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Impact of SMART Pass filter in patients with ajmaline-induced Brugada syndrome and subcutaneous implantable cardioverter-defibrillator eligibility failure: results from a prospective multicentre study

Giulio Conte ^{1,2,3*}, Fabio Cattaneo¹, Carlo de Asmundis ⁴, Paola Berne⁵, Alessandro Vicentini⁶, Mehdi Namdar⁷, Antonio Scalone⁸, Catherine Klersy⁹, Maria Luce Caputo¹, Andrea Demarchi¹, Tardu Özkartal¹, Francesca Salghetti⁴, Gavino Casu⁵, Ilaria Passarelli⁶, Stefano Mameli⁸, Dipen Shah⁷, Haran Burri ⁷, Gaetano De Ferrari⁶, Pedro Brugada ⁴, and Angelo Auricchio ^{1,2,3}

¹Division of Cardiology, Cardiocentro Ticino, Lugano, Switzerland; ²Centre for Computational Medicine in Cardiology, Faculty of Informatics, Università della Svizzera Italiana, Lugano, Switzerland; ³Faculty of Biomedical Sciences, USI, Lugano, Switzerland; ⁴Heart Rhythm Management Centre, Universitair Ziekenhuis Brussel—Postgraduate program Cardiac Electrophysiology and Pacing, Vrije Universiteit Brussel, Brussels, Belgium; ⁵Cardiology Department, Ospedale San Francesco, Nuoro, Italy; ⁶Elettrofisiologia ed Elettrostimolazione, Divisione di Cardiologia, IRCCS Policlinico S. Matteo, Pavia, Italy; ⁷Cardiology Department, University Hospital of Geneva, Switzerland; ⁸Cardiology Department, Ospedale Brotzu, Cagliari, Italy; and ⁹Service of Biometry and Clinical Epidemiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

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Aims

Ajmaline challenge can unmask subcutaneous implantable cardioverter-defibrillator (S-ICD) screening failure in patients with Brugada syndrome (BrS) and non-diagnostic baseline electrocardiogram (ECG). The efficacy of the SMART Pass (SP) filter, a high-pass filter designed to reduce cardiac oversensing (while maintaining an appropriate sensing margin), has not yet been assessed in patients with BrS. The aim of this prospective multicentre study was to investigate the effect of the SP filter on dynamic Brugada ECG changes evoked by ajmaline and to assess its value in reducing S-ICD screening failure in patients with drug-induced Brugada ECGs.

Methods and results

The S-ICD screening with conventional automated screening tool (AST) was performed during ajmaline challenge in subjects with suspected BrS. The S-ICD recordings were obtained before, during and after ajmaline administration and evaluated by the means of a simulation model that emulates the AST behaviour with and without SP filter. A patient was considered suitable for S-ICD if at least one sensing vector was acceptable in all tested postures. A sensing vector was considered acceptable in the presence of QRS amplitude >0.5 mV, QRS/T-wave ratio >3.5, and sense vector score >100. Of the 126 subjects (mean age: 42 ± 14 years, males: 61%, sensing vectors: 6786), 46 (36%) presented with an ajmaline-induced Brugada type 1 ECG. Up to 30% of subjects and 40% of vectors failed the screening during the appearance of Brugada type 1 ECG evoked by ajmaline. The S-ICD screening failure rate was not significantly reduced in patients with Brugada ECGs when SP filter was enabled (30% vs. 24%). Similarly, there was only a trend in reduction of vector-failure rate attributable to the SP filter (from 40% to 36%). The most frequent reason for screening failure was low QRS amplitude or low QRS/T-wave ratio. None of these patients was implanted with an S-ICD.

* Corresponding author. Tel: +41 918053350; fax: +41 918053173. E-mail address: giulio.conte@cardiocentro.org

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Conclusion

Patients who pass the sensing screening during ajmaline can be considered good candidates for S-ICD implantation, while those who fail might be susceptible to sensing issues. Although there was a trend towards reduction of vector sensing failure rate when SP filter was enabled, the reduction in S-ICD screening failure in patients with Brugada ECGs did not reach statistical significance.

Clinical trial registration

<https://clinicaltrials.gov> Unique Identifier NCT04504591.

Keywords

Brugada syndrome • Subcutaneous implantable cardioverter-defibrillator • SMART Pass • Screening • Eligibility • Sudden cardiac death

What's new?

- One of the five patients with Brugada electrocardiograms (ECGs) fails subcutaneous implantable cardioverter-defibrillator (S-ICD) screening when performed on Brugada type 1 ECG morphologies evoked by ajmaline challenge.
- Up to 40% of sensing vectors are not acceptable in the presence of dynamic Brugada ECG changes, due to low amplitude of the QRS complex or low QRS/T-wave ratio.
- The SMART Pass filter does not significantly reduce the proportion of subjects with an ajmaline-induced Brugada ECG and of vectors ineligible for S-ICD.
- The position of parasternal subcutaneous lead does not influence the screen-out rate of patients with Brugada ECGs or affects the number of acceptable sensing vectors.

Introduction

The subcutaneous implantable cardioverter-defibrillator (S-ICD) successfully terminates life-threatening ventricular arrhythmias, and is an established alternative to transvenous ICD (TV-ICD) in selected patients.^{1–3} Brugada syndrome (BrS) patients can be considered ideal candidates for S-ICD because they usually do not require any anti-bradycardia or anti-tachycardia pacing, but are exposed to life-long risk of transvenous lead-related complications.^{4,5}

The ICD survival benefit is usually jeopardized by the occurrence of inappropriate shocks (IAS) during follow-up, most commonly due to atrial arrhythmias, T-wave over-sensing (TWOS), lead failure, and occasionally myopotentials.^{4–6} The IAS have been reported in both TV-ICD and S-ICD although with a different rate and due to different causes.^{6,7} The TWOS which leads to R- and T-wave double-counting is by far the most frequent reason for IAS in S-ICD and can affect up to 10% of BrS patients implanted with an S-ICD.^{8,9}

The successful reduction of IAS using a novel electronic sensing filter [SMART Pass (SP) filter] in patients implanted with an S-ICD has been reported.¹⁰ The SP filter is automatically enabled during the device's set-up process if certain conditions are met.

