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Impact of physical activity on presentation and prognosis of Brugada syndrome

María Jesús Fernandez Gil,[1] Lidia María Carrillo Mora ,[1] David Fernandez Vazquez ,[1] Francisco Melgarejo,[2] Juan José Santos Mateo ,[3,4] Carmen Muñoz Esparza,[1,4] Ana Isabel Rodriguez Serrano ,[1] Marina Navarro-Penalver,[1] Juan Jose Sanchez Muñoz,[1] Francisco-Javier Gimeno-Blanes,[5] Maria Sabater-Molina ,[4,6] Juan R Gimeno [1,4]

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[1]Hospital Clínico Universitario Virgen de la Arrixaca, El Palmar, Spain
[2]Universidad Rey Juan Carlos, Mostoles, Spain
[3]Virgen de la Arrixaca University Hospital Cardiology Service, El Palmar, Spain
[4]CIBERCV, Madrid, Spain
[5]Universidad Miguel Hernández de Elche, Elche, Spain
[6]Cardiogenetic Laboratory, Universidad de Murcia Facultad de Medicina, Murcia, Spain

Correspondence to
Dr Maria Sabater-Molina; mariasm79es@hotmail.com

ABSTRACT

Introduction and objectives Brugada syndrome (BS) is a channelopathy associated with an increased risk of sudden cardiac death (SCD). Intense physical activity is a recognised trigger of life-threatening arrhythmias in long QT syndrome, catecholaminergic ventricular tachycardia syndrome and arrhythmogenic cardiomyopathy, but it is believed to be safe in BS. The objective of this study is to assess the impact of regular physical activity on the expression and prognosis of BS.

Methods 286 consecutive BS patients (aged 39.1±17.8 years old, 70.6% men) were included. Patients were classified according to the level of exercise and main discipline of sport they had practised.

Results 190 (66.4%) were sedentary, 27 (9.4%) practised light exercise, 59 (20.6%) moderate and 10 (5.3%) intense. Patients engaged in 'mixed or endurance' types of exercise were diagnosed earlier than sedentary ones (HR: 2.1; 95% CI: 1.5 to 2.9; p<0.001) and experienced syncope at a younger age (24.9±16.2 vs 37.4±18.2 years; p=0.04). Physical activity was associated with ECG sport-related changes like bradycardia (Δ 6 bpm) and a shorter QTc (Δ 21 ms) and also to a higher ST elevation in right precordial leads (Δ 0.5 mm). Physical activity was not a predictor of arrhythmic events or SCD.

Conclusions Regular physical activity was associated with a younger diagnosis and an earlier occurrence of syncopal episodes. BS patients engaged in 'mixed or endurance' sports have ECG changes associated with sport adaptation and higher ST segment elevation. Nevertheless, physical activity was not related to a higher arrhythmic risk in our cohort of patients with BS.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Brugada syndrome (BS) is a genetic channelopathy associated with sudden cardiac death (SCD). While exercise is a known risk factor for arrhythmias in other inherited cardiac conditions, it is traditionally considered safe in BS. However, the impact of regular physical activity on BS clinical expression and prognosis has not been well studied.

WHAT THIS STUDY ADDS

⇒ This study shows that regular moderate-to-intense physical activity, particularly in endurance and mixed sport disciplines, is associated with earlier diagnosis and earlier onset of syncope in BS patients. It also identifies ECG adaptations such as lower heart rate, shorter QTc and increased ST segment elevation in athletes, without an increase in arrhythmic events or SCD.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings support the safety of physical activity in BS and suggest that athletic adaptations may influence disease expression without increasing risk. These results may inform risk stratification and guide future research and clinical recommendations regarding sport participation in BS patients.

INTRODUCTION

Brugada syndrome (BS) is a hereditary channelopathy characterised by a typical pattern on the ECG with ST-segment elevation and negative T wave in V1–V2.[1–4] Diagnosis usually happens around 30–40 years of age, being more prevalent in men and is a well-known cause of sudden cardiac death (SCD). Symptoms like syncope or palpitations, related to ventricular arrhythmias, typically occur in situations with a higher vagal tone, such as during the night, at rest, after heavy meals or associated with alcohol intoxication. Fever is a typical trigger for arrhythmias.

