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Original Article

Early ganglion stellate blockade as part of two-step treatment algorithm suppresses electrical storm and need for intubation

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ABSTRACT

Background: For the treatment of patients with electrical storm (ES), we established a two-step algorithm comprising standard anti-arrhythmic measures and early ultrasound-guided stellate ganglion blockade (SGB). In this single-center study, we evaluated the short-term efficacy of the algorithm and tested the hypothesis that early SGB might prevent the need for intubations.
Methods: Overall, we analyzed data for 70 ES events in 59 patients requiring SGB (mean age 67.7 ± 12.4 years, 80% males, left ventricular ejection fraction 30.0% ± 9.1%), all with implantable cardioverter-defibrillators (ICDs).
Results: The mean time from ES onset to SGB was 13.2 ± 12.3 hours. Percentage and mean absolute reduction in shocks at 48 hours after SGB reached 86.8% (−6.3 shocks), and anti-tachycardiac pacing (ATP) declined by 65.9% (−51.1 ATPs; all $P < 0.001$). Patients with the highest sustained ventricular arrhythmia (VA) burden (shocks ≥10/48 h; ATPs 10–99/48 h and ≥100/48 h) experienced the highest percentage decrease in ICD therapy (shocks −99.1%; ATPs −92.1% and −100.0%, respectively). For clinical response by defined criteria and two outcome periods (1/no sustained VA ≤48 hours post SGB, and 2/no ICD shock or <3 ATPs/day from day 3 to discharge/catheter ablation/day 8), 75.7% and 76.1% experienced complete response, respectively. Catecholamine support, no/low-dose β-blocker therapy, polymorphic/mixed-type VA, and baseline sinus rhythm versus atrial fibrillation were more frequent in patients with early arrhythmia recurrence. Temporary Horner's syndrome occurred in 67.1%, and no other adverse events were recorded. Intubation and general anesthesia during and after SGB were not needed.
Conclusion: The presented two-step algorithm for treating ES proved efficacious and safe. The results support implementation of early SGB in routine ES management.

1. Introduction

In patients with implantable cardioverter-defibrillator (ICD), electrical storm (ES) is defined as the occurrence of ≥3 attacks of sustained ventricular tachycardia (VT) or ventricular fibrillation (VF) adequately detected and treated by shocks or anti-tachycardiac pacing (ATP) within 24 hours, with each event separated by at least 5 minutes. The annual incidence of ES ranges from 2% to 10%.[1] ES has been associated with a mortality rate of up to 14% within the first 48 hours and a 5.6- to 18-fold increase in mortality

Abbreviations: ATP, Anti-tachycardiac pacing; ES, Electrical storm; ICD, Implanted cardioverter-defibrillator; LVEF, Left ventricular ejection fraction; SGB, Stellate ganglion blockade; VA, Ventricular arrhythmia; VF, Ventricular fibrillation; VT, Ventricular tachycardia.

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risk within 3 months, depending on ICD indication and study population.[2-4] More than 50% of ES recurrences take place within two years,[5] and repeated ICD shocks associated with myocardial injury, inflammation, and fibrosis facilitate the progression of heart failure and increase morbidity and mortality.[6,7] Management is challenging and requires several strategies based on currently recognized pathophysiological mechanisms of ES. Approaches include trigger suppression (electrolyte disturbances, acute ischemia, bradycardia, drug-induced long QT, alcohol abuse, medical nonadherence, inappropriate ICD therapy), substrate modification (scar and tissue abnormalities, low ventricular function, valvular disease), and dysregulated autonomic nervous system modulation (enhanced sympathetic tone, signaling abnormalities).[8] Several algorithms have been proposed that include antiarrhythmic drugs (amiodarone, sotalol, β-blockers, procainamide, lidocaine), ICD reprogramming, sedation, and early catheter ablation.[5,9]

Recently, a decrease in enhanced sympathetic tone using neuraxial modulation techniques (thoracic epidural anesthesia, stellate ganglion blockade [SGB], surgical sympathectomy, or renal sympathetic denervation) is key in the acute management of ES.[8] Among these modalities, only SGB can be performed by a trained physician at the bedside within a few minutes, repeatedly, unilaterally (preferably left-sided), or bilaterally (if needed), and with significant short-term clinical effects.[10-13] Several ES management algorithms that include SGB have been proposed,[14,15] but the appropriate timing of SGB (early, rescue, before or after deep sedation or intubation) has not been studied. Of note, in a meta-analysis, Meng et al. found that ES management is associated with intubation and deep sedation in 37% of patients,[12] a worrisome finding because intubation and general anesthesia are associated with high in-hospital and 30-day mortality in critically ill patients, mainly because of cardiovascular complications.[16] For these reasons, investigations are needed into ways to prevent unnecessary intubation.

To our knowledge, no available data indicate when prolonged hospitalization or advanced post-procedure monitoring is required beyond 24–72 hours. This time interval has been used in several published series to differentiate between patients who do and do not experience a response to the therapy.[10,11,13] An open question is whether to continue monitoring and hospitalization in all patients or only those who experience no response until catheter ablation is required. Another open question is whether patients with high versus low shock/ATP burden experience similar responses to SGB therapy.

To address these questions, we evaluated the short-term efficacy of an adjusted, two-step algorithm, including ultrasound-guided SGB, to terminate ES and eliminate the need for ICD therapy. Our further objectives were to identify clinical parameters associated with better response to treatment, compare therapeutic efficacy between patients with high and low shock/ATP burden, and test the hypothesis that early SGB may prevent intubations in this patient population.