A sensing screening using the automated screening tool (AST) is recommended prior to S-ICD implantation to evaluate presence of

appropriate sensing vectors based on critical components of the S-electrocardiogram (ECG) signal that include QRS amplitude and QRS/T-wave ratio.^{11–13} The pre-implantation sensing screening fails in up to 18% of patients with BrS.¹⁴ The dynamic ECG changes observed in BrS that may occur spontaneously, during fever or be evoked by specific drugs can lead to potential sensing issues. Ajmaline challenge during S-ICD screening has been recently reported as a useful tool to unmask screening failure in patients with BrS and initial appropriate sensing screening.^{15–17} The value of the SP high-pass filter in reducing S-ICD screening failure in BrS patients has not been yet established. The aim of this prospective multicentre study was to investigate the ability of SP filter in appropriately discriminating dynamic Brugada ECG changes evoked by ajmaline, and to assess its value in reducing S-ICD screening failure in patients with drug-induced BrS.

Methods

Study population

This is a multicentre, prospective, single-blinded study conducted from December 2017 to May 2020 at six European centres. All consecutive patients referred for suspected BrS, undergoing ajmaline administration, were considered eligible. Exclusion criteria were prior ICD implantation, spontaneous Brugada type 1 ECG, need of anti-tachycardia/bradycardia pacing, and age <18 years. Demographic data, medical history, and baseline ECG parameters were collected. Ethics Committees of all participating centres approved the study and all patients provided informed consent before inclusion.

Subcutaneous implantable cardioverter-defibrillator screening

The S-ICD screening, using the Emblem S-ICD AST, was performed at baseline in all patients, regardless of whether they were being considered for ICD implantation. The Boston programmer (3120 ZOOM LATITUDE Programmer Recorder Monitor) was used. The screening process was performed following the S-ICD manufacturer recommendations.^{11,14} In brief, a first electrode (LA) was placed 1 cm left lateral of the xiphoid process midline, a second electrode (RA) was placed 1 cm lateral to the left sternal border and 14 cm cranial to LA electrode, and finally a third electrode (LL) was positioned at the 5th inter-costal space along the mid-axillary line. The neutral electrode was placed on the lower thorax to serve as the patient reference electrode. The resulting vectors (I, II,

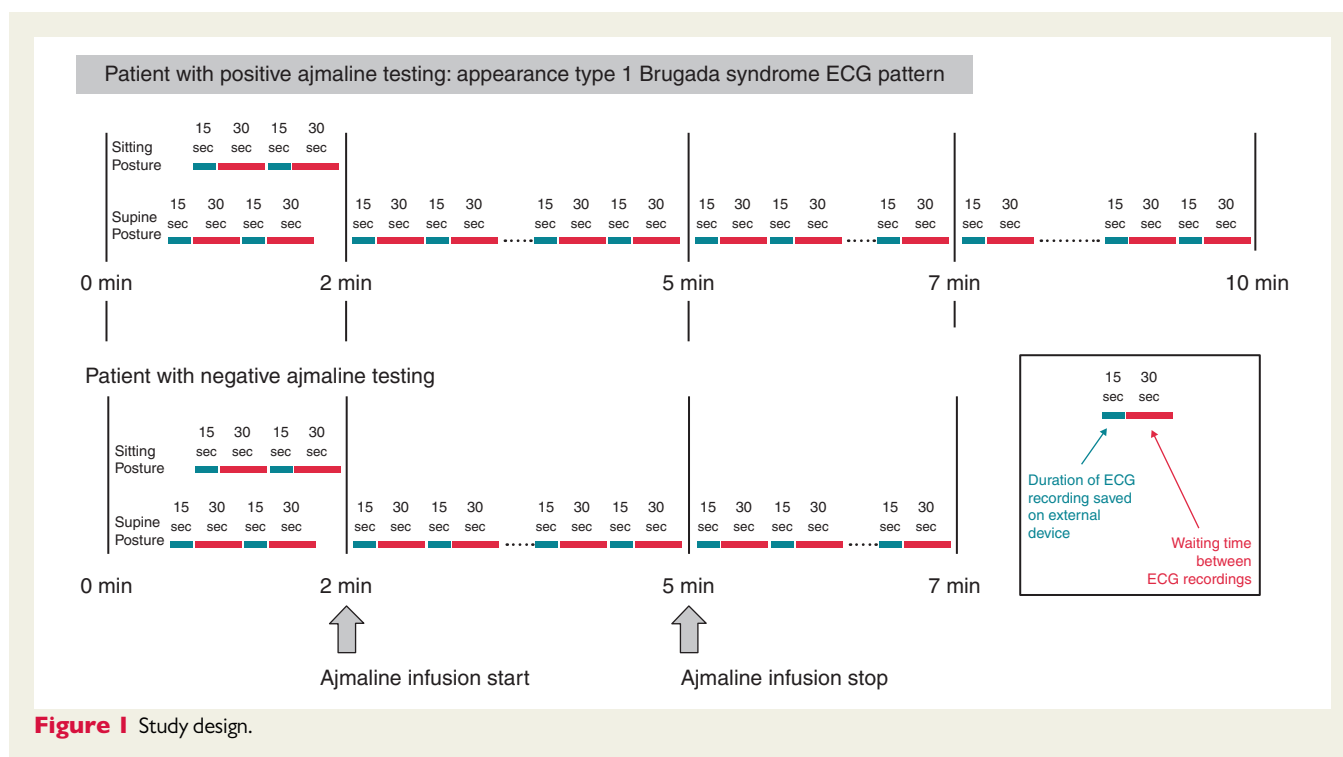


Figure 1 Study design.

and III) correspond to the alternate, secondary, and primary vectors of the S-ICD, respectively. In a limited number of patients, additional screening with right parasternal lead positions was performed (LA, 1 cm right lateral of the xiphoid process midline; RA, straight up 14 cm from LA along the right side of the sternum; and LL, same as the left parasternal position).

The S-ICD screening was repeated during ajmaline challenge. The S-ICD recordings were obtained during different phases of drug challenge (Figure 1): two recordings lasting 15 s each at both supine and sitting position before ajmaline challenge (baseline); one recording lasting 15 s starting 2 min after the beginning of ajmaline administration, or at the time of any change in ECG morphology, and followed by additional 15 s recordings until the end of ajmaline challenge (from 2 min to 5 min); and one recording lasting 15 s after termination of drug test (from 5 min to 7 min). In patients with ajmaline-induced type 1 BrS ECG pattern, additional recordings (from 7 min to 10 min, until maximal ST-segment/J point elevation started to decrease) were obtained.

