SUPPLEMENTAL MATERIAL

Table S1. Hazard Ratios for Implantable Cardioverter-Defibrillator Therapy for Ventricular Tachycardia/ Ventricular Fibrillation According to Exercise History and Clinical Characteristics in Probands.

	Unadjusted HR* (95% CI)	Model1 HR* (95%CI)	Model2 HR* (95%CI)
Exercise reduction (before presentation minus after presentation)			
Duration†	0.45 (0.26-0.77)	0.35 (0.19-0.65)	0.16 (0.05-0.54)
Dose†	0.48 (0.28-0.83)	0.29 (0.15-0.56)	0.07 (0.02-0.27)
Age at presentation (quartiles: years)			
Q1: 17.4 ± 2.5	Reference		
Q2: 26.4 ± 2.7	0.79 (0.42-1.50)		
Q3: 37.7 ± 3.9	1.02 (0.56-1.88)		
Q4: 54.9 ± 7.0	0.47 (0.24-0.95)		
Male	1.68 (1.01-2.80)		
Pathogenic / likely pathogenic variant	1.55 (0.95-2.52)		
Defibrillator for secondary prevention	1.46 (0.81-2.62)		
Syncope	0.99 (0.58-1.68)		
Family history of sudden cardiac death	1.08 (0.43-2.69)		
Non-sustained ventricular tachycardia	0.89 (0.55-1.46)		
T wave inversion on more than 3 leads	1.55 (0.81-3.00)		
Inducibility in electrophysiology study	3.48 (1.49-8.16)		
History of ventricular tachycardia ablation	1.05 (0.65-1.71)		
Right ventricle FAC ≤24% or EF ≤40%	0.97 (0.52-1.81)		
Left ventricle EF ≤ 45%	0.80 (0.36-1.76)		

* Hazard ratios were calculated comparing being in the top tertile of annual exercise duration (hours) or dose (metabolic equivalent of task –hours) and the rest in the three years before (or after) clinical presentation. † Reduction in exercise duration (or dose) was defined as being in the top tertile of reduction in annual exercise hours (or metabolic equivalent of task - hours).

Model 1: adjusted for sex, age at presentation (quartiles), primary or secondary prevention, proband status, and annual exercise duration/dose prior to clinical presentation (quartiles); **Model 2**: additionally adjusted for ablation before implant, desmosomal mutations, syncope, family history of sudden cardiac death, T wave inversions (more than 3 leads or not), right ventricular function (FAC ≤17% or EF ≤35%, FAC 17%-24% or EF 36%-40%, or other), and left ventricular function (EF ≤ 35%, EF 36%-45%, or other). HR = hazard ratio; CI = confidence interval; FAC = fractional area change; EF = ejection fraction; CI = confidence interval.

Table S2. Dose-response Relationship between Reduction in Exercise (Duration and dose) and Defibrillator Therapy for Ventricular Tachycardia/ Ventricular Fibrillation.

Exercise Reduction		Unadjusted HR (95%CI)	Model1 HR (95%CI)	Model2 HR (95%CI)	p-value for trend[†]
Duration*	Bottom	Reference	Reference	Reference	
	Middle	1.22 (0.74-2.02)	1.33 (0.75-2.37)	1.25 (0.50-3.11)	0.20
	Top	0.62 (0.36-1.07)	0.47 (0.23-0.96)	0.25 (0.06-0.97)	
Dose*	Bottom	Reference	Reference	Reference	
	Middle	1.24 (0.75-2.05)	1.36 (0.78-2.39)	0.64 (0.24-1.69)	0.01
	Top	0.63 (0.36-1.09)	0.42 (0.21-0.87)	0.10 (0.02-0.43)	

* Reduction in exercise duration (or dose) was defined as the difference between annual exercise hours (or metabolic equivalent of task – hours) after clinical presentation and that in the three years before clinical presentation.
[†] The p-values for trend were tested in model 2.
The HRs of each tertile of the difference were presented.
Model 1: adjusted for sex, age at presentation (quartiles), indication for ICD (primary or secondary prevention) , proband status, and annual exercise duration/dose prior to clinical presentation (quartiles); **Model 2**: additionally adjusted for ablation before ICD, desmosomal mutations, syncope, family history of sudden cardiac death, T wave inversions (more than 3 leads or not), right ventricular function (FAC ≤17% or EF ≤35%, FAC 17%-24% or EF 36%-40%, or other), and left ventricular function (EF ≤ 35%, EF 36%-45%, or other).
FAC = fractional area change; EF = ejection fraction; HR = hazard ratio; CI = confidence interval.

Table S3. Hazard Ratios for ICD therapy for VT/VF According to Reduction in Exercise (Duration and Dose) Stratified by Mutation Status and Indication for ICD.

		Unadjusted HR (95%CI)	Model1 HR (95%CI)	p-value for interaction[†]
Exercise Duration*				
Mutation	Positive	0.52 (0.29-0.93)	0.44 (0.20-1.00)	0.51
	Negative	0.69 (0.33-1.43)	0.41 (0.16-1.06)	
ICD Indications[††]	Primary	0.75 (0.33-1.72)	0.30 (0.08-1.07)	0.22
	Secondary	0.74 (0.44-1.24)	0.68 (0.35-1.33)	
Exercise Dose*				
Mutation	Positive	0.77 (0.44-1.38)	0.52 (0.23-1.18)	0.16
	Negative	0.67 (0.32-1.39)	0.20 (0.07-0.59)	
ICD Indications[††]	Primary	0.87 (0.38-2.00)	0.13 (0.03-0.57)	0.06
	Secondary	0.72 (0.43-1.20)	0.56 (0.29-1.10)	

 * Reduction in exercise duration (or dose) was defined as the difference between annual exercise hours (or metabolic equivalent of task – hours) after clinical presentation and that in the three years before clinical presentation.
[†] Interaction was tested in the model 1.
[††] ICD indications were defined as for primary prevention vs secondary prevention. The HRs of being in the upper half of the difference were presented.
Model1: adjusted for sex, age at presentation (quartiles), ICD indications (primary or secondary prevention), desmosomal mutation, proband status, and annual exercise duration/ dose before clinical presentation (quartiles).
ICD = implantable cardiac defibrillator; HR = hazard ratio; CI = confidence interval; VT = ventricular tachycardia; VF = ventricular fibrillation.