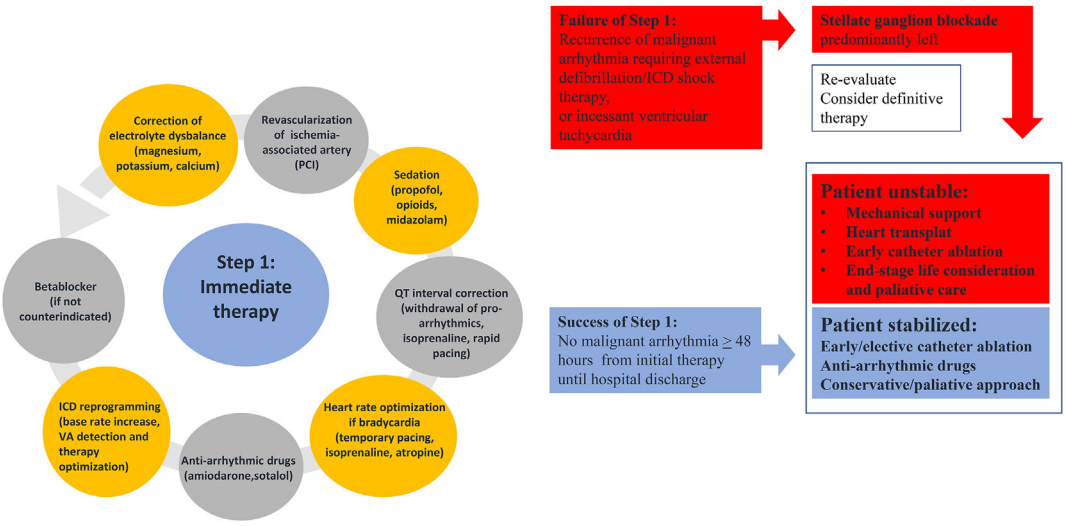
2. Methods

2.1. Treatment algorithm for ES

In 2017, an ES institutional protocol was established based on current knowledge.[1,17-19] Because thoracic epidural anesthesia and surgical cervical sympathectomy are not immediately available for our patients, a decision was made to incorporate early SGB into the treatment algorithm (Fig. 1). In each patient with ES referred to our institution, relevant cardiovascular history, medical records, electrocardiogram, and ICD interrogation for arrhythmia characteristics are obtained. The arrhythmic event is then re-classified (inappropriate therapy, phantom therapy) or confirmed as ES, and in the latter case, the on-duty arrhythmologist is consulted, and step 1 of the algorithm is initiated. This step consists of all measures and actions to clarify the cause of arrhythmia, rapidly eliminate potential triggers, and stabilize the patient. Decisions are based on mutual agreement among the attending arrhythmologist, heart failure specialist, and anesthesiologist, depending on the patient's condition. The corrective measures include immediate sedation of the patient with intravenous morphine ± midazolam to enhance the effect of opiate or dexmedetomidine if preferred by an attending physician. An arrhythmologist interrogates the implantable ICD and performs necessary inputs—in slower VT than the detection zone he/she adjusts VT zone setting or increases base rate to suppress frequent early ventricular extrasystoles (algorithm of standard ICD programming is based on guidelines[20] and shown in Supplemental Table 1). Then, intravenous substitution of kalium and magnesium up to upper-normal or supra-normal values, long-QT interval shortening by isoprenaline infusion or by increasing heart rate on implantable pacemaker/ICD or by inserting a temporary stimulation in non-device carriers follow. Intermittent overdrive stimulation may also be used to suppress frequent ventricular extrasystoles that could trigger sustained VT. If not clinically contraindicated, intravenous amiodarone is introduced at a dose of 900–1200 mg/day, and β-blocker up-titration ± intravenous bolus application of metoprolol tartrate/landiolol is initiated. The type of β-blocker used in chronic therapy is rarely replaced with another β-blocker, i.e., non-selective propranolol-type β-blocker promising a higher rate of responsiveness,[21] as this is not available in the Czech Republic. The patients with a clinical suspicion of ischemic trigger (positive troponin dynamics, new electrocardiogram changes, left ventricular ejection fraction decrease, and known previous coronary artery disease without recent coronarography <3 months) undergo acute catheterization. In case of step 1 failure, defined as recurrence of malignant ventricular arrhythmia (VA) requiring external defibrillation/ICD shock or incessant VT, the patient undergoes ultrasound-guided SGB (step 2) with a minimum of 48 hours of post-procedural electrocardiogram monitoring. Relevant interventions in step 1 continue simultaneously until clinical stabilization and/or definitive therapy, i.e., ICD implantation in non-carriers (not relevant in this case as all study subjects were ICD carriers), catheter ablation, or up-titration of β-blocker or anti-arrhythmic drugs. In hemodynamically compromised non-responders, extracorporeal membrane oxygenation is initiated as a bridge therapy to the final treatment (left ventricular assist device, heart transplantation) or myocardial recovery. A palliative approach and end-of-life considerations can also be considered in patients with end-stage heart failure. Nevertheless, in all cases, the indication for early catheter ablation, a conservative approach, other interventions, and related timing of the patient's discharge is clinically driven and left to the discretion of the attending team of specialists.

2.2. Patient cohort

This study included all consecutive patients with implantable ICD who presented with ES and underwent SGB from January 2017 to November 2021. Their relevant medical data were prospectively recorded in our database. In some patients, ES recurred within months or years. Because the clinical effect of SGB lasts for several days but is unlikely to last for weeks, we included patients as new independent SGB cases if the interval between two separate ES events was >30 days.[12,22] All patients signed an informed consent for the SGB procedure.



ICD – implanted cardioverter defibrillator; PCI – percutaneous coronary intervention; VA – ventricular arrhythmia

Figure 1. A two-step algorithm for treating ES.