Intense exercise is related to an increased risk of malignant arrhythmias in patients with cardiac diseases such as ischaemic heart disease, arrhythmogenic cardiomyopathy, hypertrophic cardiomyopathy, long QT syndrome and catecholaminergic ventricular tachycardia. All these conditions are

causes of SCD in young individuals and athletes. Patients with cardiac disease are discouraged from engaging in competitive sports and strenuous exercise.[5]

Sports are classically considered safe in patients with BS. Contrary to what happens in other cardiac conditions, a high adrenergic tone and the subsequent rise in circulating catecholamines normalise repolarisation abnormalities typical of BS. This observation is consistent with the fact that intravenous isoprenaline is the recommended therapy in life-threatening episodes of arrhythmic storms in BS.[1 3]

Although the risk of arrhythmias during exercise is not typical of BS, regular physical activity of at least moderate intensity produces electrocardiographic, morphological and functional changes in the heart, including sinus bradycardia and biventricular dilation. Vagal tone at rest and during sleep periods can be significantly increased in athletes. Individuals participating in sports in the 'mixed' and 'endurance' categories, according to the EAPC classification, where the dynamic component is higher, show greater cardiac remodelling and higher vagal tone.[5] We hypothesise that some disciplines such as cycling, long-distance running or rowing may facilitate clinical expression or impact the prognosis in patients with BS.

The objective of this study is to assess the impact of regular physical activity on the expression and prognosis of BS. We also aimed to evaluate whether the type of sport discipline related to the phenotype of the disease.

METHODS

Population and study design

This is a descriptive observational study with a population of 286 consecutive patients diagnosed with BS who were prospectively referred to an inherited cardiovascular diseases unit between 2003 and 2019. Patients were followed up annually or biannually. The main clinical variables associated with BS were collected. All syncope characteristics were reviewed and analysed, then classified as arrhythmic (cardiological or suspected arrhythmic origin) or vasovagal syncope. Age at the first syncope and age at the first arrhythmic syncope were recorded. Information regarding physical activity level was collected prospectively and verified by phone surveys with a structured questionnaire to obtain data on the exercise performed during the 3 years preceding the diagnosis. Participants were asked about their physical activity level and classified according to the concept of a 'typical week'.[6] Only physical activity time estimated to increase >70% maximum heart rate was considered. Moderate physical activity level was defined between >2 and <5 hours per week, and intense physical activity was defined as >5 hours per week. To facilitate comparisons ensuring enough cases, those who were sedentary or engaged in light physical activity were grouped as sedentary/light exercise (S/L) and those who were engaged in more than 2 hours per week were grouped as moderate/intense exercise (M/I) (figure 1).

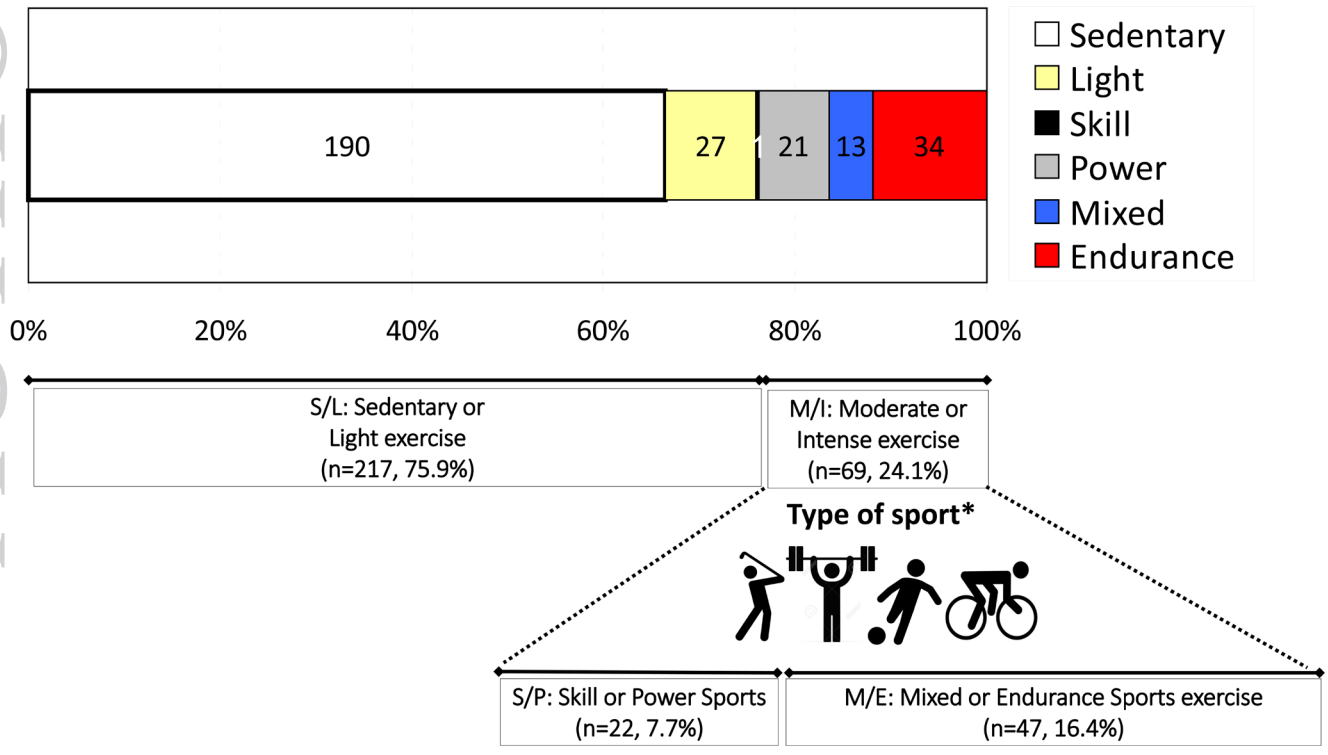

Figure 1 Physical activity 'typical week' 3 years prior to diagnosis of BS. Light (<2 hours/week), moderate (2–5 hours/week) and intense (>5 hours/week) physical activity estimated at >70% maximum heart rate. *Type of sports from Pelliccia *et al*.[5] BS, Brugada syndrome.