Ajmaline challenge

Ajmaline (1 mg/kg) was administered intravenously over a 5 min period to unmask the diagnostic Brugada ECG. The pharmacological test was considered positive for BrS only if a Brugada type 1 ECG with a coved-type ST-segment elevation of at least 2 mm was documented in ≥ 1 right precordial leads with V1 and V2 recordings simultaneously obtained by placing electrodes at the second, third, and fourth inter-costal space. Ajmaline infusion was discontinued before reaching the target dose if QRS prolongation exceeded 30% compared with baseline interval, when frequent premature ventricular beats (PVCs) or Brugada type 1 ECG occurred or in case of high-degree atrioventricular (AV) block.

Sensing vector analysis

The S-ICD recordings obtained before, during and after ajmaline were evaluated offline using a simulation model that emulates the AST, and

then using a modified simulation model that includes the SP. The S-ICD simulation model and SP sensing filter have been extensively described elsewhere.¹⁰ A sensing vector was considered acceptable in the presence of following criteria: QRS amplitude >0.5 mV, QRS/T-wave ratio >3.5 , and sense vector score >100 . Sensing vectors presenting a score below the threshold score were considered borderline despite displaying adequate QRS amplitude and QRS/T-wave ratio.

The S-ICD eligibility at patient level was determined based on the appropriateness of each sensing vector at baseline and during ajmaline challenge. A patient was considered suitable for S-ICD if at least one appropriate sensing vector remained unchanged during all pharmacological test phases. As an example, if a patient at baseline screening had primary and secondary as passing vectors, but only alternate at ajmaline challenge, overall, this patient was considered as not eligible for an S-ICD implant.

Statistical analysis

Data are given as mean \pm standard deviation (SD), if continuous, and as counts and percentages, if categorical. A two-sided P value <0.05 was considered statistically significant. Stata software (StataCorp, TX, USA) was used for computation. Multivariable logistic models for the proportion of failure were fitted both at vector and at patient level, with calculation of Huber–White robust standard errors, while clustering on patient, to account for the lack of independence with patients. Test phase, use of SP filter, and ajmaline challenge results were included in the model, together with their 2- and 3-way interactions, to assess if the proportion of failure over the test phases depends on the use of SP and ajmaline challenge result. Separate analysis was performed both at vector and patient level including only vectors and patients, respectively, which passed the baseline screening.

Table 1 Clinical and ECG characteristics of study population

Clinical characteristics	Overall population (126)	Positive ajmaline (46)	Negative ajmaline (80)	P-value
Age (years), mean ±SD	41.8 ± 13.7	45.5 ± 12	39.5 ± 14	0.02
Male, n (%)	77 (61)	31 (79)	46 (70)	0.34
BMI (kg/m ²)	24.6 ± 4.3	24.6 ± 3.6	24.5 ± 4.4	0.65
Family history of SCD, n (%)	29 (23)	9 (19.5)	20 (25)	0.51
Asymptomatic, n (%)	77 (61)	30 (59)	47 (65)	0.57
Syncope, n (%)	32 (25.4)	12 (26)	20 (25)	1.00
Aborted SCD, n (%)	2 (1.6)	0	2 (3)	0.53
Previous atrial arrhythmia, n (%)	22 (17.6)	4 (9)	18 (23)	0.18
Sick sinus syndrome, n (%)	3 (2.4)	1 (2)	2 (2.5)	1.00
VT/VF inducibility at EP, n (%)	1/12 (9)	1/12 (9)	–	–
SCN5A gene mutation, n (%)	3/15 (20)	3/15 (20)	–	–
PR duration (ms)	153 ± 30	158 ± 25	150 ± 33	0.25
QRS duration (ms)	96 ± 16	103 ± 17	92 ± 15	0.0002
QTc duration (ms)	403 ± 25	403 ± 23	404 ± 26	0.71
Brugada type 2 ECG, n (%)	36 (28.6)	19 (21)	17 (41)	0.02
Right bundle branch block, n (%)	36 (28.6)	17 (37)	19 (24)	0.15

BMI, body mass index; EP, electrophysiology study; SCD, sudden cardiac death; VF, ventricular fibrillation; VT, ventricular tachycardia.

Results

Study population

Clinical and ECG features of study population are summarized in Table 1. Ajmaline challenge unmasked BrS in 46 patients (36.5%). No adverse events or ventricular arrhythmias occurred during drug test. There were no significant differences in baseline clinical characteristics of patients with positive and negative ajmaline challenge. Patients with drug-induced BrS presented with longer baseline QRS duration compared with patients with negative ajmaline (103 ± 17 vs. 92 ± 15 ms, *P* < 0.01). None of BrS patients was implanted with an S-ICD.

Patient screening failure

Of the 126 patients, 13 (10%) failed S-ICD screening at baseline and 19 (15%) during ajmaline challenge. Baseline and ajmaline screening failure rate was reduced to 7% and 13%, respectively, when SP was enabled (Table 2, simulation model).

Screening failure at baseline was found in seven BrS patients (15%). During ajmaline-induced ECG changes, the screening failed in seven further patients leading to an overall screening failure rate of 30%. The application of the SP filter reduced the failure rate to 24%, though this difference was not statistically significant (Figure 2).

No baseline ECG or clinical parameter was associated with S-ICD screening failure.

Sensing vector analysis

A total of 6786 sensing vector recordings were obtained (1800 at baseline, 3036 during ajmaline, and 1950 after ajmaline) from patients with positive (2505 vectors) and negative ajmaline challenge (4281 vectors). Overall, 463 vectors (26%) failed the screening at baseline, while 623 vectors (32%) during ajmaline challenge.

In patients with drug-induced Brugada type 1 ECG, 196 vectors (30%) failed the screening at baseline and 340 (40%) during ajmaline (Table 2). Vector failure rate in BrS patients was significantly higher compared with patients with negative ajmaline challenge (30% vs. 23% at baseline, 40% vs. 26% during ajmaline; *P* < 0.05). Moreover, in BrS patients, when SP filter was enabled, vector failure rate decreased non-significantly from 40% to 36%.

Screening failure rate over all test phases of the primary and alternate vectors was comparable between Brugada and non-Brugada cases, whereas the secondary vector failed more frequently in BrS patients if compared with non-Brugada subjects (40% vs. 14%, *P* < 0.01).

