Anxiety and depression in inherited channelopathy patients with implantable cardioverter-defibrillators

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BACKGROUND Implantable cardioverter-defibrillators (ICDs) are an effective treatment in some patients with inherited heart disease, including inherited channelopathies, yet they have also been shown to impact patients' psychological health.

OBJECTIVE We sought to improve understanding of the level of anxiety and depression as well as device acceptance among inherited channelopathy patients with an ICD.

METHODS Eligible patients seen at Johns Hopkins Hospital were sent a survey, which included the Hospital Anxiety and Depression Scale (HADS), Cardiac Anxiety Questionnaire (CAQ), and the Florida Patient Acceptance Survey (FPAS). Student t tests and χ^2 tests were used to identify associations with abnormal anxiety and depression scores.

RESULTS Among eligible patients (n = 65), 32 individuals (49%) completed the survey. The rate of device-related complications was 34%, and 41% of patients experienced 1 or more ICD shocks. Twelve patients (38%) had an abnormal HADS anxiety subscore and 5 patients (16%) had an abnormal HADS depression subscore (score ≥ 8). Secondary-prevention ICDs were associated with an

abnormal HADS anxiety subscore (P = .03). Experiencing ICD shock(s), device complications, age, sex, and family history of sudden cardiac death were not statistically associated with anxiety or depression. Overall, respondents demonstrated high device acceptance by FPAS (79.9 ± 2.9, maximum total score 100) and moderately high cardiac-specific anxiety by CAQ total score (1.53 ± 0.12).

CONCLUSION A high prevalence of generalized anxiety was identified among inherited channelopathy patients with ICDs. High device acceptance and lack of association with ICD shocks or complications indicate that further research is necessary to understand this increased incidence.

KEYWORDS Anxiety; Brugada syndrome; Cardiac electrophysiology; Depression; Implantable cardioverter-defibrillator (ICD); Inherited heart disease; Long QT syndrome

Introduction

Inherited heart disease, which includes inherited channelopathies and familial cardiomyopathies, can increase the risk of sudden cardiac arrest. Implantable cardioverter-defibrillators (ICDs) are indicated in a subset of these patients for primary and secondary prevention of life-threatening ventricular arrhythmias.[1,2] Although ICDs reduce the rate of sudden cardiac arrest effectively, these devices are not without risk. Patients can experience complications that arise acutely during the implantation of the ICD, from everyday use, and from repeat surgical procedures.[3–5] These devices may also negatively impact the psychological health of patients. Among inherited heart disease patients as well as the general cardiology population, ICD shocks, both appropriate and inappropriate, have previously been

associated with increased anxiety and depression. However, this effect has not been consistently demonstrated, as other studies found that many patients living with ICDs enjoy a quality of life consistent with age-matched controls and have a high level of satisfaction with their device.[1,3,6–8]

To best care for patients with inherited heart disease, it is necessary to improve understanding of the impact of ICDs on their mental health. This has been better studied in familial cardiomyopathies, such as hypertrophic cardiomyopathy (HCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC), as well as in congenital heart disease.[9–11] Although both familial cardiomyopathies and channelopathies have an underlying genetic cause and are associated with sudden cardiac death, the disease course varies between these conditions. Familial cardiomyopathies are characterized by progressive structural cardiac changes, which can lead to heart failure symptoms. In contrast, a life-threatening arrhythmia is generally the first clinical manifestation of inherited channelopathies, and patients typically

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KEY FINDINGS

- Inherited channelopathy patients with implantable cardioverter-defibrillators (ICDs) have a high prevalence of generalized anxiety, similar to other inherited heart disease cohorts of patients with structural heart changes.

- Generalized anxiety was associated with an ICD placed for secondary prevention of sudden cardiac arrest.

- Patients with inherited channelopathies and ICDs demonstrate high device acceptance and moderately high cardiac-specific anxiety.

remain free of heart failure symptoms. Additionally, there are distinct differences with respect to the indications for primary-prevention ICD implantation, which are well established for patients with familial cardiomyopathies but not for patients with inherited channelopathies.[12]

Differences in both the treatment and clinical course of patients with inherited channelopathies compared to patients with familial cardiomyopathies may lead to different mental health outcomes, which necessitates separate evaluation of these 2 populations. Yet there is a paucity of this type of data for inherited channelopathies, which include congenital long QT syndrome, Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia. In this study, we sought to determine the prevalence of 2 of the most common mental health disorders, anxiety and depression, among inherited channelopathy patients with ICDs as well as to measure device acceptance and cardiac-specific anxiety in this population.