2.3. Ultrasound-guided SGB

All SGB procedures were performed by a trained electrophysiologist or specialist in acute cardiology experienced in ultrasound-guided punctures of vascular bundles, pericardium, or pleura, with the anesthesiologist available on-call. The technique has been described in detail previously.[23] Briefly, with the patient in the supine position and the head aiming at the contralateral shoulder, the operator used a linear ultrasound probe to detect landmark structures, including the internal jugular vein, internal carotid artery, longus colli muscle, and transverse protrusion of the C6 vertebra, typically recognized for its pointed shape (Chassaignac tubercle). The probe was then moved a little caudally to reach the C7 vertebra, with its flattened transverse protrusion. Next, under sterile conditions and real-time ultrasound guidance, a 21G puncture needle was introduced along the longitudinal axis of the probe to reach the ganglion, and 7 mL of 0.5% bupivacaine was injected. Then, the needle was withdrawn and the puncture site was covered with a sterile tampon. The patient then rested for 2 hours in a semi-sitting position to allow for gravitational distribution of the anesthetic along the sympathetic tract, with no food intake allowed in this period.

During the study, left-sided SGB was preferred over right-sided or bilateral SGB. The choice of puncture site was left to the operator's discretion, depending on patient status and inferred VA cause. In patients with ischemia-induced VA, blockade of both or only the right stellate ganglion could have been considered and performed. Such a decision was supported by previous findings that indicated the involvement of both stellate ganglia in afferent cardiac signaling.[24,25]

2.4. Definition and assessment of endpoints

The primary study endpoints were absolute and relative reduction in ICD therapy (shock/ATP) to treat sustained VA in the first 48 hours after SGB related to the number of shocks/ATPs within the last 48 hours before the SGB procedure. Secondary study endpoints included the ability to suppress VA until definitive therapy or safe discharge from the hospital. The need for intubation was assessed during the whole period of ES management.

Clinical outcome also was evaluated in two post-SGB periods. The first period encompassed the 48 hours after the procedure (i.e., ≤48 hours). A response was defined as experiencing no ICD shocks or ATPs (i.e., no sustained VA) during these first 48 hours, and cases not meeting this criterion were considered non-responders, including those with repeat SGB within 48 hours. We took this approach to determine the number of acute complete responders who might be considered stabilized and excluded from further monitoring after the 48-hour arrhythmia-free observational period yet experience shock recurrence after 48 hours post-procedure. The second period (i.e., >48 hours) was defined as beginning from day 3 to discharge/catheter ablation/day 8 (whichever came first) to identify patients not fulfilling the criteria of ongoing ES after 48 hours post SGB (with possible VA recurrences within the first 48 hours). Cases were defined as responders if there was no further ICD shock or <3 ATPs/day; otherwise, they were defined as non-responders, including those with repeat SGB until day 8. We applied this approach to investigate the number and characteristics of patients who could be safely excluded from extended monitoring beyond 48 hours.

Relevant clinical parameters were compared between the responder and non-responder cases for each outcome period to identify factors significantly associated with acute treatment success and further VA recurrence.

2.5. Safety analysis

Safety endpoints included the occurrence of ipsilateral Horner's syndrome (partial ptosis, miosis, facial anhidrosis, and apparent enophthalmos). We also included other possible SGB periprocedural complications such as blood aspiration, intra-arterial injection, vocal cord paresis, phrenic nerve palsy, dysphagia, pneumothorax, puncture site infection, and hematomas.

2.6. Statistical analysis

Patient characteristics were described using standard descriptive statistics (mean, standard deviation, median, 25% and 75% quartiles [interquartile range {IQR} Q1; Q3], minimum and maximum). Categorical parameters were described using absolute

and relative frequencies. The changes in the absolute and relative number of ICD shocks and ATPs 48 hours before and after the SGB procedure were calculated for individual ES cases and then for each case group, expressed as mean and median values, as follows: 1/ Absolute change = number of therapies before—number of therapies after the SGB; and 2/Relative change = 100% - (number of therapies after/number of therapies before the SGB * 100%). The results were evaluated using the Wilcoxon signed-rank test for continuous parameters, and the Chi-square or Fisher's exact test for categorical parameters. Wilcoxon rank sum test for continuous parameters was used to compare values between subgroups of responders and non-responders. All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA) at the 5% level of significance ($\alpha = 0.05$). Graphical visualizations were performed using Excel and PowerPoint (Microsoft Corporation, Redmond, WA, USA), except for the Sankey chart of β-blocker distribution that was generated using a free version of the software available on www.sankeymatic.com. Because of the study design, the tests were performed for exploratory and not confirmatory purposes.

The study was approved by the Ethics Committee of Agel Trinec-Podlesi Hospital and was conducted in accordance with the provisions of the Declaration of Helsinki. All patients signed informed consent to participate in the registry.

3. Results

3.1. Patient characteristics

From January 2017 to November 2021, a total of 87 SGB procedures were performed. To avoid potential interference and bias in the assessment of SGB clinical efficacy, 15 SGB procedures within the previous 30 days and an additional 2 SGB procedures followed by early catheter ablation in <48 hours were excluded (Fig. 2). Thus, 70 SGB procedures performed in 59 patients (80% male, mean age 67.7 years) were included in the study (Table 1). The median left ventricular ejection fraction (LVEF) was 28.5% (15%–60%), and 34.3% of patients had atrial fibrillation as the basal rhythm. Ischemic heart disease was the arrhythmia etiology in 60%, 72.9% of ES events were caused by monomorphic VT, and 68.6% of patients experienced combined ICD therapy (both ATPs and shocks) to treat ES. Extracorporeal membrane oxygenation was applied in 3 (4%) cases.

3.2. SGB

The index SGB procedures were performed within 13.2 ± 12.3 hours of ES onset. Left-sided SGB was performed in 65 (93%), right-sided SGB in 1 (1%), and bilateral SGB in 4 (6%) patients. A second SGB was required in 8 (11.4%) cases at an average of 1.8 ± 1 days since the first procedure.

