Specificity of Elevated Intercostal Space ECG Recording for the Type 1 Brugada ECG Pattern

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Background: Right precordial (V1–3) elevated electrode placement ECG (EEP-ECG) is often used in the diagnosis of Brugada syndrome (BrS). However, the specificity of this has only been studied in smaller studies in Asian populations. We aimed to study this in a larger European population.

Methods: Two different populations consisting of healthy subjects were used. A total of 340 subjects were included, 80% were men, the median age was 43 year (interquartile range: 31–51) and all were of European ethnicity.

Results: No type 1 ECG patterns were identified but 16 (4.7%) subjects with a type 2 ECG and 32 (9.4%) subjects with a type 3 ECG were identified in any lead placement. In total 43 (13%) subjects had any BrS ECG pattern in any lead placement. The specificity was 100% (one-sided 97.5% CI: 99%) for the use of EEP-ECG to uncover type 1 pattern. For type 2 pattern the specificity was 95% (95% CI: 92–97%) and for type 3 pattern 91% (95% CI: 88–94%).

Conclusions: Elevated electrode placement ECG in the diagnosis of BrS seems to have a very high specificity with regards to the finding of a type 1 ECG pattern in a European population; conversely a finding of a type 2 or 3 pattern is of a significantly lower specificity and should perhaps be disregarded.

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Brugada syndrome; ECG; elevated electrode placement

INTRODUCTION

Brugada syndrome (BrS) is a primary arrhythmia syndrome characterized by the occurrence of malignant ventricular arrhythmias often during rest or sleep.¹ A Requirement for the diagnosis of BrS is the finding of the characteristic type 1 Brugada electrocardiogram (ECG) pattern in the right pre-

cordial leads (V1–3). This ECG pattern is characterized by a coved ST-segment elevation ≥ 2 mm (0.2 mV) followed by a negative T wave.² The diagnosis of BrS can often be difficult to make as the presence of a type 1 ECG pattern fluctuates significantly over time even in definitely diagnosed BrS patients.³

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To improve the sensitivity of the ECG recording for detecting the diagnostic type 1 pattern two different techniques are typically used: (1) pharmacologic provocation testing using a sodium-channel blocker (flecainide, ajmaline, pilsicainide, or procainamide), and (2) elevated electrode placement ECG (EEP-ECG). EEP-ECG employs the use of higher than normal placement of the right precordial leads (V1–V3) when recording an ECG in a patient suspected of having the syndrome.⁴ Usually three ECGs are recorded, one with normal electrode placement of V1–3 (V1–2 in intercostal space 4), one with V1–3 elevated one intercostal space (+1 ICS), and one with V1–3 elevated two intercostal spaces (+2 ICS). The aim is to improve the sensitivity of the examination as Brugada ECG patterns are more prevalent with elevated electrode placement.²

Some prior studies have investigated the specificity of EEP-ECG using healthy controls, but they have been relatively small and only performed in Asian populations.^{5–9} As BrS seems to be more prevalent in Asian than in European populations it is unsure whether findings can be translated to populations of European ancestry.^{10–12}

In this study we aim to investigate the specificity of recording ECGs with elevated electrode placement for the type 1 Brugada pattern in a European population.

METHODS

Populations

Two populations were used: The first population consisted of Danish civil aviation pilots undergoing routine health examinations at University Hospital Rigshospitalet, Copenhagen, Denmark. All ECGs were recorded by the same investigator (MT) using a standardized protocol. The inclusion criteria for this population were age between 16 and 75 years. Exclusion criteria were any form of structural heart disease (IHD, CHF, etc.), history of syncope, and family history of SD under the age of 50 years, intake of any medications with known effect on the cardiovascular system. Subjects with arterial hypertension were not excluded.

The second population consisted of subjects with no apparent heart disease determined by negative personal and family history, normal physical examination and normal standard resting 12-lead ECG, who were not taking any medications with known effect on the cardiovascular system. These

ECGs were acquired at St. George's, University of London, UK as part of a research project approved by the local Ethics Committee.¹³

Definitions

The presence of R' was defined as a clear discernable positive reflection at the end of the QRS complex at least 0.5 mm of height, the presence of BrS type 1, 2, and 3 ECG patterns as noted in the second Brugada Syndrome consensus report,² J-point elevation measured as the first point of the inflection on the upstroke of the S wave, ST-segment elevation measured only when a horizontal part of the ST segment existed. All measurements were rounded down to nearest mm.