The type of sport was classified according to the EAPC classification as 'skill', 'power', 'mixed' and 'endurance'.[5] For statistical analysis, 'skill' and 'power' were grouped together, and 'mixed' and 'endurance' were grouped together.

Patients who were unresponsive (n=30) or deceased (n=14) at the time of the questionnaire data collection were excluded. Only subjects with type 1 pattern, either spontaneous or after pharmacological testing with sodium channel blockers, were included in our analysis.

For detailed electrocardiographic subanalysis, the sample was reduced to those who had at least one digital ECG (n=131, 47.2%) that could be analysed by the computer system. The first available digital ECG for each patient was selected. ECGs were performed at rest, in supine position, and standard 12-lead ECG was obtained. In 151 (52.8%) participants, only printed ECG was available and they were excluded from this subanalysis.

Patient involvement

Patients were informed about the study's purpose, the tests they would undergo (such as ECG and questionnaires), and how their data would be analysed. The importance of publishing the results to benefit future research and patient care was also emphasised.

Definition of events

SCD was defined as the unexpected natural death from a cardiac cause within a short time period, generally ≤1 hour from the onset of symptoms. For SCD or equivalent, we also included resuscitated cardiac arrest and appropriate ICD discharge.

Statistical analysis

IBM SPSS Statistics V.25.0 for Windows software was used for statistical analysis. Quantitative variables are expressed as mean and SD. Qualitative variables are expressed as absolute numbers and percentages. For the comparison of two qualitative variables, Pearson's χ^2 test or Fisher's exact test was used. Student's t-test for independent samples was used for the comparison of quantitative variables. Univariate survival analysis was performed to evaluate the relationship of a predictor factor with the time

Table 1 Baseline characteristics of BS patients based on level of physical activity

	Level of physical activity			
	Sedentary or light (S/L)	Moderate or intense (M/I)	Total	P value
n	217 (75.9%)	69 (24.1%)	286 (100%)	
Gender				
Male	137 (63.1%)	65 (94.2%)	202 (70.6%)	<0.001
Female	80 (36.9%)	4 (5.8%)	84 (29.4%)	<0.001
Proband	157 (72.4%)	55 (80.9%)	212 (74.4%)	0.16
Diagnosis age	40.5 (18.0)	34.4 (16.3%)	39.1 (17.8)	0.01
Diagnosis reason				
Unknown	13 (6.0%)	3 (4.3%)	16 (5.6%)	0.77
Incidental	104 (47.9%)	43 (62.3%)	147 (51.4%)	0.04
Symptoms	42 (19.4%)	12 (17.4%)	54 (18.9%)	0.72
SCD	7 (3.2%)	1 (1.4%)	8 (2.8%)	0.68
Family screening	50 (23.0%)	10 (14.5%)	60 (21.0%)	0.13
Spontaneous type I pattern	73 (33.6%)	27 (39.1%)	100 (35.0%)	0.40
Family history of BS	96 (44.2%)	27 (39.1%)	123 (43.0%)	0.45
Family history of SCD	71 (33.6%)	14 (20.9%)	85 (30.6%)	0.05
Positive genotype*	28 (18.1%)	8 (19.0%)	36 (18.3%)	0.88
Atrial fibrillation	14 (6.6%)	4 (6.0%)	18 (6.4%)	1.00
Syncope	58 (26.7%)	15 (21.7%)	73 (25.5%)	0.41
Arrhythmic syncope	27 (13.2%)	10 (14.7%)	37 (13.6%)	0.75
Age at 1st syncope	37.4 (18.2)	25.7 (13.9)	35.1 (17.9)	0.01
Age at 1st arrhythmic syncope	42.1 (19.5)	34.2 (17.5)	40.1 (19.1)	0.26
Abnormal EP procedure*	13 (28.9%)	1 (20.0%)	14 (28.0%)	1.00
ICD insertion	34 (16.6%)	11 (15.9%)	45 (15.7%)	0.96
SCD or equivalent	9 (4.1%)	3 (4.3%)	12 (4.2%)	1.00

*% in relation to total.
BS, Brugada syndrome; EP, electrophysiology procedure; ICD, implantable cardioverter defibrillator; SCD, sudden cardiac death.

until diagnosis of BS (diagnosis age), using the Kaplan-Meier method and the log-rank test for significance.