3.3. Clinical outcomes

No patients required intubation or general anesthesia as part of ES management. Catheter ablation as a definitive therapy was employed during the index hospitalization after 7 ± 5 (2–22) days since the SGB procedure in 22 (31%) cases. In addition, seven catheter ablation procedures were performed after discharge within 60 days of the SGB. In-hospital mortality was 8.8%, with three deaths from cardiovascular causes and three from non-cardiovascular causes. Overall 30-day case-based mortality rate was 12.9%.

3.4. Primary study endpoint

Within the first 48 hours after SGB, ICD shocks declined by 86.8% (absolute mean reduction, 6.3 shocks), and any sustained VT/VF detected and treated by ICD declined by 87.4% overall (absolute mean reduction, 57.4 delivered therapies; all $P < 0.001$). Patients with higher arrhythmia burden before SGB (shocks <10/48 h vs. >10/48 h; ATPs <10/48 h vs. 10–99/48 h vs. >100/48 h) experienced greater improvement (shocks −85.6% vs. −99.1%; ATPs −50.3% vs. −92.1% vs. −100.0%) (Table 2, Fig. 3). Significant improvement was found irrespective of ischemic vs. non-ischemic VA etiology (Supplemental Fig. 1).

To demonstrate the most common ("expected") efficacy of the SGB procedure within 48 hours in an exploratory analysis of arrhythmia burden reduction, absolute ICD shock reduction ranging from 0 to 10 and/or ATPs ranging from 0 to 20 occurred in 68.7% of the ES cases. One patient experienced an increase in both, and one patient experienced a post-SGB decrease in shocks but an increase in ATPs (Supplemental Fig. 2).

3.5. Secondary study endpoints

During the period ≤48 hours after SGB, 53 (75.7%) patients experienced a response, remaining free from ICD shock and ATPs,

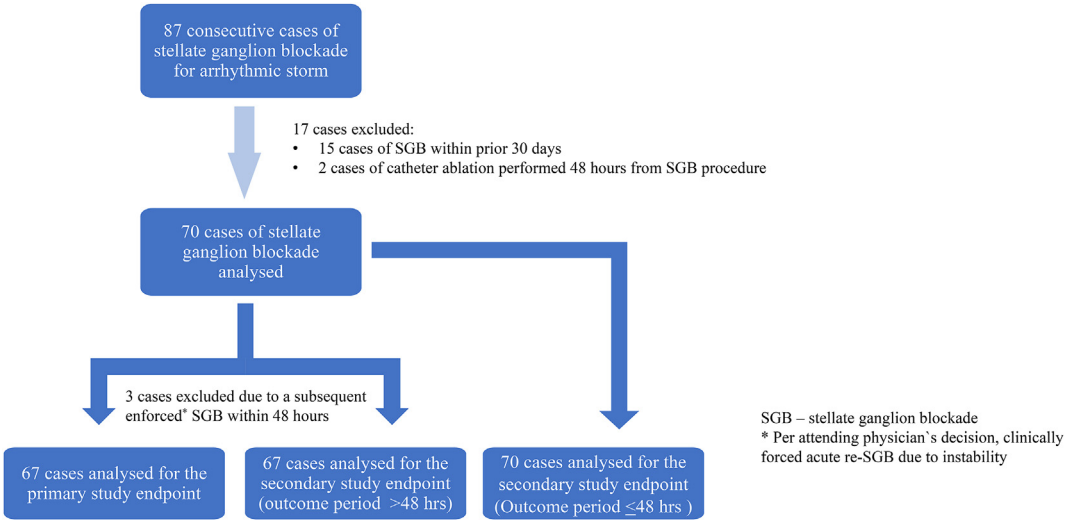


Figure 2. Study flowchart.

Table 1
Patient characteristics.

Parameter	Subgroups	Statistic	Number of SGBs (N = 70)
Number of patients	Total	n	59
	Patients with 1 SGB	n	51
	Patients with >1 SGB	n	8
Age (years)		n	70
		Mean (SD)	67.7 (12.44)
		Min; Max	31; 86
Sex	Male	n (%)	56 (80.0)
	Female	n (%)	14 (20.0)
Ethnicity	Caucasian	n (%)	70 (100)
Diabetes mellitus		n (%)	20 (28.6)
LVEF	All	n	70
		Mean (SD)	30.0 (9.05)
		Min; Max	15; 60
	≤35%	N (%)	54 (77.1)
		Mean (SD)	26.1 (5.21)
		Min; Max	15; 35
	>35%	N (%)	16 (22.9)
		Mean (SD)	43.4 (5.92)
		Min; Max	37; 60
Etiology of arrhythmia	Ischemic	n (%)	42 (60.0)
	Revascularized	n (%)	38 (90.5)
	Non-ischemic	n (%)	28 (40.0)
	LQT	n (%)	3 (10.7)
	HOCM	n (%)	1 (3.6)
	Other non-ischemic	n (%)	24 (85.7)
Base rhythm on ECG	AF	n (%)	24 (34.3)
	SR	n (%)	46 (65.7)
ICD therapy	Shocks and ATPs	n (%)	48 (68.6)
	Shocks only	n (%)	19 (27.1)
	ATPs only	n (%)	3 (4.3)
Type of arrhythmia	MMVT	n (%)	51 (72.9)
	PMVT	n (%)	9 (12.9)
	VF	n (%)	8 (11.4)
	MIX	n (%)	2 (2.9)
Medication at the time of SGB	β-blocker use	n (%)	64 (91.4)
	Amiodarone intravenous	n (%)	55 (78.6)
	Catecholamines	n (%)	8 (11.4)
	Digoxin	n (%)	4 (5.7)
	Trimecain	n (%)	4 (5.7)
	Sotalol	n (%)	1 (1.4)
ECMO		n (%)	3 (4.3)
Hospitalization	Overall	n (%)	68 (97.1)
	Duration of hospitalization (days)	n	68
		Mean (SD)	11.2 (7.84)
		Min; Max	1; 34
	Death during hospitalization	n (%)	6 (8.8)
	Cardiovascular	n (%)	3 (50.0)
	Non-cardiovascular	n (%)	3 (50.0)
BSG Site	LGSB	n (%)	65 (92.9)
	BILAT	n (%)	4 (5.7)
	RGSB	n (%)	1 (1.4)
Time from storm to SGB (hours)	Overall	n	70
		Mean (SD)	13.2 (12.32)
		Min; Max	0; 44
	Ischemic etiology	n	42
		Mean (SD)	13.3 (12.00)
		Min; Max	0; 44
	Non-ischemic etiology	n	28
		Mean (SD)	13.1 (13.01)
		Min; Max	0; 44
Horner's syndrome		n (%)	47 (67.1)
Catheter ablation	Overall	n (%)	34 (49.3)
	During index hospitalization	n (%)	22 (31.4)
	Up to 60 days after SGB	n (%)	29 (41.4)
	Days from SGB to catheter	n	22
	ablation during hospitalization	Mean (SD)	7.0 (5.32)
		Min; Max	2; 22

