Genetic arrhythmia syndromes and sport: who can play?

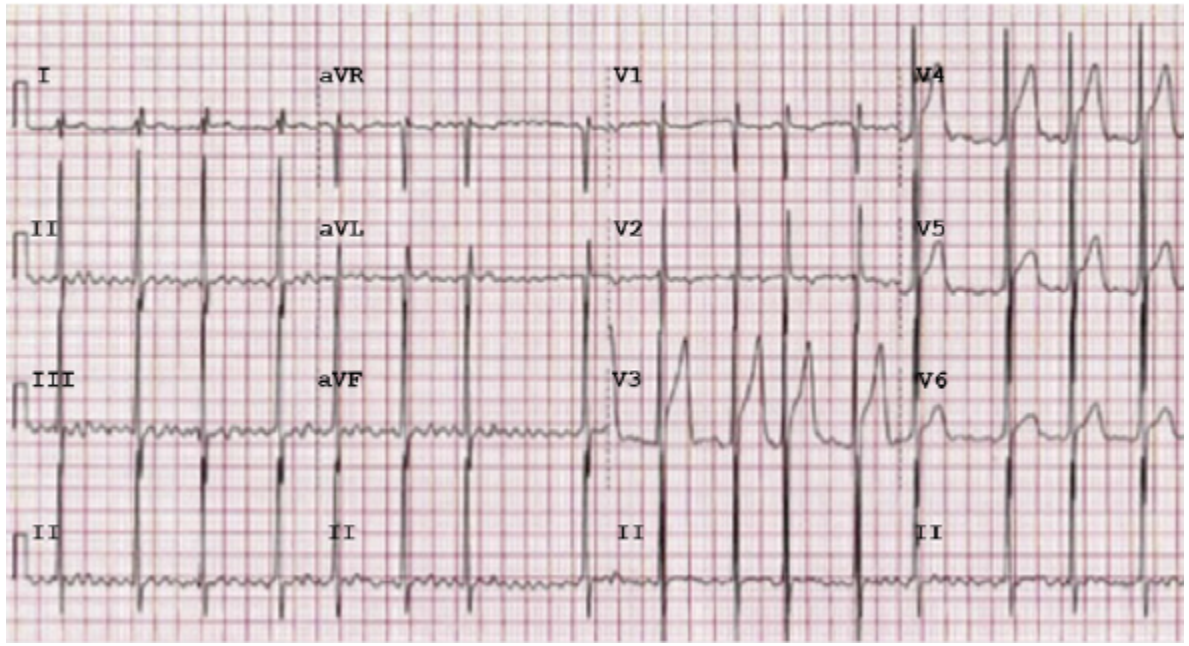
Maria Miszczak-Knecht

The Children Memorial Health Institute,

Warsaw, Poland

Genetic arrhythmia syndrome;

-Long QT Syndrome
-Brugada Syndrome
-Catecholamic Polymorphic Ventricular Tachycardia
-Early Repolarization Syndrome
-Short QT Syndrome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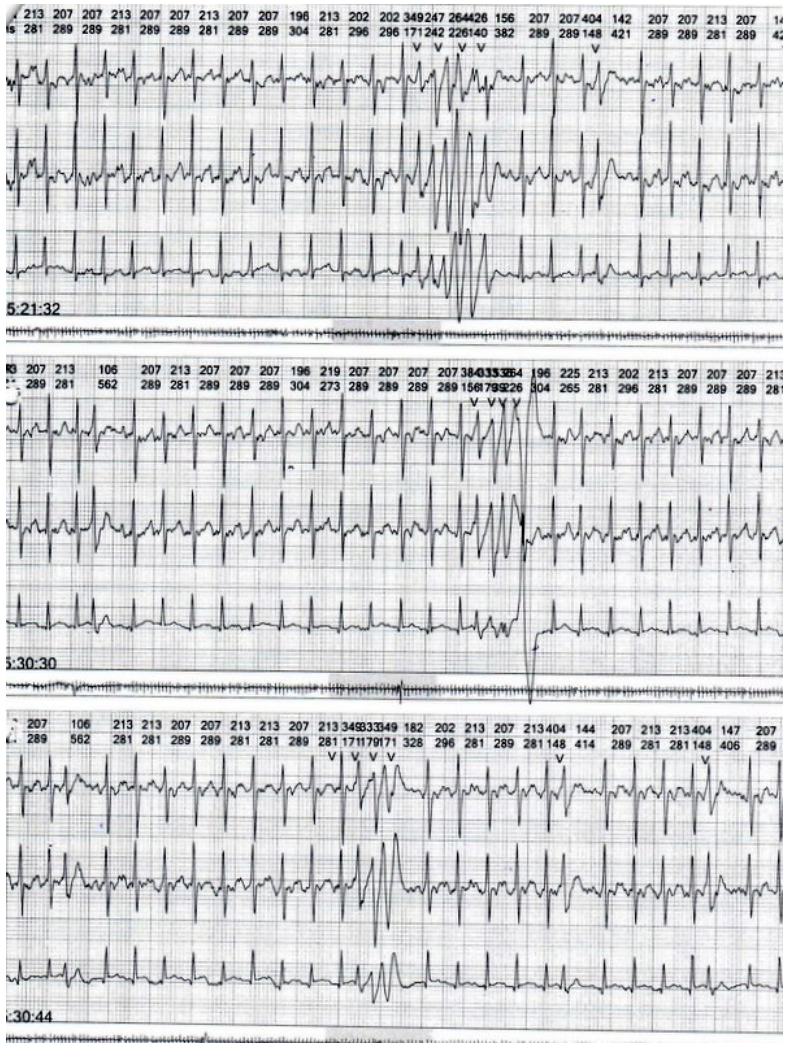
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Does Sports Activity Enhance the Risk of Sudden Death in Adolescents and Young Adults?