Multivariate regression analysis was performed to study the predictive influence of different variables, using binary logistic regression and Cox regression. Results with a p<0.05 were considered statistically significant.

RESULTS

General characteristics of the population

A population of 286 patients with BS (mean age 48.9±14.7 years, 70.6% men) was studied. The most frequent reason for diagnosis was incidental in 147 (51.4%) participants, followed by family screening in 60 (21.0%), presence of symptoms in 54 (18.9%) and resuscitated cardiac arrest in 8 patients (2.8%). The diagnosis type was pharmacological induction in 186 patients (65.0%), and spontaneous in the other 100 (35.0%) patients. Mean age at diagnosis was 39.1±17.8 years. Family history of BS was present in 123 (43.0%) patients and history of sudden death (SCD) in the family in 85 (30.6%) participants.

Regarding symptoms, 73 (25.5%) patients had a history of syncope. 37 (14.6%) had a history of documented arrhythmic syncope, and 44 patients (16.1%) have had vasovagal syncope. The age of first arrhythmic syncope was 40.1±19.1 years.

There were 18 (6.4%) patients with a history of atrial fibrillation. 45 (15.7%) were carriers of an implantable cardioverter defibrillator. The average follow-up time of the patients was 71.5±54.5 months.

Physical activity level

69 (24.1%) patients fall under the moderate or intense (M/I) activity group, whereas 217 (75.9%) were sedentary or engaged in light activity (S/L). In the M/I activity group, there were more men (65, 94.2%). Incidental diagnosis was more frequent in the M/I group (43, 62.3% vs 104, 47.9%, p=0.04). A similar rate of spontaneous type I pattern was found in both groups (27, 39.1% vs 73, 33.6% p=0.40). Diagnosis of BS occurred at a younger age in the higher levels of physical activity group (M/I) (34.4±16.3 vs 40.5±18.0 years, p=0.01). Age of the first syncope was also younger in the M/I group (25.7±13.9 vs 37.4±16.1 years, p=0.0001) (table 1).

In the Kaplan-Meier analysis for the probability of BS diagnosis, a significant association was confirmed between the level of physical activity and an earlier age at diagnosis (figure 2A). The median age at diagnosis for those engaging in intense activity was 28.0±11.9 years (95% CI: 4.8 to 51.2), while for non-athletes, it was 45.0±1.4 years (95% CI: 42.2 to 47.8) (p=0.001) (online supplemental table 1).

Type of sports

Table 2 shows patient characteristics based on the type of sport practised according to the EAPC classification.[5] Among patients with M/I physical activity, a distinction was made between those performing skill or power sports (S/P) (group 2, 22 (7.7%)) and those performing mixed or endurance sports (M/E) (group 3, 47 (16.4%)). The group 1 consisted of non-athletes, composed of BS patients with S/L physical activity.

There were more men in both types of sports compared with non-athletes (group 3, 22 (100%), group 2, 43 (91.5%) vs group 1, 137 (63.1%), p<0.001 for group 3 vs 1 and for group 2 vs 1).

In the Kaplan-Meier analysis for age at diagnosis, a significant association was obtained with the level of physical activity. Practising M/I physical activity (compared with the S/L) was associated with an earlier age at diagnosis (HR: 1.6, 95% CI: 1.2 to 2.1, p=0.001) (figure 2A).