Methods
Survey content

This study was approved by a Johns Hopkins Institutional Review Board and followed the ethical norms and standards in the Declaration of Helsinki. Eligible participants provided informed consent through voluntary completion of the survey after reading informed consent documentation. The "Living with an Inherited Channelopathy" survey collected self-reported data on demographics, personal medical history, family history, and device history, including previous ICD shocks and device complications. Data extracted from the patients' electronic medical record (EMR) were ICD indication (primary vs secondary), age, and race.

Additionally, 3 validated mental health scales were included. The Hospital Anxiety and Distress Scale (HADS) is divided into 2 subscales, with subscores ≥ 8 considered abnormal and indicative of possible clinically significant

Table 1 Demographic, family history, and diagnosis information of respondents and nonrespondents

	Respondents (N = 32)	Nonrespondents (N = 33)	P value
Average age, years	45.0	42.4	P = .48
Race, n (%)			
White (non-Hispanic)	27 (84.4)	27 (81.8)	P = .76
Black	3 (9.4)	2 (6.1)	
Asian	1 (3.1)	1 (3.0)	
Other/unknown	1 (3.1)	3 (9.1)	
Sex (female), n (%)	17 (53)	20 (60)	P = .54
Activity level, n (%)			
None	2 (6.3)	NA	NA
Light activity	11 (34.4)		
Moderate activity	18 (56.3)		
Competitive activity	1 (3.1)		
Diagnosis, n (%)			
Long QT syndrome	16 (50)	19 (57)	P = .75
Brugada syndrome	12 (37.5)	10 (30)	
CPVT	0 (0)	1 (3)	
Other	4 (12.5)	3 (10)	
Diagnosis date, n (%)			
<1 year	0 (0)	0 (0)	P = .44
1–5 years	7 (21.9)	10 (30)	
>5 years	25 (78.1)	23 (0)	
Family history of SCD, n (%)			
No	11 (34.4)	NA	NA
Yes	4 (12.5)		
Possibly, not proven	15 (46.9)		
Unknown	2 (6.3)		

All included data were from patient self-report upon completion of the questionnaire, with the exception of age and race. A diagnosis of "other" was defined as a patient with clinical evidence of an inherited channelopathy but who was not diagnosed with a known syndrome through genetic testing. Data from nonrespondents were collected from their electronic medical record. Age, sex, diagnosis, and time since diagnosis were not found to be statistically different between respondents and nonrespondents.

CPVT = catecholaminergic polymorphic ventricular tachycardia; SCD = sudden cardiac death.

Table 2 Implantable cardioverter-defibrillator history among inherited channelopathy patients

	Respondents (N = 32)
ICD indication	
Primary prevention	21 (65.6)
Secondary prevention	11 (34.4)
ICD type	
Transvenous	27 (84.4)
Subcutaneous	5 (15.6)
ICD shock experienced	13 (40.6)
Appropriate	6
Inappropriate	5
Unknown	4
Number of shocks	
None, but ATP	3 (9.4)
None	16 (50)
1	4 (12.5)
2–5	3 (9.4)
6–10	2 (6.3)
11–20	2 (6.3)
>20	2 (6.3)
ICD complications	11 (34%)
ICD complication type	
Lead fracture	5 (15.6)
Device or lead recall	4 (12.5)
Premature battery depletion	2 (6.3)
Complication at implant	1 (3.1)
Other	4 (12.5)

All data are presented as n (%).

All data were collected by patient self-report, with the exception of ICD indication, which was taken from the patients' electronic medical records. Approximately one-third of our cohort experienced a complication related to their ICD. Thirteen patients experienced at least one ICD shock, with some patients previously experiencing both appropriate and inappropriate shocks.

ATP = antitachycardia pacing; ICD = implantable cardioverter-defibrillator.

Table 3 Hospital Anxiety and Depression Scale, Cardiac Anxiety Questionnaire, and Florida Patient Acceptance Survey total scores and subscores of respondents

	Respondents (N = 32)
HADS*	
Anxiety (HADSa)	6.6 ± 0.80
Depression (HADSd)	2.7 ± 0.58
Total FPAS[†]	79.9 ± 2.9
Return to Function	80.9 ± 3.7
Positive Appraisal	80.9 ± 3.6
Device-Related Distress[‡]	21.9 ± 3.1
Body Image[‡]	19.1 ± 4.1
Total CAQ[§]	1.53 ± 0.12
Fear	1.68 ± 0.14
Avoidance	1.17 ± 0.15
Attention	1.65 ± 0.13

CAQ = Cardiac Anxiety Questionnaire; FPAS = Florida Patient Acceptance Survey; HADS = Hospital Anxiety and Depression Scale.