Multivariable logistic models

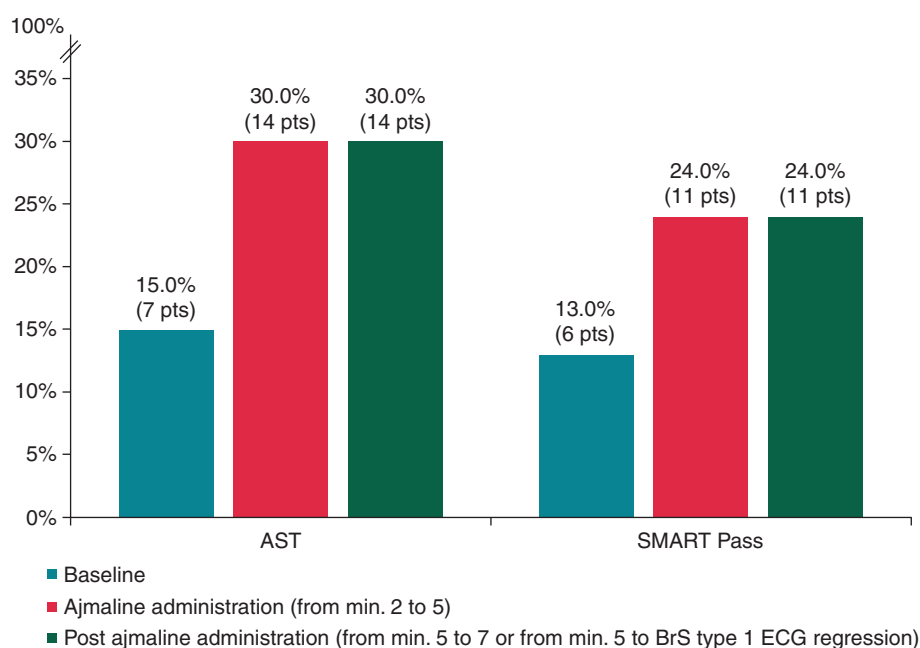
The proportion of vectors failing the screening is summarized in Table 2, upper part. They were of similar magnitude for the two simulation models (AST without and with SP) and by ajmaline challenge results. The failure rate estimated from the multivariable logistic model is shown in Figure 3. Failure rates changed similarly in all four combinations of simulation model and drug test result; indeed, there was no difference over the test phases neither depending on the use of SP filter nor on the ajmaline challenge result (3-way interaction *P* = 0.251); similarly, 2-way interactions (test phase and SP use, test phase and drug test result, SP and drug test result) did not reach statistical significance (*P* = 0.052, *P* = 0.162, *P* = 0.737, respectively). Analysis excluding vectors failing baseline screening showed similar results (*P* = 0.111, *P* = 0.199, *P* = 0.197, respectively).

A similar behaviour regarding failure rates was elicited at patient level (Table 2, lower part).

A multivariable analysis showed that the screen-out rate was independent from both SP filter application and drug test result (3-way interaction *P* = 0.317), as shown in Figure 3. None of the 2-way interactions (test phase and SP use, test phase and drug test result, SP

Table 2 Proportions of screening failures at the vector and patient level during different ajmaline challenge phases using the Automated Screening Tool with and without SMART Pass (SP) filter.

	N	Automated screening tool (SP disabled)			Automated screening tool (SP enabled)		
		All N (%)	Negative ajmaline N (%)	Positive ajmaline N (%)	All N (%)	Negative ajmaline N (%)	Positive ajmaline N (%)
Vector							
Baseline	1800	463 (26)	267 (23)	196 (30)	411 (23)	234 (20)	177 (27)
Ajmaline administration	3036	867 (29)	482 (24)	385 (38)	775 (25)	427 (21)	348 (35)
Post-ajmaline administration	1950	623 (32)	283 (26)	340 (40)	529 (27)	221 (20)	308 (36)
Patient							
Baseline	126	13 (10)	6 (7)	7 (15)	9 (7)	3 (4)	6 (13)
Ajmaline administration	126	19 (15)	10 (12)	9 (20)	16 (13)	8 (10)	8 (18)
Post-ajmaline administration	126	14 (11)	5 (6)	9 (20)	10 (8)	4 (5)	6 (13)

**Figure 2** Subcutaneous implantable cardioverter-defibrillator screening failure rates before and after ajmaline challenge in patients with BrS (N = 46). BrS, Brugada syndrome.

and drug test result) were significant ($P = 0.521$, $P = 0.397$, $P = 0.294$, respectively). Analysis excluding patients failing baseline screening showed similar results ($P = 0.324$, $P = 0.144$, $P = 0.935$, respectively). No substantial differences were seen from the initial model with no interaction becoming significant when considering a patient suitable for S-ICD in the presence of at least two sensing vector acceptable in all tested posture (Supplementary material online, Figure S1).

Vectors screening failure causes

The most common cause for screening failure was low QRS amplitude (<0.5 mV), followed by a QRS/T-wave ratio <3.5 , as shown in Figure 4. These failure criteria were equally present in both patient

groups although more prominently in patients with drug-induced BrS type 1 ECG. Figure 5 shows different AST outcomes (FAIL/PASS) depending on if signal was SP filtered (SP disabled/enabled) in two patients with ajmaline-induced Brugada type 1 ECG (PASS, panel A; FAIL: panel B).

Right parasternal electrode position analysis

In 26 patients, screening was additionally performed with the lead placed in right parasternal position. Of them, six patients (483 vectors) tested positive for BrS. In these patients, vectors' failure rate was comparable between left parasternal and right parasternal