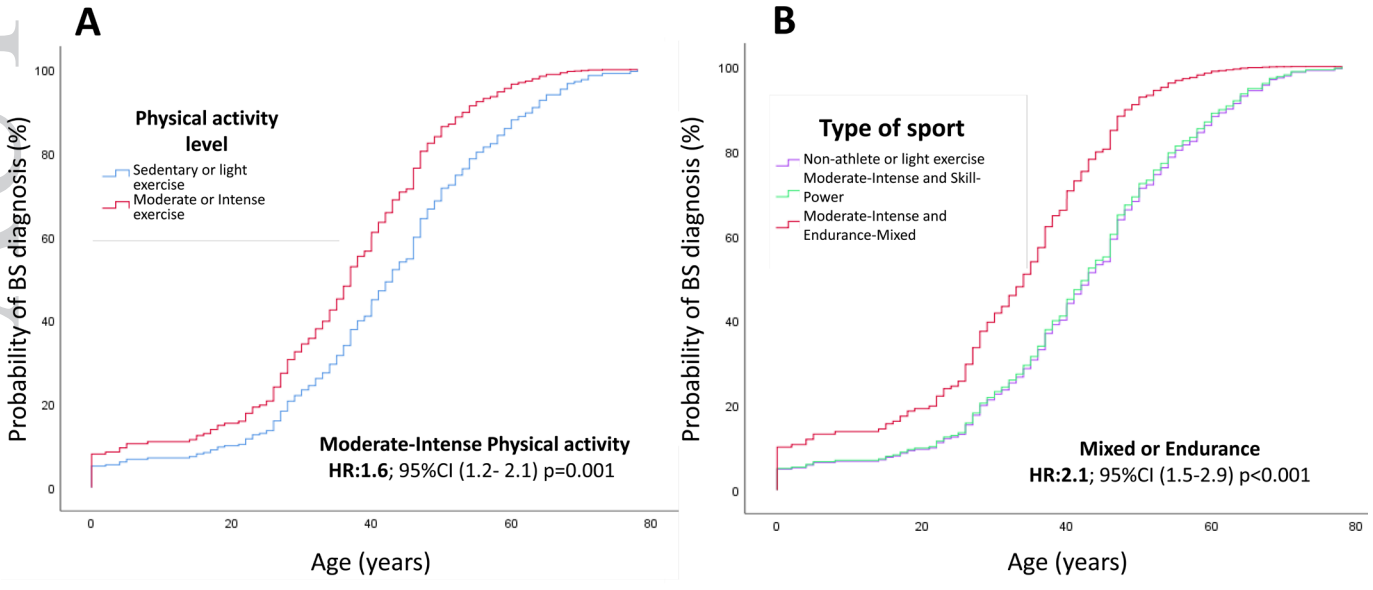

Figure 2 BS, Brugada syndrome

Table 2 Baseline characteristics of BS patients based on type of sport

	Type of sports					
	Non-athlete (group 1)	Skill/power (group 2)	Mixed/endurance (group 3)	Total	P value G1 vs G3	P value G1 vs G2
n	217 (75.9%)	22 (7.7%)	47 (16.4%)	286 (100%)		
Gender						
Female	80 (36.9%)	0 (0%)	4 (8.5%)	84 (29.4%)	<0.001	<0.001
Male	137 (63.1%)	22 (100%)	43 (91.5%)	202 (70.6%)	<0.001	<0.001
Proband	157 (72.4%)	17 (77.3%)	38 (80.9%)	212 (74.1%)	0.15	0.62
Diagnosis age	40.5 (18.0)	39.5 (18.9)	32.1 (14.5)	39.1 (17.8)	0.003	0.81
Diagnosis reason						
Unknown	13 (6.0%)	1 (4.5%)	2 (4.3%)	16 (5.6%)	1.00	1.00
Incidental	104 (48.1%)	11 (50.0%)	32 (68.1%)	147 (51.6%)	0.01	0.85
Symptoms	42 (19.4%)	5 (22.7%)	5 (10.6%)	60 (21.1%)	0.06	0.97
SCD	7 (3.2%)	0 (0%)	1 (2.1%)	8 (2.8%)	1.00	1.00
Family screening	50 (23.1%)	5 (22.7%)	5 (10.6%)	60 (21.1%)	0.06	0.97
Spontaneous type 1 pattern	73 (33.6%)	10 (45%)	17 (36%)	100 (35.0%)	0.74	0.27
Family history of BS	96 (44.2%)	13 (59.1%)	14 (29.8%)	123 (43.0%)	0.07	0.18
Family history of SCD	71 (33.6%)	2 (9.1%)	12 (26.7%)	85 (30.6%)	0.36	0.02
Positive genotype*	28 (18.1%)	2 (14.3%)	6 (21.4%)	36 (18.3%)	0.67	1.00
Atrial fibrillation	14 (6.5%)	3 (13.6%)	1 (2.1%)	18 (6.3%)	0.48	0.19
Syncope	58 (26.7%)	5 (22.7%)	10 (21.3%)	73 (25.5%)	0.44	0.68
Arrhythmic syncope	27 (13.2%)	4 (19.0%)	6 (12.8%)	37 (13.6%)	0.94	0.50
Age at 1st syncope	37.4 (18.2)	27.2 (8.8)	24.9 (16.2)	35.1 (17.9)	0.04	0.06
Age at 1st arrhythmic syncope	42.1 (19.5)	35.3 (22.1)	33.5 (16.0)	40.1 (19.1)	0.32	0.52
Abnormal EP procedure*	13 (29%)	0 (0%)	1 (33%)	14 (28.0%)	1.00	1.00
ICD insertion	34 (16%)	3 (14%)	8 (17%)	45 (16.0%)	0.82	1.00
SCD or equivalent	9 (4%)	0 (0%)	3 (6.4%)	12 (4.2%)	0.45	1.00

*% in relation to total.
BS, Brugada syndrome; EP, electrophysiology procedure; ICD, implantable cardioverter defibrillator; SCD, sudden cardiac death.

Comparison between athletes (mixed/endurance) and non-athletes (S/L)

Regarding diagnosis type, incidental diagnosis was significantly more frequent in the M/E sports group compared with S/L group (32, 68.1% vs 104, 48.1%, p=0.01). There were no other significant differences between groups regarding diagnosis type, spontaneous type 1 pattern or medical history of syncope (any syncope or arrhythmic syncope).