AF, atrial fibrillation; ATP, anti-tachycardiac pacing; ECG, electrocardiogram; ECMO, extracorporeal membrane oxygenation; HOCM, hypertrophic obstructive cardiomyopathy; ICD, implanted cardioverter-defibrillator; LQT, long QT syndrome; LVEF, left ventricular ejection fraction; SGB, stellate ganglion blockade; SR, sinus rhythm; VT, ventricular tachycardia.

Table 2
ICD therapy to treat malignant ventricular arrhythmias 48 hours before and 48 hours after the SGB procedure (overall and by groups of arrhythmia burden).

Parameter	Group	Statistic	48 hours before SGB	48 hours after SGB	Absolute difference (after - before)	Percentage difference (after - before)	p-value
Arrhythmias before and after SGB (overall)							
Shocks	overall	n	67	67	67	67	<.0001
		Mean (SD)	6.612 (11.958)	0.269 (0.978)	−6.343 (11.866)	−86.8 (33.3)	
		Median (Q1; Q3)	3 (2; 5)	0 (0; 0)	−3 (−5; −2)	−100 (−100; −100)	
		Min; Max	0; 67	0; 7	+2; −67	+40; −100	
ATP	overall	n	67	67	67	66	<.0001
		Mean (SD)	52.313 (224.649)	1.209 (4.287)	−51.104 (224.81)	−65.9 (46.3)	
		Median (Q1; Q3)	6 (0; 20)	0 (0; 0)	−5 (−16; 0)	−100 (−100; 0)	
		Min; Max	0; 1700	0; 31	+10; −1700	+28.6; −100	
Shocks & ATP	overall	n	67	67	67	67	<.0001
		Mean (SD)	58.925 (224.681)	1.478 (4.636)	−57.448 (224.917)	−87.4 (39.6)	
		Median (Q1; Q3)	11 (5; 31)	0 (0; 0)	−10 (−31; −4)	−100 (−100; −100)	
		Min; Max	2; 1703	0; 31	+7; −1703	−100; +175	
Arrhythmias before and after SGB (by group)							
Shocks	<10/48 hours before	n	61	61	61	61	<.0001
		Mean (SD)	3.393 (2.052)	0.246 (0.96)	−3.148 (2.212)	−85.6 (34.7)	
		Median (Q1; Q3)	3 (2; 5)	0 (0; 0)	−3 (−5; −2)	−100 (−100; −100)	
		Min; Max	0; 9	0; 7	+2; −9	+40; −100	
	≥10/48 hours before	n	6	6	6	6	0.0313*
		Mean (SD)	39.333 (20.637)	0.5 (1.225)	−38.833 (20.213)	−99.1 (2.2)	
		Median (Q1; Q3)	37.5 (29; 55)	0 (0; 0)	−37.5 (−52; −29)	−100 (−100; −100)	
		Min; Max	10; 67	0; 3	−10; −67	−94.5; −100	
ATP	<10/48 hours before	n	43	43	43	42	<.0001
		Mean (SD)	2.907 (3.161)	0.721 (2.313)	−2.186 (3.554)	−50.3 (50.7)	
		Median (Q1; Q3)	2 (0; 5)	0 (0; 0)	−1 (−4; 0)	−61.1 (−100; 0)	
		Min; Max	0; 9	0; 10	−9; +10	+28.6; −100	
	10-99/48 hours before	n	21	21	21	21	<.0001
		Mean (SD)	39.286 (26.073)	2.381 (6.874)	−36.905 (26.298)	−92.1 (16.8)	
		Median (Q1; Q3)	32 (12; 61)	0 (0; 0)	−30 (−58; −12)	−100 (−100; −100)	
		Min; Max	10; 97	0; 31	−6; −97	−49.2; −100	
	≥100/48 hours before	n	3	3	3	3	0.2500*
		Mean (SD)	851.667 (803.556)	0 (0)	−851.667 (803.556)	−100 (0)	
		Median (Q1; Q3)	753 (102; 1700)	0 (0; 0)	−753 (−1700; −102)	−100 (−100; −100)	
		Min; Max	102; 1700	0; 0	−102; −1700	−100; −100	

P-value of Wilcoxon signed-rank test.
* Statistic results were likely influenced by a low patient number in the group. Despite this fact, the clinical significance of the % reduction of the therapy is undoubtable.
ATP, anti-tachycardiac pacing; ICD, implantable cardioverter-defibrillator; SGB, stellate ganglion blockade.
Plus sign "+" in the output marks increase of therapies, minus sign '−' marks decrease of therapies.