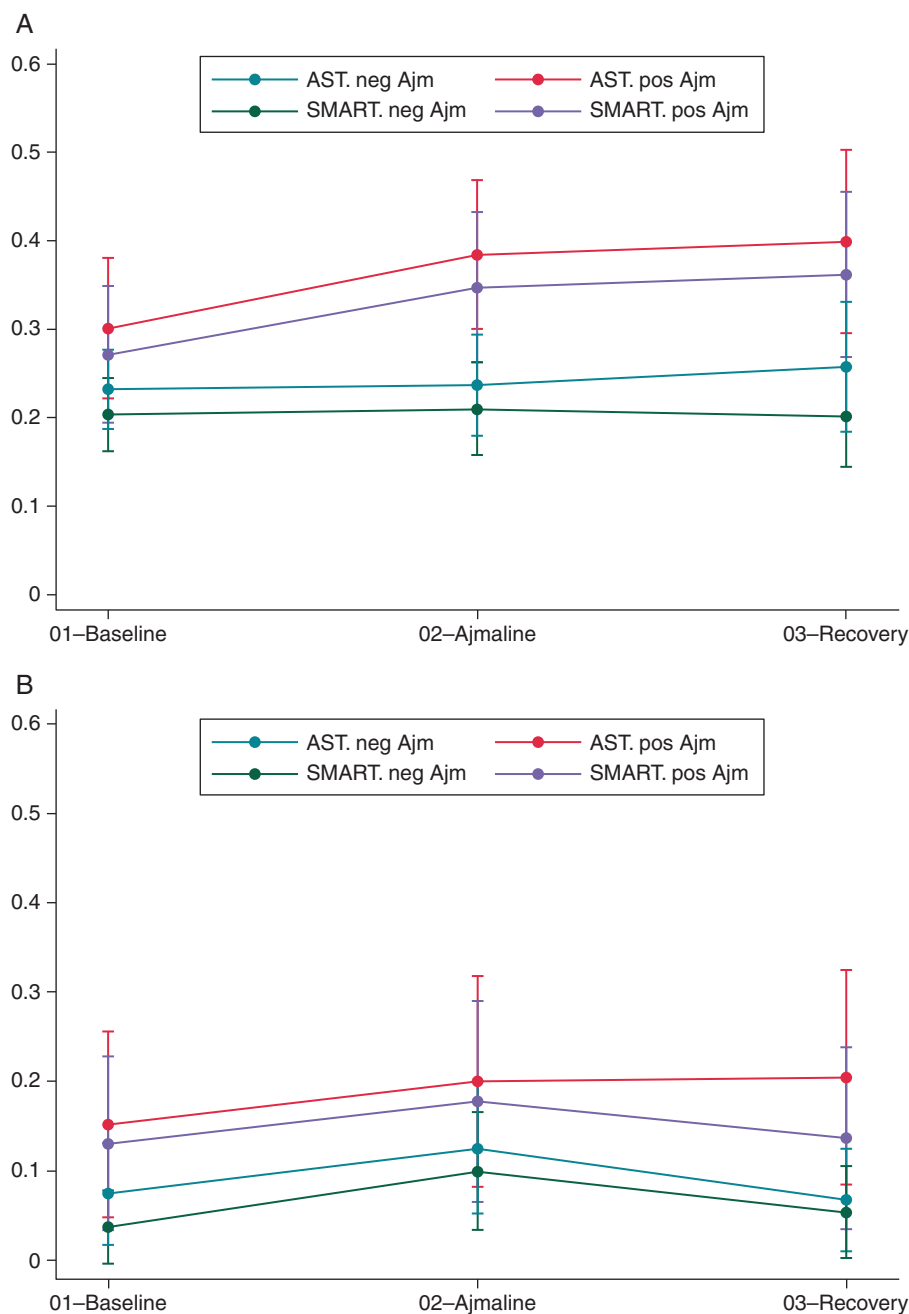


Figure 3 Proportion of failure from logistic multivariable model (panel A: vector level; panel B: patient level).

position (24% vs. 21%; $P = 0.45$). The vectors' screen-out rate in the two positions remained unchanged with SP filter (21% vs. 22%, $P = 0.82$).

Discussion

To the best of our knowledge, this is the first study assessing the impact of the SP filter in patients with drug-induced BrS. Our results

indicate that a sizable proportion of patients with a confirmed BrS type 1 ECG would not qualify for an S-ICD due to low amplitude of the QRS complex or low QRS/T-wave ratio. The proportion of BrS patients and vectors ineligible for S-ICD was not significantly reduced by the SP filter. Moreover, the position of parasternal subcutaneous lead did not influence the screen-out rate of BrS patients nor the number of usable sensing vectors. These study results are novel, and considerably expand our current knowledge on the use of S-ICD in a large group of patients with inherited primary arrhythmia syndrome.

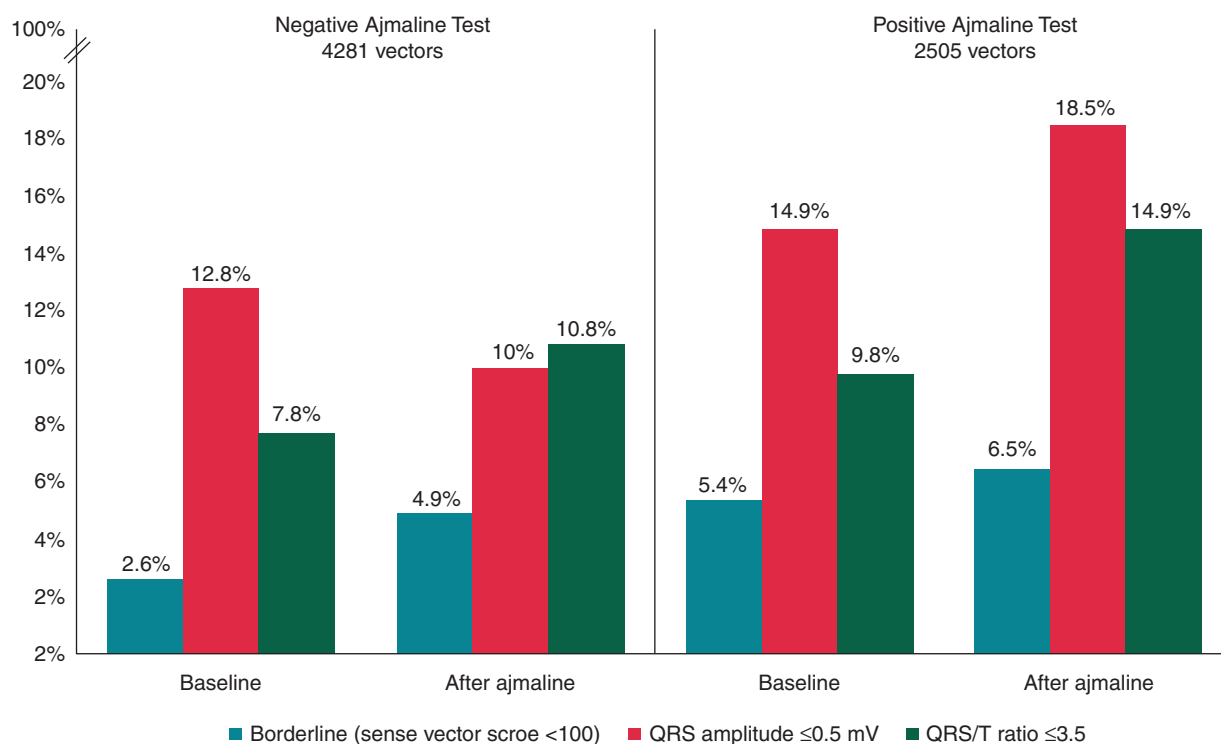


Figure 4 Causes of vector screening failure (without SP filter). SP, SMART Pass.