As for the age at diagnosis, significant differences were observed, with a younger age at diagnosis in the group of patients performing M/E sports compared with S/L group (32.1±14.5 vs 40±18.0 years, p=0.003). Age of first syncope was also lower in the M/E group compared with S/L group (24.9±16.2 vs 37.4±18.2 years, p=0.04). There were no significant differences in atrial fibrillation or arrhythmic events between groups.

Figure 2B shows the Kaplan-Meier analysis for the age at diagnosis according to the sports discipline. Probability of diagnosis was earlier for M/E sports disciplines compared with S/L patients (HR: 2.1, 95% CI: 1.5 to 2.9, p<0.001).

Comparison between athletes (skill/power) and non-athletes (S/L)

There were no significant differences in the reason for diagnosis, age at diagnosis, diagnosis type (spontaneous or pharmacological), history of syncope or arrhythmic events between S/P group participants and S/L group. Only a trend towards a younger age at first syncope was observed in the S/P sports group compared with S/L group (27.2±8.8 vs 37.4±18.2 years, p=0.06).

Online supplemental table 2 lists the demographic, sports and clinical characteristics of BS patients engaged in high-intensity physical activity.

Digital ECG analysis

Digital ECG analysis (available in n=131, 45.8% of the cohort) was conducted to assess whether the intensity of physical activity (98, 73.7% S/L physical activity, 33,

Table 3 ECG features of BS patients based on level of physical activity

Level of physical activity	Sedentary or light (S/L)	Moderate or intense (M/I)	Total	P value
n	98 (74.8%)	33 (25.2%)	131 (100%)	0
Age at ECG recorded	46.9 (14.4)	38.5 (10.5)	44.8 (14)	0.002
Heart rate	72.5 (12)	66.6 (11.6)	71 (12.1)	0.02
P wave duration (ms)	109.9 (28.4)	117.3 (25.3)	111.7 (27.8)	0.19
PR interval duration (ms)	170.2 (29.2)	167.1 (25.6)	169.4 (28.2)	0.58
QRS duration DII (ms)	99.2 (18.9)	102.2 (18.2)	100 (18.7)	0.42
QRS maximum amplitude limb leads (mV)	16.9 (6.6)	15.6 (5.7)	16.6 (6.4)	0.29
QRS maximum amplitude precordial leads (mV)	24.5 (8.6)	27.6 (8)	25.2 (8.5)	0.07
J point maximum amplitude (mV)	2.1 (1.2)	2 (1.1)	2.1 (1.2)	0.67
Number of leads with J point elevation	1.7 (1.2)	2 (1.3)	1.8 (1.2)	0.21
J point total elevation (mV)	5.3 (2.6)	5.4 (2.8)	5.3 (2.7)	0.71
Maximum amplitude ST elevation (mV)	2 (1.4)	2.5 (1.3)	2.1 (1.4)	0.07
Number of leads with ST segment elevation	2.8 (2.7)	3.8 (2.2)	3.1 (2.6)	0.08
ST segment total elevation (mV)	8.7 (6.3)	10.1 (4.5)	9 (5.9)	0.24
Maximum amplitude ST elevation V1-V3 (mV)	1.9 (1.4)	2.4 (1.4)	2 (1.4)	0.05
Total ST elevation V1–V3 (mV)	3.5 (2.7)	4.2 (2.2)	3.7 (2.6)	0.21
QTc interval duration DII	401.6 (30.1)	380.4 (28.5)	396.1 (31)	0.001
Number of leads with negative T waves	2.6 (1)	2.4 (0.8)	2.5 (1)	0.32

BS, Brugada syndrome.

26.3% M/I physical activity) or sports discipline (24, 18.0% M/E sports and 9, 6.8% S/P sports) affected any parameters associated with electrical cardiac remodelling in BS patients (table 3).

Patients with BS engaged in M/I physical activity had a significantly lower heart rate (66.6±11.6 vs 72.4±11.9 bpm, p=0.02), and shorter QTc intervals (Bazett correction) compared with S/L patients (QTc II: 380.4±28.5 vs 401.6±30.0 ms, p=0.001). The amplitude of ST segment elevation in right precordial leads (V1–V3) was higher in those engaged in M/I physical activity compared with S/L individuals (2.4±1.4 vs 1.9±1.4 mV, p=0.05).

Regarding the analysis by sports discipline, comparison was made separately between non-athletes (S/L) versus S/P sports and S/L versus M/E sports. Heart rate was lower in the M/E sports group compared with S/L group (64.9±10.6 vs 72.4±11.9 bpm, p=0.01), which was not significant in the S/P sports group compared with S/L individuals. QTc interval was significantly shorter in both the M/E sports and S/P sports groups compared with S/L group (QTc II: 377.6±31.8 ms in M/E, 389.0±12.8 ms in S/P, 401.6±30.1 ms in S/L, p=0.001 and p=0.04, respectively). Amplitude of ST segment elevation in right precordial leads was numerically higher in the sports groups but did not reach statistical significance compared with non-athletes.