Domenico Corrado, MD, PHD,* Cristina Basso, MD, PHD,† Giulio Rizzoli, MD,‡
Maurizio Schiavon, MD,§ Gaetano Thiene, MD†

Table 1. Characteristics of Sudden Death Victims

	Athletes (n = 55)	Non-Athletes (n = 245)	p Value
Mean age (yrs)	23.1 ± 7	23.9 ± 9	1.0
Gender			
Males	50	170	0.002
Females	5	75	
Circumstances of death			
Exercise-related	49 (89%)	22 (9%)	< 0.0001
During effort	40	15	
After effort	9	7	
Unrelated to exercise	6 (11%)	225 (91%)	
Medical history			
Familial history of SD	5 (9%)	27 (11%)	0.8
Previous symptoms	18 (32%)	56 (23%)	0.2
ECG abnormalities/ arrhythmias	22 (40%)	36/63 (57%)	0.1

an increased risk of SD,
nhanced mortality, but it
onditions predisposing to
J Am Coll Cardiol 2003;

36th Bethesda Conference: Egibility Recommendations for Competitive Athlets with Cardiovascular Abnormalities. BJ.Maron, DP.Zipes. JACC 2005;45:1313-1375

Cardiovascular pre-participation screening on young competitive athlets for prevention of suden death: proposal for common European protocol. Consensus Statement of the Study Group of Sport Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericaridial Diseases of the ESC, D.Corrado i wsp. Europ Heart J 2005;26:516-524

Recommendations and Cosiderations Related to Preparticipation Screening for Cardiovascular Abnormalities in Competitive Athlets: 2007 Update. A Scientific Statement from AHA. BJ.Maron, PD.Thompson Circulation 2007;115:1643-1655

Bethesda Conference #36 and the ESC Consensus Recommendations Revisited. A Comparison of U.S. and European Criteria for Eligibility and Disqualification of Competitive Athletes With Cardiovascular Abnormalities. A. Pelliccia, DP Zipes, BJ. Maron.JACC 2008;52:1990–1996

Diagnosis of LQTS based on criteria

- 470ms male
- 480ms female

Symptomatic **only** class IA

Asymptomatic class IA (exception: LQT3 genetically proved)

Genotype-positive/phenotype-negative can participate **in all sports** (exception LQT1-swimming)

Diagnosis of LQTS based on criteria

- 440ms male
- 460ms female

No form of competitive sports

Genetic test are recommended

Genotype-positive/phenotype-negative **no** competitive sports

Return to play? Athletes with congenital long QT syndrome

Jonathan N Johnson,[1] Michael J Ackerman[1,2,3]

Group of 130 patients with LQTS

Aged 6-40 yr, mean 11.5±7

Mean QTc 471±46 ms

Mean follow up period 650 pt-yr

Sport category:

27 pts basketball

16 pts competitive dance/gymnastics

15 pts soccer

7 pts (American) football

Table 3 Demographics of athlete participation relative to the Bethesda and ESC guidelines

	Against ESC but within Bethesda	Contrary to both ESC and Bethesda	p Value
Number of patients	70	60	
Age at diagnosis (years)	11±7	12±6	NS
Sex (male/female)	41/29	29/31	NS
Average QTc (ms)	444±23	501±46	<0.0001
Genotype			
LQT1	41 (59%)	33 (55%)	NS
LQT2	20 (29%)	21 (35%)	NS
LQT3	8 (11%)	3 (5%)	NS
Multiple	1 (1%)	3 (5%)	NS
History of symptoms	1 (1%)	28 (47%)	<0.0001
β-Blockers	55 (79%)	57 (95%)	<0.008
ICD	0	20 (33%)	<0.0001
Follow-up available (years)	5.1±2.9	5.0±3.0	NS

No deaths, no LQT-triggered cardiac events, no ICD related complications

Executive summary: HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes

Europace 2013

Expert Consensus Recommendations on ***LQTS Therapeutic Interventions***

All LQTS patients who wish to engage in competitive sports ***should be*** referred to a clinical expert for the evaluation of risk.

AHA/ACC SCIENTIFIC STATEMENT

Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Preamble, Principles, and General Considerations

A Scientific Statement From the American Heart Association and American College of Cardiology

Conceald genetic syndrome
-can participaty in any kinds of competetive sports
-under special codition:

It is reasonable for an asymptomatic athlete with genotype-positive/phenotype-negative (i.e., concealed channelopathy) LQTS, CPVT, BrS, early repolarization syndrome, idiopathic ventricular fibrillation, or short-QT syndrome to participate in all competitive sports with appropriate precautionary measures, including 1) avoidance of QT-prolonging drugs for athletes with LQTS (http://www.crediblemeds.org), 2) avoidance of drugs that exacerbate the BrS in affected athletes (http://www.brugadadrugs.org), 3) electrolyte/hydration replenishment and avoidance of dehydration for all, 4) avoidance or treatment of hyperthermia from febrile illnesses or training-related heat exhaustion or heat stroke for athletes with either LQTS or BrS, 5) acquisition of a personal automatic external defibrillator as part of the athlete's personal sports safety gear, and 6) establishment of an emergency action plan with the appropriate school or team officials *(Class IIa; Level of Evidence C)*.

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JACC 2015

For athletes with a suspected/diagnosed cardiac channelopathy, a comprehensive evaluation by a heart rhythm specialist or genetic cardiologist with sufficient experience and expertise with these disorders is recommended *(Class I; Level of Evidence C)*.

LQTS patients

	LQT1	LQT2	LQT3
Gene frequency (%)	35	30	10
Gene	*KCNQ1*	*KCNH2*	*SCN5A*
Ion channel current	I_{Ks}	I_{Kr}	I_{Na}
Contribution to action potential			
Clinical event triggers	Exercise and sympathetic tone	Auditory, emotion	Sleep
Response to β-blockade	+++	++	+

Aziz, Cardiol Young 2017

LQTS1 (KCNQ1-Kv7.1 chanel)

Loss of function Iks current

-creates a sensitivity to QT prolongation

-crucial to adaptive QT shortening during sympathetic activation

QT prolongation during exercise and late in recovery

LQTS2 (KCNH2-Kv11.1)

Loss of function Ikr current rapid delayed rectifier

- responsible for phase 2 repolarization

Normal QT adaptation to exercises

Symptoms trigger auditory and emotion

LQTS3 (SCN5A Nav1.5 chanel)

Gain of function in INa channel

-responsible for phase 0 of the action potential

-prolongs repolarization

Genetic status is responsible for clinical presentation
Interpretation of genetic results is still challenging

Symptoms during rest or sleep

RISK STRATIFICATION

- Jervell and Lang-Nielsen or Thimoty syndrome
- QTc > 500ms
- presence of T wave alternans
- Syncope before 7yr
- Syncope or cardiac arrest in 1st year of life

JACC Clin Electrophysiol. 2015 ; 1(1-2): 62–70. doi:10.1016/j.jacep.2015.03.006.