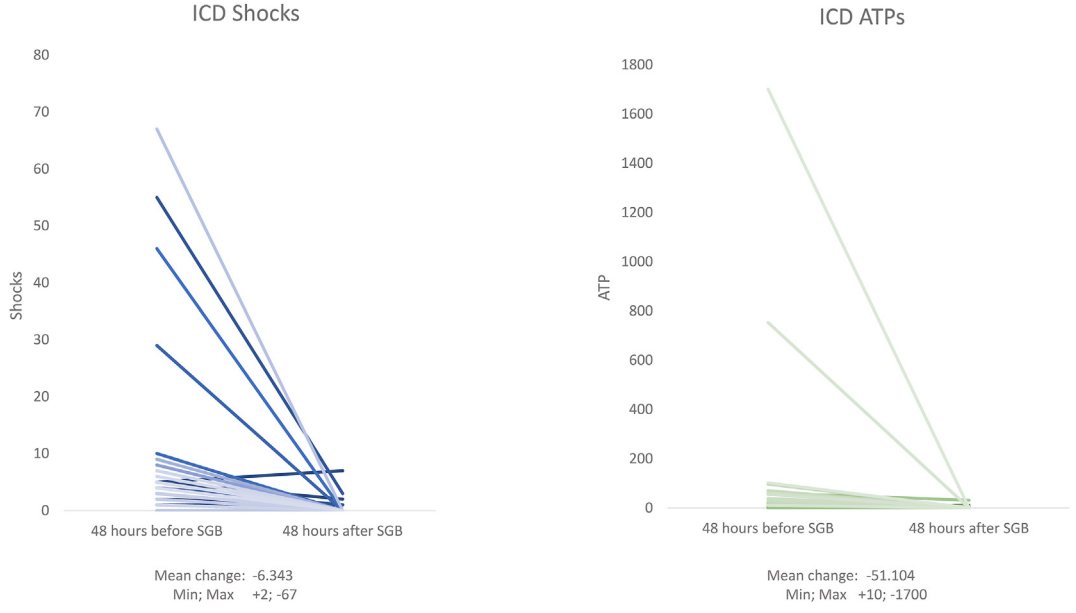


Figure 3. ICD shock and ATP therapy in patients with ES before and after the SGB procedure.

and 17 did not. The patients with baseline atrial fibrillation expressed a higher responsiveness rate than the patients with baseline sinus rhythm ($P = 0.025$). Among the "early" responders, 8 (15.1%) patients later experienced recurrent VA before discharge/catheter ablation/day 8.

During the >48-hour post-SGB period, 51 (76.1%) patients experienced a response, with no further ICD shock or <3 ATPs/day, and 16 did not. Patients not experiencing a response were less frequently receiving β-blockers ($P < 0.001$) and more often needed catecholamine support ($P = 0.05$) or presented with polymorphic VT/mixed-type VT (Table 3).

3.6. Periprocedural anti-arrhythmic medication

In order to evaluate the effect of two major anti-arrhythmic drugs, β-blockers and intravenous amiodarone, on responsiveness rates for both post-SGB periods, a more detailed analysis was performed. Amiodarone was used in 78.6% of cases at a standard dose of 900–1200 mg daily and did not significantly affect responsiveness rates to SGB in either group (Table 3). The β-blocker therapy was monitored with respect to a recommended daily dosing at certain time periods before and after the SGB procedure. The distribution of β-blocker average daily doses at home, during the last 48 hours before SGB, during the first 48 hours after SGB, and later until ablation/discharge/day 8 did not vary significantly between responders and non-responders in either post-SGB study definition (Table 4a). Nevertheless, there was a significant difference with respect to whether the β-blocker dose was decreased, sustained, or increased periprocedurally between responders and non-responders per definition one, but not two. Responders per definition one (i.e., ≤48 hours) had significantly frequently increased their β-blocker dose (from none to any dose or from none or <50% daily dose to ≥50% daily dose; or introduced/switched to intravenous β-blocker) within the last 48 hours before SGB compared with their home dose (Table 4b). The distribution and dynamics of β-blocker dosing across time periods are demonstrated in Fig. 4.

Concerning the anti-arrhythmic medication at discharge/day 8, 74.3% of patients were receiving a combination therapy of amiodarone and β-blocker, of which the dose of ≥50% recommended daily dose was reached in 44.3% of patients. A significant difference was found in the distribution of anti-arrhythmic drugs between responders and non-responders per definition two, but not one. Responders per definition two (i.e., >48 hours) had at least one anti-arrhythmic drug in therapy (amiodarone, β-blocker, or sotalol) and a higher representation of β-blockers than non-responders (97.9% vs. 76.2%), as shown in Table 5.

3.7. Safety and tolerability of SGB

SGB procedures were well tolerated, with 67.1% having an episode of temporary ipsilateral Horner's syndrome that resolved within 24 hours. The incidence did not significantly differ between responders and non-responders during either outcome period (≤48 hours and >48 hours). In addition, no clinically relevant adverse events (blood aspiration, intra-arterial bupivacaine injection, vocal cord paresis, pneumothorax, puncture site infection, large hematomas) were observed.

4. Discussion

To the best of our knowledge, this is the largest single-center case series analysis of percutaneous SGB as part of the predefined treatment algorithm of ES performed in patients with ICDs at high risk of sudden cardiac death. The type and burden of malignant arrhythmia were prospectively collected and analyzed in all participants, and this study yielded several key findings. First, the presented two-step algorithm was quite effective, with an 87% reduction in all events of ICD shocks at 48 hours after SGB. Second, almost a quarter of patients did not experience a complete response to algorithm-guided therapy and had recurrent ventricular arrhythmias after the 48-hour observational period, whether the ≤48-hour period was arrhythmia-free or not. Third, there were no adverse events or reactions associated with the SGB procedure except for temporary Horner's syndrome in two-thirds of cases. Finally, there was zero need for intubation and general anesthesia as part of ES management in patients when the algorithm was applied.