Physical activity and severity of phenotype in BS

For the study of phenotypic severity in BS, and its possible association with physical activity, a multivariate analysis was conducted where arrhythmic syncope and spontaneous type I diagnosis were defined as dependent variables. Independent variables included sex, age at diagnosis, level of physical activity and sports discipline. Neither level of physical activity nor type of sports was a predictor of arrhythmic syncope (OR: 1.3, 95% CI: 0.6 to 3.0, p=0.52, for M/I activity vs S/L; OR: 1.1, 95% CI: 0.7 to 1.7, p=0.7 for M/E sports vs S/L). The only predictor of spontaneous type I diagnosis was male sex (OR: 3.0, 95% CI: 1.6 to 5.6, p<0.001).

Physical activity and BS-associated events

Neither intensity of physical activity (M/I) nor sports discipline (M/E or S/P) was a predictor of arrhythmic syncope or SCD in univariate or multivariate survival analysis (figure 3).

However, the presence of spontaneous type I pattern on the ECG and a history of arrhythmic syncope were significantly associated with a higher risk of SCD or equivalent (HR: 3.3, 95% CI: 1.0 to 11.1, p=0.05 and HR: 5.3, 95% CI: 1.7 to 16.9, p=0.005, respectively).

DISCUSSION

Previous publications on physical activity in BS have focused on ECG morphology, acute repolarisation

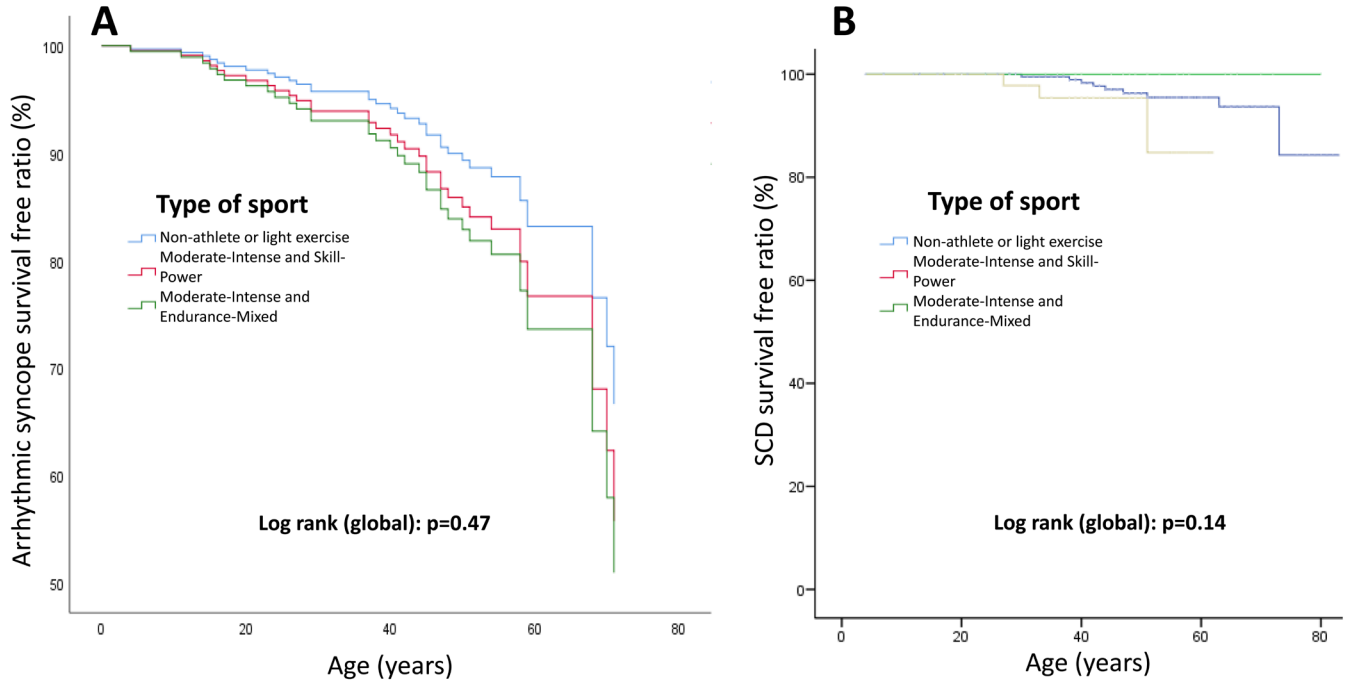

Figure 3 SCD, sudden cardiac death.

changes and development of arrhythmias during exercise stress tests in general BS cohorts, irrespective of physical activity.[7–10] It has been proved that vagal hypertonia predominant in the recovery phase facilitates the expression of the typical type 1 pattern. Nonetheless, no clear temporal association between ST elevation in the recovery phase and onset of arrhythmias has been established.[11 12]

There are no specific publications on BS in athletes. This is the first study comparing BS expression based on regular physical activity and sports discipline. A survey based on the 'typical week' in 3 years prior to diagnosis was used for classifying physical activity intensity, and sports discipline was categorised according to the EAPC classification.[5 6] Additionally, an analysis of ECG features related to BS and electrical remodelling was performed in the subset of participants with available digitised ECG.