Subcutaneous implantable cardioverter-defibrillator eligibility of Brugada syndrome patients

An S-ICD screening test is recommended before S-ICD implantation to evaluate appropriate sensing though not predicting S-ICD efficacy. The S-ICD eligibility is examined using a screening test based on the ECG, namely the AST using the manufacturer's programmer. The S-ICD eligibility in patients with inherited primary arrhythmia syndrome is usually as high as 95% in patients with idiopathic ventricular fibrillation, early repolarization syndrome or long-QT syndrome; in contrast, in patients with BrS, the S-ICD eligibility is about 82%. Our data confirm the findings by Olde Nordkamp *et al.*¹⁶ and Conte *et al.*¹⁴ but in a much larger patient cohort and assessed in a prospective, multi-centre study.

We found that the vast majority (about 90%) of patients with a suspected BrS could be considered eligible for an S-ICD when their resting ECGs do not show a typical type 1 BrS ECG pattern. Differently from all previous studies conducted in BrS patients, we performed an offline analysis by processing the ECG thus, mimicking the SP filter, a 9 Hz high-pass filter integrated in the device, which markedly reduces T-wave amplitude. Somehow surprising was the fact that the SP filter did not change significantly the proportion of BrS patients' eligibility which remained as high as 85% at resting condition. When a type-1 BrS ECG was evident, the S-ICD eligibility markedly reduced to 70%, thus confirming previous reports.^{16,18} This proportion did not statistically change and remained 76% even after the use of the SP filter. Our findings, in the largest population of BrS

patients so far tested for S-ICD, suggest a potentially important role for ajmaline challenge during the pre-implantation screening process of BrS patients. Of note, ajmaline administration may suggest what could occur in the ECG spontaneously, but the clinically relevant 'predictability' of ajmaline challenge to what actually could happen in a patient has not been shown. Furthermore, our results highlight the clinical unmet need to further improve the sensing algorithms specific for a sizable group of young patients who are ideal candidates for S-ICD therapy.

The risk of inappropriate shocks by subcutaneous implantable cardioverter-defibrillator

The clinical advantage of the S-ICD over the TV-ICD is partially offset by the higher frequency of IAS, most frequently due to TWOS.¹⁹ The recent prospective, randomized comparison of subcutaneous with TV-ICD therapy (PRAETORIAN) trial reported a 9.7% IAS rate.² The cause of the IAS was cardiac oversensing (predominantly T waves) in 60% of S-ICD patients. In the PRAETORIAN study, the SP sensing filter was either not available or not activated in about 80% of patients.² Unlike PRAETORIAN, the understanding outcomes with the S-ICD in primary prevention patients with low ejection fraction (UNTOUCHED) trial reported a 4.1% rate of IAS at 18 months follow-up. The most common cause of IAS was TWOS which was present in 1.6% of patients.³ The large difference in the proportion of IAS was most likely due to use of contemporary S-ICD programming

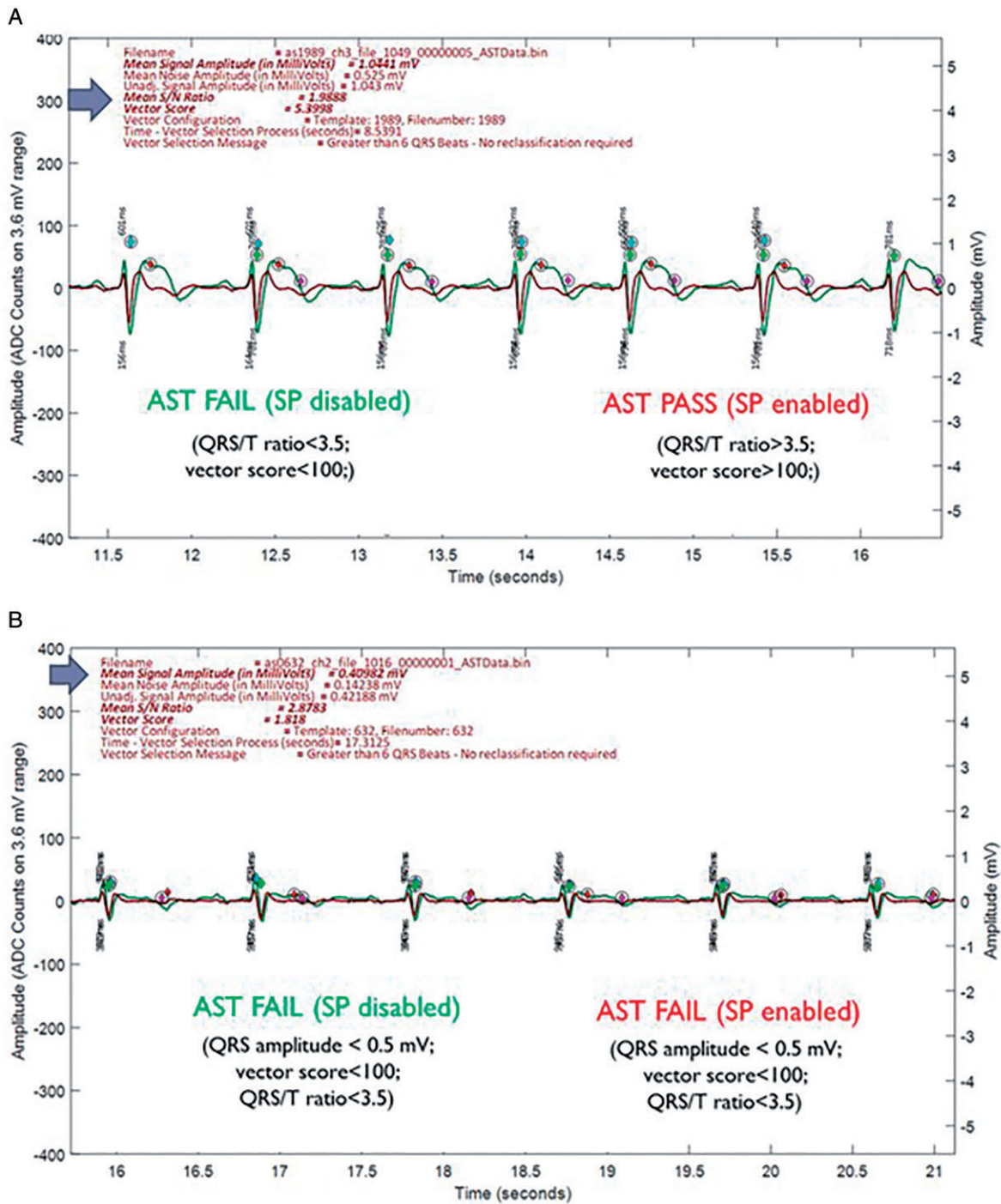


Figure 5 Different Automated Screening Tool outcomes depending on if signal was SP filtered (red) in two patients with ajmaline-induced Brugada type 1 ECG (PASS, panel A; FAIL: panel B). The blue/green dots are associated to R wave peaks while red/pink dots relate to T-wave peaks and are used by the simulation model to compute QRS amplitudes and R–T ratio. The dots are associated with the absolute values of the peaks. ECG, electrocardiogram; SP, SMART Pass.