The study design and population varied significantly from previous reports. The study included only patients with an implanted ICD to enable recording complete arrhythmia history prior to ES and during hospitalization, achieve a relatively homogeneous group of patients not having been recently resuscitated, and avoid sudden arrhythmic deaths after the termination of extended acute monitoring at an intensive care unit. Previously published case series enrolled consecutive ES patients, among whom 9.1% to 70% had ICDs. Those patients were often post-resuscitation, intubated, and received inotropic therapy. Therefore, β-blocker use was comparatively less during the course of SGB (35%–45% vs. 91.4% in our study); a mechanical cardiac support system because of pump failure was required more often (up to 50% compared with 4.3% in our study), and in-hospital mortality was higher (23.3%–36.4% vs. 8.6% in our study). Similar to our findings, most patients in earlier studies had ischemic etiology of the arrhythmia and LVEF of around 30%.[10,11,13] Other characteristics of participants in these studies were described heterogeneously in each of the publications, making comparison difficult. Concerning the type of arrhythmia, monomorphic VT seemed to be more common in our study than that reported in previous studies (10%–50% vs. 73% in our study).[10,12,26] The reason might be a high percentage of primary preventive indications in our study for ICD in patients with chronic ischemic heart disease/dilated cardiomyopathy who typically manifested with re-entry, substrate-dependent monomorphic tachycardia. Regarding the type of arrhythmia and responsiveness to SGB, the data in literature is missing. Our results suggested a similar efficacy of SGB to treat and prevent recurrences of VAs within 48 hours in those presenting with either monomorphic or polymorphic tachycardia, or VF; polymorphic and mixed-type tachycardia seemed to respond less effectively to SGB and became recurrent after the 48-hour observational period in 44.4% and 100%, respectively (Table 3).

Of note, none of the previous papers mentioned a time delay between the ES onset and SGB.[10,11,13] The SGB procedure was performed according to local protocols either unilaterally, bilaterally, or even repeatedly, but commonly as the last therapeutic option, presumably with a longer delay. In this study, the mean delay was 13.2 ± 12.3 hours and was similar between patients with ischemic and non-ischemic arrhythmias (Table 1). Within this period, the first step of the algorithm (immediate therapy) was initiated to suppress ES (Fig. 1). If a recurrent arrhythmia occurred anytime during this step, then immediate/early SGB was performed with no further delay in most cases during electrolyte infusion, prior to revascularization or sedation of the patient, and regardless of concomitant therapy (e.g., anti-thrombotics). Consequently, in ES cases with a very short delay, a "carryover" effect of the medical/interventional therapy that had been started shortly before SGB and could not have been fully expressed, needs to be considered.

The algorithm including the early SGB approach was efficacious in reducing the ICD therapy burden at 48 hours. The effect on reductions in ICD shock therapy was more pronounced than effects on ATP burst therapy, which is clinically important from the

Table 3
Secondary analysis results of clinical response to treatment algorithm per outcome period applied in patients with ES.