Sports Participation in Genotype Positive Children With Long QT Syndrome

Peter F. Aziz, MD[*], **Tammy Sweeten, MS**[†], **Ramon L. Vogel, MD**[†], **William J. Bonney, MD**[†], **Jacqueline Henderson, RN**[†], **Akash R. Patel, MD**[‡], and **Maully J. Shah, MBBS**[†]

103 sport participant with geneticlly proof LQTS

Followed for 750 patients/year

NO DEATHS

NO ABORTED CARDIAC ARREST

NO SYNCOPE

Return to play? Athletes with congenital long QT syndrome

Jonathan N Johnson,[1] Michael J Ackerman[1,2,3]

Who can play?

1. Extensive assessment of phenotype status
2. Discussion with child and parents-if there is any object for safety concern the child is disqualified
3. BB therapy particular in LQT1, LQT2
4. Avoiding: QT prolonging drug
   dehydratation
   electrolyt derangements
   overheating
5. Personal AED (if ICD not implanted)
6. „Buddy” a person who knows what to do in case

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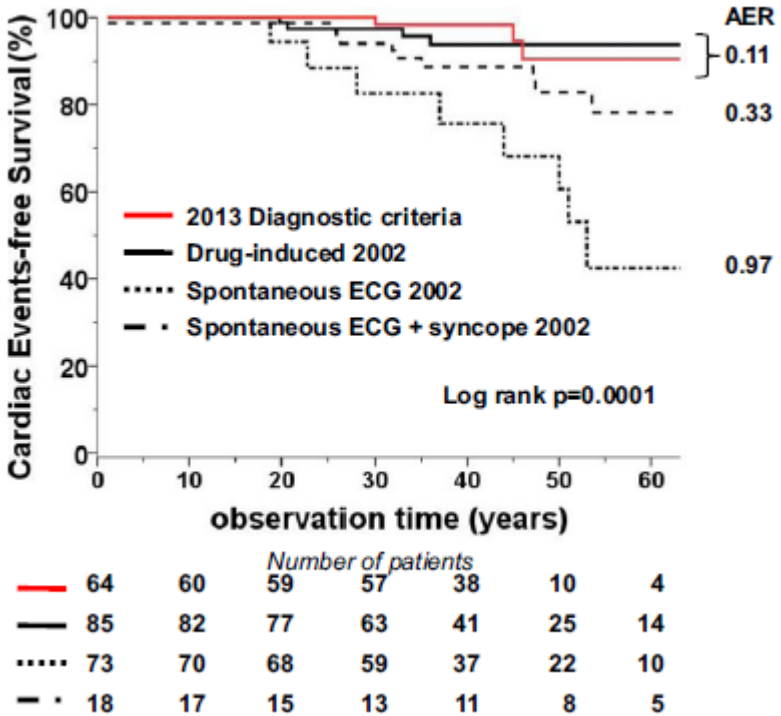
A Scientific Statement From the American Heart Association and American College of Cardiology

Competitive sports participation may be considered for an athlete with either previously symptomatic or electrocardiographically evident BrS, early repolarization syndrome, or short-QT syndrome assuming appropriate precautionary measures and disease-specific treatments are in place and that the athlete has been asymptomatic on treatment for at least 3 months *(Class IIb; Level of Evidence C)*. If therapy includes an ICD, refer to the Task Force 9 report (2).



Clinical Presentation and Outcome of Brugada Syndrome Diagnosed With the New 2013 Criteria

ANTONIO CURCIO, M.D., PH.D.,* ANDREA MAZZANTI, M.D.,† RAFFAELLA BLOISE, M.D.,† NICOLA MONTEFORTE, M.D.,† CIRO INDOLFI, M.D.,*,‡ SILVIA G. PRIORI, M.D., PH.D.,†,§ and CARLO NAPOLITANO, M.D., PH.D.†

J-Wave syndromes expert consensus conference report: Emerging concepts and gaps in knowledge☆,☆☆

Charles Antzelevitch, PhD, FHRS[a,*], Gan-Xin Yan, MD, PhD[b], Michael J. Ackerman, MD, PhD[c], Martin Borggrefe, MD[d], Domenico Corrado, [e], Jihong Guo, MD[f], Ihor Gussak, MD, PhD[g], Can Hasdemir, MD[h], Minoru Horie[i], Heikki Huikuri, MD[j], Changsheng Ma, MD[k], Hiroshi Morita, MD, PhD[l], Gi-Byoung Nam, MD, PhD[m], Frederic Sacher, MD, PhD[n], Wataru Shimizu, MD[o], Sami Viskin, MD[p], Arthur A.M. Wilde, MD, PhD, FHRS[q,r]