ECG Recording and Analyses

ECGs were recorded either as three separate ECGs, one for each electrode placement or as two 15-lead ECGs where the three extra leads were used for either +1 ICS or +2 ICS lead placements. All ECGs were recorded electronically using a General Electric MAC 5500 ECG recorder or CardioSoft 6.01 resting digital recorders (GE Healthcare Products, Milwaukee, WI, USA) with the same technical characteristics (500 Hz, 4.88 μ V amplitude resolution). ECGs were stored as XML files and imported into a custom-made ECG server for analyses. Analyses were carried out by one of the investigators (A.G.H.) on screen using a built-in magnifier function. All findings were recorded separately for V1, V2, and V3 for each lead placement and BrS ECG patterns was classified according to the definitions given by the second consensus report on BrS.² All interval measurements were taken from the built in 12SL Marquette algorithm found in GE ECG recorders.

Statistical Analyses

Differences between means or medians were assessed using the unpaired Student's *t*-test or the Wilcoxon rank-sum test. Differences between proportions were assessed using the χ^2 test. The Clopper-Pearson method was used to calculate confidence intervals for the specificity. All analyses were done using Stata 11 (StataCorp LP).

The study was approved by the regional ethics committee (H-B-2009-023) and the Danish Data Protection Agency.

Table 1. Clinical and ECG Characteristics

	No Brugada ECG Pattern	Brugada ECG Pattern	P-value
Population size, n (%)	297 (87%)	43 (13%)	
Age, median (IQR)	43 (31–52)	43 (32–49)	0.59
Male gender, n (%)	241 (80%)	37 (86%)	0.38
Blood pressure mm Hg, median (IQR)			
Systolic*	134 (126–140)	138 (130–141)	0.28
Diastolic*	76 (70–83)	77 (74–82)	0.55
Body mass index, mean (SD)*	25 (2.8)	24 (3.0)	0.04
ECG measures, mean (SD)			
Beats per minute	62 (11)	62 (10)	0.76
PR interval, ms	160 (24)	160 (21)	0.96
QRS duration, ms	96 (11)	96 (10)	0.88
QTc interval (Bazett's), ms	410 (24)	407 (22)	0.43

*Data only available for n = 243 subjects.

Table 2. Prevalence of Brugada Type 1–3 ECG Patterns for Different Lead Placements

	Type 1	Type 2	Type 3
+0 ICS	0	0	3 (0.9%)
+1 ICS	0	9 (2.4%)	10 (3.0%)
+2 ICS	0	11 (3.3%)	24 (7.10%)
Any lead placement	0	16 (4.7%)	32 (9.4%)

RESULTS

A total of 353 healthy subjects were included, 248 from the Danish cohort and 105 from the English cohort. Because of non-European ethnicity 13 subjects were excluded. The population consisted of 276 (81%) men, the median age was 43 year (interquartile range: 31–51).

Clinical characteristics divided into Brugada ECG pattern and non-Brugada ECG patterns groups are summarized in Table 1. The two groups were similar on all variables except with regards to body mass index where a significant difference was seen ($P = 0.04$) with the Brugada ECG pattern group being slightly leaner than the non-Brugada ECG patterns group (24.1 vs. 25.3).

No type 1 ECG patterns were identified but 16 (4.7%) subjects with a type 2 ECG and 32 (9.4%) subjects with a type 3 ECG was identified in any lead placement. The prevalence of Brugada ECG patterns increased with increasingly elevated lead placements (Table 2). In total 43 (13%) subjects had any Brugada ECG pattern in any lead placement. Examples of Brugada ECG patterns can be seen in Figure 1.

The above data results in a specificity of 100% (one-sided 97.5% CI: 99%) for the use of EEP-ECG to uncover type 1 patterns, the only diagnostic pat-

tern for BrS. For type 2 pattern the specificity was 95% (95% CI: 93–97%) and for type 3 pattern 91% (95% CI: 87–94%).

Of the subjects without any Brugada patterns at +0 ICS ($n = 337$) 15 developed a type 2 pattern and 25 developed a type 3 pattern at higher lead placements.

An incomplete right bundle-branch block (IRBBB) defined as the existence of an R' wave in lead V1 was also highly correlated to increasingly elevated lead placements: at +0 ICS 18 (5.3%) had an R' wave in V1, at +1 ICS it was 45 (13.3%), and at +2 ICS it was 120 (36%). The median amplitude of the R' wave (when present) stayed the same (2 mV).

The population with a type 2 ECG pattern ($n = 16$), shown in Table 3, were predominantly males (15/16), albeit not significantly different from the rest of the population ($P = 0.22$). Age wise the population is also similar to the rest of the population (42 vs. 40 years, $P = 0.52$). With regards to PR interval, QRS duration, and QTc interval the two populations were also similar (data not shown).