(discrimination algorithms active from 200–250 b.p.m.), and the systematic use of the SP sensing filter.³

Patients with S-ICD and inherited primary arrhythmia syndrome represent only a minority of patients (4.7%) included in the

PRAETORIAN and none of the UNTOUCHED trial.^{2,3} Therefore, most of the available data about IAS in S-ICD patients and inherited primary arrhythmia syndromes are coming from small, non-randomized controlled study cohorts. In a pooled analysis of the

EFFORTLESS and IDE study, 10% of study population was represented by patients with inherited primary arrhythmia syndromes; the estimated 3-year IAS rate was 13%.²⁰ A similar IAS rate (13%) was reported by a Dutch cohort with a higher proportion (23%) of patients with inherited primary arrhythmia syndromes,²¹ as well as by Casu *et al.* who reported an IAS rate of 14% in a cohort of BrS patients.⁹ Finally, a sub-analysis of EFFORTLESS S-ICD study by Lambiase *et al.*,²² including 83 patients with BrS, reported an IAS rate of 8.5% in S-ICD patients with inherited primary arrhythmia syndromes, which was similar to the IAS rate (12.5%) of patients with other cardiac pathologies. Collectively, these studies indicate a relatively higher proportion of IAS in patients with BrS treated with an S-ICD, but these data represent populations before SP was available. Recently, Rudic *et al.*²³ reported low prevalence (3%) of IAS in a single-centre study including 62 S-ICD patients with inherited primary arrhythmia syndromes.

The TWOS in S-ICD occurs more frequently in S-ICD than TV-ICD because S-ICD sensing algorithm is based on fixed bipolar electrogram (vector) recorded on body surface thus may show a P wave, a QRS complex, and a T wave. Although the S-ICD has up to three different sensing vectors (the primary, secondary, and alternate sensing vector), only one of them is used for sensing; once a vector is selected, it cannot be automatically changed by the device but only during device interrogation with the programmer. Therefore, the S-ICD sensing algorithm is particularly sensitive to dynamic variation in R-wave and/or T-wave amplitude on a given vector. The SP sensing filter significantly reduces the T-wave amplitude and its clinical use markedly reduces the frequency of IAS. Recently, a prospective blinded evaluation of the SP sensing filter has demonstrated that enabling the SP sensing filter reduces one-year IAS by 50% in the real-world population.²⁴ However, no specific information on the rate of BrS patients was reported in this study. Processing of the signals performed in this study attempts to simulate an implanted S-ICD system thus, to unmask potential dynamic (drug-induced) S-ICD sensing failure in BrS patients, especially during changes in R- and T-wave amplitude induced by ajmaline. Our data on the reduction of the individual vector screening failures during ajmaline, especially in those patients who presented a type 1 BrS ECG pattern, strongly support the beneficial use of the SP sensing filter in these patients, and let us anticipate a reduction in the number of IAS due to TWOS during spontaneous ST-T change in this challenging group of patients. The possibility of ECG templating during ajmaline-induced Brugada type 1 ECG and dynamic vector change in case of failure would be of great value and could increase in the future the number of BrS patients suitable for an S-ICD.

Implant position and QRS/T-wave signal analysis

In selected patients, a right parasternal lead position may provide a useful alternative appropriate S-ICD sensing configuration.²⁵ In our study, placement of right parasternal S-ICD leads in BrS patients did not significantly affect the vectors screen-out rate (21% right parasternal vs. 22% left parasternal). No data on modified S-ICD lead placement have been reported in BrS patients so far. Okamura *et al.*²⁶ evaluated right-sided electrode placement for T-wave sensing in patients with congenital heart disease. Use of bilateral parasternal

ECG screening in these patients reduced the S-ICD eligibility failure rate from 21% to 12%.

Limitations

Our study has a certain number of limitations. First, it is a study conducted in a relatively small number of patients, most of them without any indication to ICD therapy. Specific information on S-ICD IAS is not available in our study population, since none of the enrolled patients was implanted with an S-ICD. Therefore, no conclusion can be made on the potential IAS risk of these patients. To avoid any side effect or pro-arrhythmic event and ensure patient's safety, screening was not repeated at sitting position during the ajmaline peak. Moreover, the study included patients with drug-induced type 1 BrS ECGs. The relationship between ajmaline-induced ECG changes and ECG changes that occur spontaneously in BrS patients receiving an S-ICD has not been yet established.

Conclusions

One of the five patients with BrS fails S-ICD screening during the appearance of Brugada type 1 ECG evoked by ajmaline. The BrS patients who pass the sensing screening during ajmaline challenge can be considered good candidates for S-ICD implantation, while patients who fail might be exposed to sensing issues. Although there was a trend towards reduction of vector sensing failure rate when SP filter was enabled, the reduction in S-ICD screening failure in BrS patients attributable to the SP filter did not reach statistical significance. Further refinement of the sensing algorithm is warranted to increase the number of BrS patients eligible for S-ICD.

Supplementary material

Supplementary material is available at *Europace* online.

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Data availability

The data will be shared on reasonable request to the corresponding author.