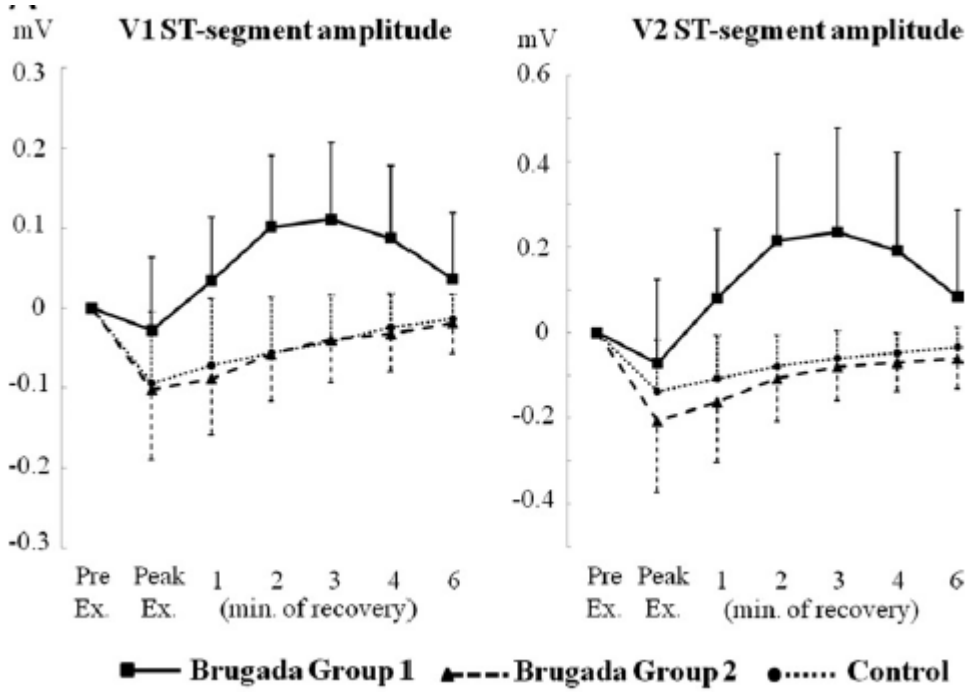
Proposed Shanghai Score System for diagnosis of Brugada syndrome.