*HADS score was calculated based on respondents' answers to the questions of HADS. A score ≥8 is considered abnormal and indicative of clinically significant anxiety or depression.

[†]FPAS scores were calculated and reported on a scale from 0 to 100.

[‡]For two of the FPAS subscores a result closer to 0 is more favorable.

[§]CAQ scores are reported on a 5-point Likert scale. All scores reported as mean ± standard error of the mean.

anxiety (HADSa) or depression (HADSd).[13] The Cardiac Anxiety Questionnaire (CAQ) is an 18-item 5-point Likert scale survey divided into subscores for fear, avoidance, and heart-focused attention, which are reported from 0 to 4, with higher scores indicating worse anxiety.[14] The Florida Patient Acceptance Survey (FPAS) is an 18-item 5-point Likert scale survey with subscores for Return to Function, Device-related Distress, Body Image, and Positive Appraisal. Total FPAS score and subscores are reported between 0 and 100, with a higher total score indicating higher device acceptance.[15]

Survey administration

A cross-sectional survey was administered to adult patients with a clinical or genetic diagnosis of an inherited channelopathy and an ICD who were identified via the Center for Inherited Heart Diseases registry at the Johns Hopkins Hospital (Baltimore, MD). Exclusion criteria included lack of an ICD, death, age at screening (<18 years), and diagnosis of a cardiomyopathy.

Among this cohort, eligible patients with a valid e-mail address in their EMR were provided a personalized Web link to the survey, which was administered using Qualtrics

(Provo, UT). Individuals who did not respond to the survey after 2 e-mail reminders were mailed a paper copy as well as a link to the online version. Patients who did not have a valid e-mail address were only mailed the letter described above. All patient contact occurred between June 23 and July 23, 2020.

Statistical analysis

Student t tests and χ^2 tests were used to compare demographic data between respondents and nonrespondents as well as to identify associations with abnormal HADS subscores. A P value less than .05 was considered to be statistically significant. Data are presented as average ± standard error of the mean.

Results

Among a cohort of 65 eligible participants, 32 patients (49%) returned the completed survey, either online (n = 27, 84%) or by mail (n = 5, 16%). Among respondents, the average age was 45 years, and the majority of patients identified as white (84%) and female (53%). Age and sex were not significantly different between respondents and nonrespondents (Table 1).

The majority of respondents carried a diagnosis of either congenital long QT syndrome (n = 16, 50%) or Brugada syndrome (n = 12, 38%). Time since diagnosis was greater than 5 years prior to survey completion for the majority of individuals (n = 25, 78%). Diagnosis and time since diagnosis were not significantly different between respondents and nonrespondents. Family history of sudden cardiac death was

positive in 4 patients (13%) and possible but unproven in 15 patients (47%) (Table 1).

Eleven patients (34%) received an ICD for primary prevention of sudden cardiac arrest while 21 patients (66%) had secondary-prevention ICDs. Thirteen patients (41%) reported experiencing at least one ICD shock, including 5 (16%) who previously had received at least one inappropriate shock. Three patients (9.4%) experienced only antitachycardia pacing and no shocks, while 16 respondents (50%) reported never receiving therapy from their device. The overall rate of device-related complications was 34%, which includes self-report of lead fracture, recall, premature battery depletion, and/or complication at the time of implant (Table 2).

The average HADSd subscale score was 2.7 ± 0.58 (range 0–10), and 5 patients (16%) had an abnormal score indicative of clinically significant depression. The average HADSa subscale score was 6.6 ± 0.80 (range 0–16), and 12 patients (38%) had an abnormal score indicative of clinically significant anxiety (Table 3). A secondary-prevention ICD compared to a primary-prevention ICD was statistically associated with an abnormal HADSa subscore ($P = .03$) but not with an abnormal HADSd subscore ($P = .19$). Age, sex, family history of sudden cardiac death, experiencing an ICD shock, and experiencing an ICD complication were not statistically associated with an abnormal HADSa or HADSd subscore (Supplemental Table 1).

