for young individuals with relatively bad shock histories; however, the genetic etiology of ARVD/C may also play a role. Although family history was not a significant predictor of device-specific anxiety, regardless of whether a patient already had a documented family history at the time of questionnaire completion, all had been counseled that their family members were at increased risk of developing ARVD/C. Inherited diseases carry unique anxieties over health risks of family members, particularly children.25 In the relatively few studies focusing on adjustment in patients and families with inherited cardiac disease, anxiety and depression have been identified as persistent issues.36

Limitations

Our cross-sectional retrospective study design limits study findings in several ways. First, the wide variation in time since first ICD implant limits our ability to assess the short-term impact of clinical events on psychosocial adjustment. Additionally, retrospective registry-based data collection combined with a long follow-up time in some patients precluded comprehensive collection of ICD-related complications periprocedure and during follow-up. This limited our ability to assess these factors as predictors of adjustment. Finally, our approach to sample recruitment and registry-based data collection did not allow comparison of psychosocial adjustment in athletes and other study participants.

Our study population also limits the generalizability of results. First, our study included only adults, although there is a subset of patients with ARVD/C who had an ICD implanted as teens. Second, comparison of subjects with and without devices was not feasible, owing to near-universal device placement among patients with ARVD/C in this largely North American cohort, although device implantation is rarer in other locations. Unfortunately there are no data available (in this or prior studies) on baseline anxiety or depression in patients with ARVD/C, which would contribute to maladjustment otherwise presumed to be device-related. Third, while our study population is fairly large, given the prevalence of ARVD/C, the sample size may have limited our power to detect predictors of psychosocial adjustment with a smaller effect size. Finally, study participants all chose to enroll in a research registry and, hence, are a potentially biased sample. Patients with ARVD/C not enrolled in research may differ from our population.

Finally, the timing of questionnaire administration at enrollment in the ARVD/C Registry precluded investigating the influence of genetic test result on psychosocial adjustment, as many participants were in the process of considering genetic testing, arranging testing, or awaiting the test result at the time of questionnaire administration. As participants are completing follow-up questionnaires, this issue will be addressed in a future study.
Clinical Implications

Although the majority of individuals who have an ICD to treat ARVD/C appear to have good device acceptance and no evidence of clinically significant anxiety or depression, a significant minority may have poorer adjustment. Patients with ARVD/C, particularly those who are young, have higher-than-typical levels of body image concerns and device-related distress. Anxiety levels appear to be elevated beyond what is the norm for ICD patients as well. Poor device adjustment, although unfavorable in and of itself, was additionally associated with increased likelihood of clinically significant depression and anxiety. Factors associated with poor adjustment included: (1) younger age; (2) having a device implanted recently; (3) having at least 1 ICD shock; and (4) having a poorer functional capacity. Assessment of these factors may be easily accomplished in a clinical setting. Patients with multiple risks may then be provided opportunities to discuss ICD-related concerns further. A low threshold for a mental health referral would also be appropriate. Furthermore, providing anticipatory guidance, to younger individuals in particular, that psychosocial adjustment issues related to the device are common and treatable, may ameliorate some of the distress evident in this subgroup.

The results of this study likely have applicability not only to caring for individuals with ARVD/C but also for those with other inherited cardiomyopathies (HCM, familial DCM) and arrhythmia syndromes (Long QT, Brugada syndrome, CPVT, etc.), for which ICDs are implanted to prevent sudden cardiac death. Similar to ARVD/C, individuals with these conditions have an ICD implanted at a young age and include a higher proportion of affected girls and women than other ICD populations. Perhaps, most critically, these patients similarly live within the psychosocial milieu of a family affected by an inherited cardiac disease associated with sudden death, with the associated risks of anxiety, guilt, loss or potential loss, and stigma. Future research into adjustment to life with an ICD in this population would provide insight into the broader applicability of the current findings.

Acknowledgments

We are grateful to the ARVD/C patients and families who have made this work possible.

Sources of Funding

The Johns Hopkins ARVD Program (http://www.ARRVD.com) is supported by the Bogle Foundation, the Healing Hearts Foundation, the Campanella family, the Wilmerding Endowments, and the Dr Francis P. Chiaramonte Private Foundation. The authors wish to acknowledge funding from the St Jude Medical Foundation, Medtronic Inc, and Boston Scientific Corp.

Disclosure

Dr Calkins receives research support from Boston Scientific, Medtronic, and St Jude Medical and is a consultant for Medtronic. Dr Sears serves as a consultant to Medtronic and has research grants from Medtronic. All funds from Medtronic are directed to East Carolina University. Dr Sears also has received speaker honorarium from Medtronic, Boston Scientific, St Jude Medical, and Biotronik. All relationships are considered “minor” and are less than $10 000 annually.

References

Arrhythmogenic right ventricular dysplasia cardiomyopathy (ARVD/C) is an inherited cardiomyopathy characterized by frequent life-threatening arrhythmias and right ventricular dysfunction. Patients are often treated with an implantable cardioverter defibrillator (ICD). Due to a younger age at ICD implant, higher proportion of female patients, and higher frequency of ICD discharge than the average patient with an ICD, as well as the inherited nature of the disease, we anticipated that our population might be at particularly high risk for difficulties adjusting to the device. Eighty-six adults with ARVD/C and an ICD completed a questionnaire measuring ICD-specific and generalized anxiety, device acceptance, and depression. Although the majority had good device acceptance and no evidence of clinically significant anxiety or depression, a significant minority had poorer adjustment. Patients with ARVD/C, particularly those who are young, had higher-than-typical levels of body image concerns and device-related distress. Anxiety levels were elevated beyond what is the norm for patients with an ICD as well. Poor device adjustment, although unfavorable in and of itself, was additionally associated with increased likelihood of clinically significant depression and anxiety. Factors associated with poor adjustment included: (1) younger age; (2) having a device implanted recently; (3) having at least 1 ICD shock; and (4) having a poorer functional capacity. Assessment of these factors may be easily accomplished in a clinical setting. Patients with multiple risks may then be provided opportunities to discuss ICD-related concerns further. A low threshold for a mental health referral may also be appropriate.
General and Disease-Specific Psychosocial Adjustment in Patients With Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy With Implantable Cardioverter Defibrillators: A Large Cohort Study
Cynthia A. James, Crystal Tichnell, Brittney Murray, Amy Daly, Samuel F. Sears and Hugh Calkins

_Circ Cardiovasc Genet._ 2012;5:18-24; originally published online January 11, 2012; doi: 10.1161/CIRCGENETICS.111.960898

_Circulation: Cardiovascular Genetics_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 1942-325X. Online ISSN: 1942-3268

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circgenetics.ahajournals.org/content/5/1/18

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation: Cardiovascular Genetics_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation: Cardiovascular Genetics_ is online at:
http://circgenetics.ahajournals.org//subscriptions/