DISCUSSION

We report the hitherto largest study of the specificity of elevated electrode placement ECG for detecting Brugada ECG patterns. In total 340 healthy subjects was included and no Brugada type 1 patterns was found, but 16 (4.7%) subjects with a type 2 ECG and 32 (9.4%) subjects with a type 3 ECG was identified. This resulted in a specificity of 100% with a one-sided 97.5% CI of 99% with regards to Brugada type 1, meaning a very high specificity. As the prevalence of type 2 or 3 patterns were quite high at especially +1 and +2 ICS,

Figure 1. Examples of ECG patterns classified as Brugada and non-Brugada patterns.

Table 3. Characteristics of Subjects with a Type 2 Brugada Pattern

Gender	Age	+0 ICS	+1 ICS	+2 ICS	HR	PQ	QTc	R-axis
Male	21	–	Type 2–V2	R'–V1/V2	73	138	427	54
Male	21	–	R'–V2	Type 2–V3	68	172	399	60
Male	27	–	Type 2–V2	Type 3–V3	60	156	374	74
Male	30	–	Type 2–V2	Type 2–V2/V3	69	136	413	54
Male	33	–	R'–V2	Type 2–V3	71	172	417	26
Male	34	–	Type 2–V2	Type 2–V2	56	188	360	17
Male	34	–	R'–V1/V2	Type 2–V3	57	166	383	20
Male	42	R'–V1	R'–V1/V2/V3	Type 2–V3	56	136	449	61
Male	43	–	–	Type 2–V2	51	138	407	83
Male	43	–	Type 2–V2	Type 3–V2	62	164	410	64
Male	46	–	–	Type 2–V2	73	196	420	87
Male	46	R'–V1	Type 2–V2	Type 2–V3	62	150	418	78
Male	46	–	Type 2–V2	Type 3–V2	59	186	399	66
Female	48	–	R'–V1	Type 2–V3	54	160	402	52
Male	51	–	–	Type 2–V2	74	152	432	1
Male	62	Type 3–V1/V2	Type 2–V3	Type 3–V3	48	200	414	78

The most severe pattern for each lead placement is reported along with the lead where it was identified.

this resulted in a specificity of 95% and 91% with regards to type 2 or 3 patterns, indicating that these patterns should probably be disregarded in the setting of EEP-ECG, at least in an a priori low-risk population.

Other studies of EEP-ECG conducted in Asian populations have shown similar results. Shimizu et al. investigated a population of 40 healthy Japanese men (mean age 47 years, SD 14) and found no Brugada ECG patterns during EEP-ECG.⁷ Sangwatanaroj et al. examined 53 healthy Thais and found no Brugada type 1 ECG patterns.⁶ Hisamatsu

et al. studied 206 Japanese men in a screening study, recording +0 and +1 ICS ECGs, and found two subjects with a type 1 patterns, six with a type 2 patterns and four with a type 3 patterns.⁸ Finally Shin et al. examined 225 healthy Korean men (mean age 44 years, SD 13) and found three type 2 patterns.⁵ These findings suggest that Brugada ECG patterns are more prevalent in Japan than in other countries.

To our knowledge no studies of EEP-ECG have been conducted in Europeans but a recent German study examining 4,149 individuals and did not

detect any type 1 or 2 Brugada patterns in standard leads.⁹ Another recent Danish study though, found 13 out of 18,974 subjects with either a type 2 or type 3 pattern, but no type 1 patterns were found.¹⁴

The population in our study reflected the typical age and gender distribution of a BrS population. The largest BrS population (n = 1029) reported so far, had 72% men and a median age of 45 years,¹⁵ and the second largest (n = 334) had 76% men and a mean age of 42 years.¹⁶ These numbers are comparable to our study population with 80% men and a median age of 43 years.

It is also noteworthy how significant an influence right precordial electrode placement has on the existence of an R' wave, and thus, by most definitions, the existence of an IRBBB, as the prevalence of this increased from 5.4% at +0 ICS to 36% at +2 ICS. This indicates that this pattern has little to do with bundle-branch block, as also suggested by others.¹⁷

Limitations

We cannot exclude that some of the subjects in our study at a later time would develop BrS, although taking into consideration the very low prevalence of BrS and the fact that our population excluded those with a history of syncope or sudden death in the family this seems highly unlikely.

CONCLUSION

Elevated electrode placement ECG seems to have a very high specificity with regards to the finding of a type 1 Brugada ECG pattern in a European population. Conversely a finding of a type 2 or 3 pattern is of a significantly lower specificity and should probably be disregarded.

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