The average total CAQ score in this cohort was 1.53 ± 0.12, with subscores of 1.68 ± 0.14 for fear, 1.17 ± 0.15 for avoidance, and 1.65 ± 0.13 for attention (Table 3). The average total patient acceptance score by FPAS was 79.9 ± 2.9 (maximum score 100). The Return to Function and Positive Appraisal subscores were 80.9 ± 3.7 and 80.9 ± 3.6, respectively, indicating that the patients perceived that they were able to perform well in everyday life despite their device and had an overall positive regard for the intervention. Two FPAS subscores are considered more favorable closer to 0; therefore the Device-Related Distress and Body Image subscores were elevated at 21.9 ± 3.1 and 19.1 ± 4.1 respectively (Table 3).

Discussion

Recognizing the prevalence and level of psychological distress among individuals with inherited channelopathies with ICDs is important in order to improve patient care and outcomes in this patient population. Anxiety and depression are associated with worse clinical outcomes in cardiology patients.[16–18] Both the diagnosis of a genetic condition and having an ICD are known to lead to higher prevalence of anxiety and depression; therefore, it is imperative to better understand patients at the intersection of these 2 populations.[19,20]

Our results add to the existing, albeit limited, literature of HADS results in patients with inherited heart disease, with and without ICDs (Figure 1).[1,9–11,21,22] In our study, 38% of respondents had an abnormal HADSa subscore and 16% had an abnormal HADSd subscore. This is consistent with the known prevalence of psychological distress in approximately one-third of patients with inherited heart conditions.[1,19] For example, in a cohort of ARVC patients with ICDs from our institution, the prevalence of anxiety was 31% (6.2 ± SD 3.9) and the prevalence of depression was 9% (3.7 ± SD 2.8) by HADS.[9] The comparable level of anxiety and depression among our patients and inherited cardiomyopathy patients indicates psychosocial screening is warranted in all inherited heart disease patients.

Our respondents reported a high rate of complications related to their device (34%), although this is comparable to the rate in a previous report of long-term follow-up of a cohort of inherited heart disease patients with ICDs (33% at 10 years).[23] We only identified a statistical association between secondary-prevention ICDs and anxiety by HADS; however, our small sample size may have prevented us from identifying additional associations that have previously
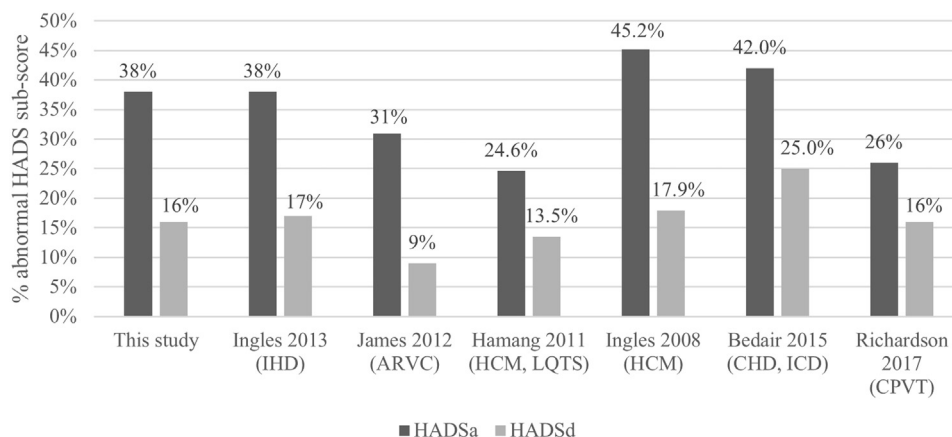