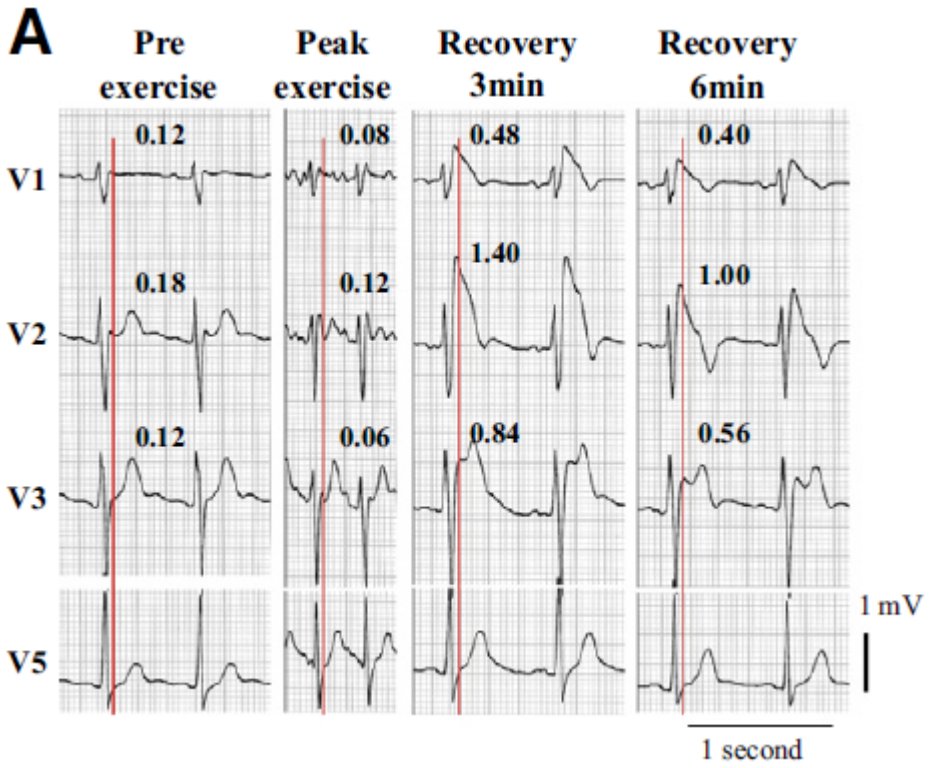
	Points
I. ECG (12-Lead/Ambulatory)	
A. Spontaneous type 1 Brugada ECG pattern at nominal or high leads	3.5
B. Fever-induced type 1 Brugada ECG pattern at nominal or high leads	3
C. Type 2 or 3 Brugada ECG pattern that converts with provocative drug challenge	2
*Only award points once for highest score within this category. One item from this category must apply.	
II. Clinical History*	
A. Unexplained cardiac arrest or documented VF/polymorphic VT	3
B. Nocturnal agonal respirations	2
C. Suspected arrhythmic syncope	2
D. Syncope of unclear mechanism/unclear etiology	1
E. Atrial flutter/fibrillation in patients o30 years without alternative etiology	0.5
*Only award points once for highest score within this category.	
III. Family History	
A. First- or second-degree relative with definite BrS	2
B. Suspicious SCD (fever, nocturnal, Brugada aggravating drugs) in a first- or second-degree relative	1
C. Unexplained SCD o45 years in first- or second- degree relative with negative autopsy	0.5
*Only award points once for highest score within this category.	
IV. Genetic Test Result	
A. Probable pathogenic mutation in BrS susceptibility gene	0.5
Score (requires at least 1 ECG finding)	
≥3.5 points: Probable/definite BrS	
2–3 points: Possible BrS	

Augmented ST-Segment Elevation During Recovery From Exercise Predicts Cardiac Events in Patients With Brugada Syndrome

Hisaki Makimoto, MD,* Eiichiro Nakagawa, MD, PHD,† Hiroshi Takaki, MD, PHD,*
Yuko Yamada MD,* Hideo Okamura, MD,* Takashi Noda, MD, PHD,* Kazuhiro Satomi, MD, PHD,*
Kazuhiro Suyama, MD, PHD,* Naohiko Aihara, MD,* Takashi Kurita, MD, PHD,‡
Shiro Kamakura, MD, PHD,* Wataru Shimizu, MD, PHD*

Suita and Osaka, Japan





Gr1 BrS with type I 37% Gr 2 BrS without changes in ECG 67%

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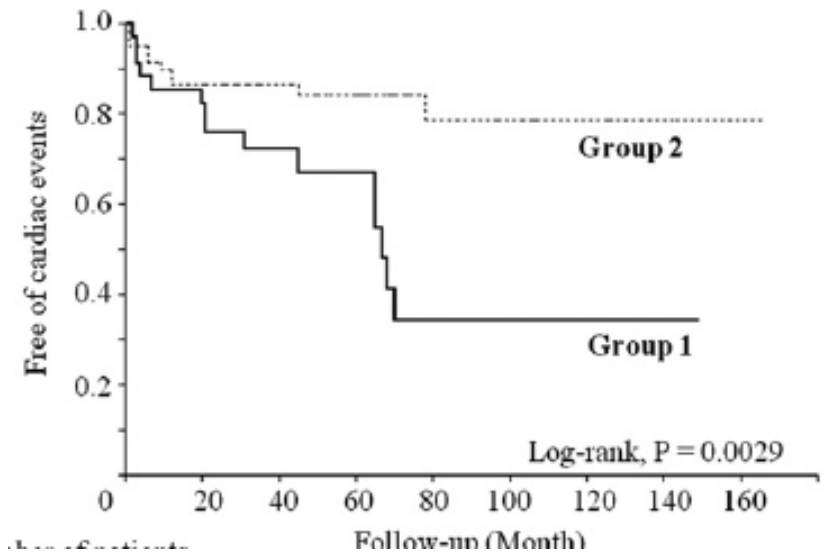

Who can play?

Individual approach to sport qualifications

Don’t know

-how take to account the specific genotype or mutation or localization

-how does specific sport type trigger arrhythmia