References

- Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J et al. ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: the task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the Europe. *Europace* 2015;**17**:1601–87.
- Knops RE, Olde Nordkamp LRA, Delnoy PHM, Boersma LVA, Kuschyk J, El-Chami MF, et al.; PRAETORIAN Investigators. Subcutaneous or transvenous defibrillator therapy. *N Engl J Med* 2020;**383**:526–36.
- Gold MR, Lambiase PD, El-Chami MF, Knops RE, Aasbo JD, Bongiorni MG et al. Primary results from the understanding outcomes with the S-ICD in primary prevention patients with low ejection fraction (UNTOUCHED) trial. *Circulation* 2020;**143**:7–17.
- Conte G, Sieira J, Ciconte G, de Asmundis C, Chierchia GB, Baltogiannis G et al. Implantable cardioverter-defibrillator therapy in Brugada syndrome: a 20-year single-center experience. *J Am Coll Cardiol* 2015;**65**:879–88.
- Sacher F, Probst V, Maury P, Babuty D, Mansourati J, Komatsu Y et al. Outcome after implantation of a cardioverter-defibrillator in patients with Brugada syndrome: a multicenter study-part 2. *Circulation* 2013;**128**:1739–47.
- Auricchio A, Hudnall JH, Schloss EJ, Sterns LD, Kurita T, Meijer A et al. Inappropriate shocks in single-chamber and subcutaneous implantable cardioverter-defibrillators: a systematic review and meta-analysis. *Europace* 2017;**19**:1973–80.
- Rordorf R, Casula M, Pezza L, Fortuni F, Sanzo A, Savastano S et al. Subcutaneous versus transvenous implantable defibrillator: an updated meta-analysis. *Heart Rhythm* 2021;**18**:382–91.
- Burke MC, Gold MR, Knight BP, Barr CS, Theuns DAMJ, Boersma LVA et al. Safety and efficacy of the totally subcutaneous implantable defibrillator: 2-year results from a pooled analysis of the IDE study and EFFORTLESS Registry. *J Am Coll Cardiol* 2015;**65**:1605–15.
- Casu G, Silva E, Bisbal F, Viola G, Merella P, Lorenzoni G et al. Predictors of inappropriate shock in Brugada syndrome patients with a subcutaneous implantable cardiac defibrillator. *J Cardiovasc Electrophysiol* 2021;**32**:1704–11.
- Brisben AJ, Burke MC, Knight BP, Hahn SJ, Herrmann KL, Allavatam V et al. A new algorithm to reduce inappropriate therapy in the S-ICD system. *J Cardiovasc Electrophysiol* 2015;**26**:417–23.
- EMBLEM S-ICD, EMBLEM MRI S-ICD User's Manual. Boston Scientific Corporation: MN, USA, 2015.
- Zeb M, Curzen N, Allavatam V, Wilson D, Yue A, Roberts P et al. Sensitivity and specificity of the subcutaneous implantable cardioverter defibrillator pre-implant screening tool. *Int J Cardiol* 2015;**195**:205–9.
- Sakhi R, Yap SC, Michels M, Schinkel AFL, Kauling RM, Roos-Hesselink JW et al. Evaluation of a novel automatic screening tool for determining eligibility for a subcutaneous implantable cardioverter-defibrillator. *Int J Cardiol* 2018;**272**: 97–101.
- Conte G, Kawabata M, de Asmundis C, Taravelli E, Petracca F, Ruggiero D et al. High rate of subcutaneous implantable cardioverter-defibrillator sensing screening failure in patients with Brugada syndrome: a comparison with other inherited primary arrhythmia syndromes. *Europace* 2018;**20**:1188–93.
- Conte G, Regoli F, Moccetti T, Auricchio A. Subcutaneous implantable cardioverter-defibrillator and drug-induced Brugada syndrome: the importance of repeat morphology analysis during ajmaline challenge. *Eur Heart J* 2016;**37**: 1498.
- Olde Nordkamp LRA, Conte G, Rosenmöller BRAM, Warnars JLF, Tan HL, Caputo ML et al. Brugada syndrome and the subcutaneous implantable cardioverter-defibrillator. *J Am Coll Cardiol* 2016;**68**:665–6.
- Özkartal T, Auricchio A, Conte G. Ajmaline infusion during automated screening in Brugada syndrome and spontaneous Type 1 electrocardiogram unmasks non-suitability for subcutaneous implantable cardioverter-defibrillator. *Eur Heart J* 2019;**40**:1888–9.
- Brugada P. The variability of the electrocardiogram in Brugada syndrome: implications for subcutaneous implantable cardioverter-defibrillator candidacy. *Rev Port Cardiol* 2020;**40**:39–40.
- Olde Nordkamp LR, Brouwer TF, Barr C, Theuns DA, Boersma LV, Johansen JB et al. Inappropriate shocks in the subcutaneous ICD: incidence, predictors and management. *Int J Cardiol* 2015;**195**:126–33.
- Burke MC, Gold MR, Knight BP, Barr CS, Theuns DAMJ, Boersma LVA et al. Safety and efficacy of the totally subcutaneous implantable defibrillator: 2-year results from a pooled analysis of the IDE study and EFFORTLESS Registry. *J Am Coll Cardiol* 2015;**65**:1605–15.
- Olde Nordkamp LR, Dabiri Abkenari L, Boersma LV, Maass AH, de Groot JR, van Oostrom AJ et al. The entirely subcutaneous implantable cardioverter-defibrillator: initial clinical experience in a large Dutch cohort. *J Am Coll Cardiol* 2012;**60**:1933–9.
- Lambiase P, Eckardt L, Theuns DA, Betts TR, Kyriacou AL, Duffy E et al. Evaluation of subcutaneous implantable cardioverter-defibrillator performance in patients with ion channelopathies from the EFFORTLESS cohort and comparison with a meta-analysis of transvenous ICD outcomes. *Heart Rhythm* 2020;**1**: 326–35.
- Rudic B, Tülümen E, Berlin V, Röger S, Stach K, Liebe V et al. Low prevalence of inappropriate shocks in patients with inherited arrhythmia syndromes with the subcutaneous implantable defibrillator single center experience and long-term follow-up. *J Am Heart Assoc* 2017;**6**:e006265.
- Theuns DAMJ, Brouwer TF, Jones PW, Allavatam V, Donnelley S, Auricchio A et al. Prospective blinded evaluation of a novel sensing methodology designed to reduce inappropriate shocks by the subcutaneous implantable cardioverter-defibrillator. *Heart Rhythm* 2018;**15**:1515–22.
- Wilson DG, Zeb M, Veldtman G, Dimitrov BD, Morgan JM. Left and right parasternal sensing for the S-ICD in adult congenital heart disease patients and normal controls. *Pacing Clin Electrophysiol* 2016;**39**:282–90.
- Okamura H, McLeod CJ, DeSimone CV, Webster TL, Bonnicksen CR, Grogan M et al. Right parasternal lead placement increases eligibility for subcutaneous implantable cardioverter defibrillator therapy in adults with congenital heart disease. *Circ J* 2016;**80**:1328–35.