Figure 1 Literature review and comparison of Hospital Anxiety and Depression Scale (HADS) subscores among inherited heart disease patients. Comparison of HADS subscore results from this study and previous reports in the literature demonstrates that our cohort had comparable levels of generalized anxiety (HADSa) and depression (HADSd) to other inherited heart disease patients as well as to a cohort of sudden cardiac arrest patients, which included those with inherited heart disease. This finding supports the potential need to discuss and intervene in the psychological health of inherited channelopathy patients in addition to patients with structural heart disease. ARVC = arrhythmogenic right ventricular cardiomyopathy; HCM = hypertrophic cardiomyopathy; IHD = inherited heart disease; LQTS = long QT syndrome; SCA = sudden cardiac arrest.
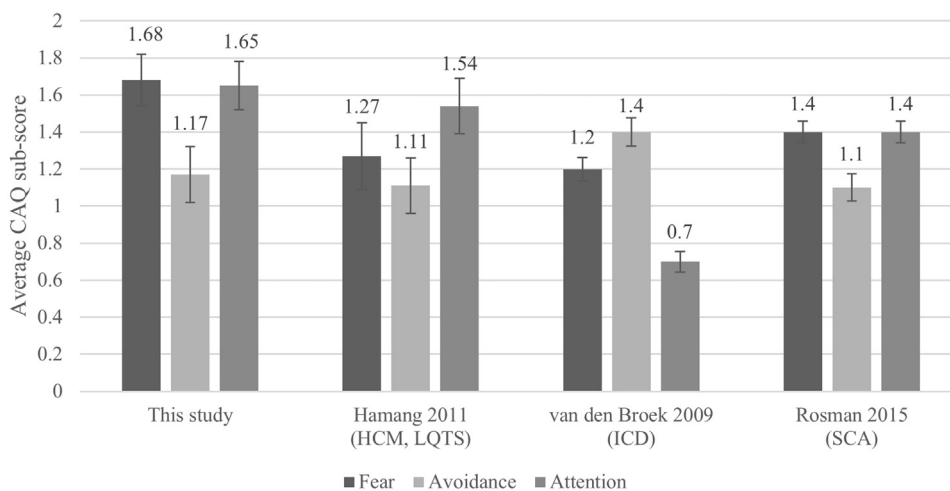
Figure 2 Literature review and comparison of Cardiac Anxiety Questionnaire (CAQ) subscores among inherited heart disease patients. Our cohort had comparable levels of cardiac anxiety to a cohort of inherited heart disease patients with structural and conduction problems. The cohort of Rosman and colleagues[25] (2015) included inherited heart disease patients. Compared to a general implantable cardioverter-defibrillator (ICD) patient population, our cohort had overall higher levels of cardiac anxiety and in a different pattern. HCM = hypertrophic cardiomyopathy; LQTS = long QT syndrome; SCA = sudden cardiac arrest.

been reported, such as female sex, history of ICD shock, and younger age.[9]

There is a lack of data on cardiac-specific anxiety in the inherited channelopathy population. We compared our results to 3 other reports of CAQ scores: an HCM/long QT syndrome cohort, a cohort of cardiology patients with ICDs, and a cohort of sudden cardiac arrest survivors, which included patients with ICDs, long QT syndrome, and HCM (Figure 2).[21,24,25] Our cohort had a similar pattern and level of cardiac anxiety to other inherited heart disease patients. However, the level of cardiac-specific anxiety in our cohort was potentially elevated and presented in a different pattern compared to the general ICD population (Figure 2).

By the total score from FPAS, both the ARVC cohort (score = 76.7) from our institution and our participants (score = 79.9) demonstrated high levels of device acceptance.[9] Strikingly, our participants' average Return to Function subscore (score = 80.9) was much higher than the ARVC population (score = 65.9). Similarly, our participants had a better Return to Function result compared to a cohort of congenital heart disease patients with ICDs (score = 69), who also had a lower total FPAS score (score = 73) than our cohort.[11] This could be due to the lack of structural heart changes and their associated symptoms in inherited channelopathies compared to ARVC and congenital heart disease. Overall, our results suggest common findings (increased generalized anxiety) yet distinct differences (higher Return to Function score) in our population compared to other inherited heart disease patients; however, these findings should be replicated in a larger cohort.

Study limitations
This study was primarily based on self-reported data, which can be exaggerated or subject to various biases. The study was also limited by the relatively small sample size, which limits the generalizability of our conclusions. By definition,

the study's results and conclusions did not include the perspectives of nonrespondents; however, demographic variables were not found to be significantly different between respondents and nonrespondents.

In the current study, we focused on the mental health of the patients at highest risk for poor outcomes, which are patients with inherited channelopathy and an ICD. Future studies are needed to compare the results of this study with the outcomes in inherited channelopathy patients without ICDs. This comparison will allow for the assessment of the level of anxiety that is related to the patient's underlying channelopathy vs related to their device.

Conclusion
We found that inherited channelopathy patients with ICDs have a high prevalence of generalized anxiety. Yet, cardiac-specific anxiety was not found to be notably higher among our respondents compared to previous reports, and the cohort demonstrated high device acceptance. Further research is needed to understand the cause for the high prevalence of anxiety among inherited channelopathy patients in order to direct targeted interventions and improve mental health outcomes in this population.

Authorship

All authors attest they meet the current ICMJE criteria for authorship.

Patient Consent

Eligible participants provided informed consent through voluntary completion of the survey after reading informed consent documentation.

Ethics Statement

This study was approved by a Johns Hopkins Institutional Review Board and followed the ethical norms and standards in the Declaration of Helsinki.

Appendix
Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hroo.2021.06.001.

Refernces

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