In the group of athlete patients, there were more males, similar to other series of athletes with other conditions and athletes from the general population. No relationship was observed between the level of physical activity or sports discipline and the type of diagnosis, whether spontaneous or pharmacologically induced.

However, for the first time, an association was demonstrated between physical activity, mainly from disciplines that produce greater morphological and electrical cardiac remodelling, such as those included in the 'mixed and endurance' group, and an earlier age of diagnosis (Δ 6 years) and an earlier onset of syncope (Δ 12 years). The finding of an earlier diagnosis in athletes might, in part, be justified by more frequent medical check-ups including an ECG. Although this potential bias would not explain the earlier onset of syncope.

The detailed analysis of ECG features, despite being a small group, did show that regular moderate to intense physical activity resulted in electrical remodelling in the hearts of BS patients in our series. Heart rate (Δ 6 bpm) and QTc interval (Δ 21 ms) were significantly lower in athletes. Regarding the typical BSECG morphology, the maximum ST elevation in V1–V3 was significantly higher (Δ 0.5 mm) in athletes compared with sedentary individuals. The changes observed in digital ECGs were primarily seen in patients who practise 'mixed' or 'endurance' sports.

Thus far, relevant QT interval alterations have not been described in BS patients. The presence of these shorter QTc values in patients practising high cardiovascular demanding sports, as well as a lower heart rate, reflects the vagal hypertonia characteristic of cardiovascular adaptation to training. Previous publications studying QT adaptation according to heart rate in BS patients compared with controls observed a greater QT lengthening during exercise.[9] However, these series do not specifically study athletes with BS.

Exercise testing in BS patients typically shows a greater decrease in heart rate in the first minute (heart rate decay), usually associated with ST segment elevation compared with healthy controls, both expressions of parasympathetic activation and sympathetic inhibition that occur in the recovery phase.[8] In our study, the first available digital ECG of BS patients was selected, being in all cases a standard 12-lead ECG recorded in a supine resting position. An analysis of ECG exercise response in athletes with BS may show more striking alterations in the recovery phase than those described in previous studies in populations not selected according to their level of physical activity.

Physical activity is considered safe in BS patients.[12] In our study, despite identifying associations between moderate to intense physical activity with age of diagnosis, age of first syncope and some electrocardiographic features, we did not find an increased risk of arrhythmic events or SCD in athletes with BS compared with sedentary individuals with BS.

Expert consensus documents and clinical practice guidelines do not include restrictions on physical activity in BS patients. However, in light of our study results, it would be desirable to conduct studies with a larger number of BS athletes to appropriately assess the impact of performing high-intensity sport disciplines such as 'mixed and endurance'on disease expression, particularly on the incidence of arrhythmias and SCD.

Limitations

The study has several limitations inherent to the rarity of the disease and small numbers. M/E athletes were younger compared with sedentary individuals. One could argue that ECG findings might have been related to the age of the individuals rather than the consequence of physical activity and that athletes might have had easier access to ECG tests. In this regard, it is important to highlight that the type of analysis based on survival estimates and Cox regression adjusts by the effect of age. There was no preparticipation programme for athletes on site in the geographical area during the period of the study that could explain an easier access of athletes to cardiac examinations.

Other limitations were the availability of digital ECGs to only a 47% of the cohort and the use of a 70% heart rate as the definition of the cut-off for the significant physical activity of 70%. In order to have accurate and automatic measurements of the ECG to limit the analysis to those with available digital ECG.

CONCLUSIONS

Among BS patients diagnosed in our clinical practice, one out of four practised moderate to high intensity physical activity in the years prior to diagnosis. Regular moderate to intense physical activity is associated with earlier age of diagnosis and earlier age of first syncope. BS patients performing sports classified as 'mixed and endurance' show ECG features like bradycardia, shorter QTc and higher ST segment elevation. Nonetheless, physical activity in BS patients in our series is not associated with a higher arrhythmic risk.

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ORCID iDs
Lidia María Carrillo Mora http://orcid.org/0000-0001-7314-9779
David Fernandez Vazquez http://orcid.org/0000-0003-4306-1447
Juan José Santos Mateo http://orcid.org/0000-0003-3546-4350
Ana Isabel Rodriguez Serrano http://orcid.org/0000-0003-0129-6504
Maria Sabater-Molina http://orcid.org/0000-0003-1352-1748
Juan R Gimeno http://orcid.org/0000-0001-5818-1754

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