Parameter		Statistic	Responders (n = 53)	Non-responders (n = 17)	p-value	Responders (n = 51)	Non-responders (n = 16)	p-value
			Outcome period ≤48 hours			Outcome period >48 hours		
Amiodarone	Yes	n (%)	41 (74.5%)	14 (25.5%)	1.0000	40 (76.9%)	12 (23.1%)	0.7429
	No	n (%)	12 (80.0%)	3 (20.0%)		11 (73.3%)	4 (26.7%)	
Base rhythm on ECG	AF	n (%)	22 (91.7%)	2 (8.3%)	**0.0246**	19 (82.6%)	4 (17.4%)	0.3677
	SR	n (%)	31 (67.4%)	15 (32.6%)		32 (72.7%)	12 (27.3%)	
β-blocker use	Yes	n (%)	49 (76.6%)	15 (23.4%)	0.6279	51 (82.3%)	11 (17.7%)	**0.0005**
	No	n (%)	4 (66.7%)	2 (33.3%)			5 (100%)	
Cardiac etiology of arrhythmia	HOCM	n (%)	1 (100%)		0.5543	1 (100%)		0.8477
	ICM	n (%)	33 (78.6%)	9 (21.4%)		31 (77.5%)	9 (22.5%)	
	LQT	n (%)	3 (100%)			2 (66.7%)	1 (33.3%)	
	NICM	n (%)	16 (66.7%)	8 (33.3%)		17 (73.9%)	6 (26.1%)	
Catecholamines	Yes	n (%)	6 (75.0%)	2 (25.0%)	1.0000	3 (42.9%)	4 (57.1%)	**0.0505**
	No	n (%)	47 (75.8%)	15 (24.2%)		48 (80.0%)	12 (20.0%)	
Age ≥50 years	Yes	n (%)	48 (77.4%)	14 (22.6%)	0.3917	45 (75.0%)	15 (25.0%)	1.0000
	No	n (%)	5 (62.5%)	3 (37.5%)		6 (85.7%)	1 (14.3%)	
Age (years)		n	53	17		51	16	
		Mean (SD)	67.3 (11.67)	68.7 (14.94)	0.3733	67.1 (12.58)	69.7 (11.90)	0.4060
		Median	68.8	74.1		68.6	72.0	
		Min; Max	31; 85	39; 86		31; 86	40; 82	
LVEF	≤30%	n (%)	33 (71.7%)	13 (28.3%)	0.5313	33 (75.0%)	11 (25.0%)	1.0000
	31%–49%	n (%)	17 (81.0%)	4 (19.0%)		15 (75.0%)	5 (25.0%)	
	≥50%	n (%)	3 (100%)			3 (100%)		
Cause direct	AHF	n (%)	8 (88.9%)	1 (11.1%)	0.7998	8 (88.9%)	1 (11.1%)	0.5794
	AMI	n (%)	7 (77.8%)	2 (22.2%)		5 (62.5%)	3 (37.5%)	
	LQT	n (%)	1 (100%)			1 (100%)		
	unknown	n (%)	37 (72.5%)	14 (27.5%)		37 (75.5%)	12 (24.5%)	
Diabetes mellitus	Yes	n (%)	18 (90.0%)	2 (10.0%)	0.1223	18 (90.0%)	2 (10.0%)	0.1191
	No	n (%)	35 (70.0%)	15 (30.0%)		33 (70.2%)	14 (29.8%)	
Gender	Male	n (%)	41 (73.2%)	15 (26.8%)	0.4917	43 (81.1%)	10 (18.9%)	0.0815
	Female	n (%)	12 (85.7%)	2 (14.3%)		8 (57.1%)	6 (42.9%)	
Horner's syndrome	Yes	n (%)	34 (72.3%)	13 (27.7%)	0.3467	36 (81.8%)	8 (18.2%)	0.1302
	No	n (%)	19 (82.6%)	4 (17.4%)		15 (65.2%)	8 (34.8%)	
Midazolam	Yes	n (%)	28 (73.7%)	10 (26.3%)	0.6660	25 (67.6%)	12 (32.4%)	0.0683
	No	n (%)	25 (78.1%)	7 (21.9%)		26 (86.7%)	4 (13.3%)	
Other anti-arrhythmics	Digoxin	n (%)	3 (75.0%)	1 (25.0%)	0.1303	3 (75.0%)	1 (25.0%)	0.3287
	None	n (%)	48 (78.7%)	13 (21.3%)		46 (78.0%)	13 (22.0%)	
	Sotalol	n (%)		1 (100%)			1 (100%)	
	Trimecain	n (%)	2 (66.7%)	1 (33.3%)		2 (66.7%)	1 (33.3%)	
Prior revascularization	Yes	n (%)	30 (76.9%)	9 (23.1%)	0.7914	29 (76.3%)	9 (23.7%)	0.9656
	No	n (%)	23 (74.2%)	8 (25.8%)		22 (75.9%)	7 (24.1%)	
Type of arrhythmia	Mixed	n (%)	1 (50.0%)	1 (50.0%)	0.4479		2 (100%)	**0.0220**
	MMVT	n (%)	37 (72.5%)	14 (27.5%)		40 (81.6%)	9 (18.4%)	
	PMVT	n (%)	8 (88.9%)	1 (11.1%)		5 (55.6%)	4 (44.4%)	
	VF	n (%)	7 (87.5%)	1 (12.5%)		6 (85.7%)	1 (14.3%)	
Time from storm to SGB (h)	Overall	n	53	17		51	16	
		Mean (SD)	14.4 (12.88)	9.6 (9.85)	0.1644	14.0 (13.19)	12.7 (9.54)	0.8947
		Median	44783	44778		44752	44662	
		Min; Max	0; 44	0; 29		0; 44	1; 29	
	Early (0–12 h)	n	29	8		28	9	
		Mean (SD)	4.4 (3.74)	3.8 (3.67)	0.6312	3.9 (3.52)	5.3 (4.20)	0.3212
		Median	44745	44622		44653	6.0	
		Min; Max	0; 12	1; 11		0; 11	1; 12	
	Late (13–48 h)	n	24	6		23	7	
		Mean (SD)	26.4 (9.11)	21.0 (6.79)	0.2037	26.2 (9.75)	22.2 (4.08)	0.5236
		Median	44644	44580		44705	44614	
		Min; Max	13; 44	14; 29		13; 44	16; 29	

P-value of Chi-squared or Fisher test for categorical variables, Wilcoxon rank sum test for continuous variables for comparison of responders and non-responders.
Detailed description of responders and non-responders for each definition in text.
Univariate comparison, $p < 0.05$ (in bold) is statistically significant and expresses a significant difference in distribution of variables between responders and non-responders for each parameter.
AF, atrial fibrillation; ATP, anti-tachycardiac pacing; NICM, non-ischemic cardiomyopathy; ECG, electrocardiogram; ECMO, extracorporeal membrane oxygenation; HOCM, hypertrophic obstructive cardiomyopathy; ICD, implanted cardioverter-defibrillator; ICM, ischemic cardiomyopathy; LQT, long QT syndrome; LVEF, left ventricular ejection fraction; MMVT, monomorphic ventricular tachycardia; NICM, non-ischemic cardiomyopathy; PMVT, polymorphic ventricular tachycardia; RFA, radiofrequency ablation; SGB, stellate ganglion blockade; SR, sinus rhythm; VF, ventricular fibrillation.

patient's perspective. The median number of defibrillation events at 48 hours decreased from 3 (IQR: 2–5) to 0 (IQR: 0 to 0), which is comparable to previous findings by Fudim et al. (5.5 [IQR: 2.0 to 15.8] to 0 [IQR: 0 to 3.8]).[10] In a review of 38 cases by Meng et al., the number of external defibrillations or ICD shocks substantially decreased from 10.00 ± 9.10/day to 0.05 ± 0.22/day. Their data suggested that the total arrhythmia burden prior to SGB could have played an important role in the effectiveness of SGB. For this reason,

Table 4a
Average β-blocker daily doses used by subjects in certain time periods and comparison between responders and non-responders per study definition one and two.

Time period	β-blocker therapy	Definition ONE				Definition TWO			
		Total	Responders	NON responders	p	Total	Responders	NON responders	p
		%	%	%		%	%	%	
P1	no BB	20.0%	20.8%	14.3%	0.172	19.1%	21.4%	33.3%	0.782
	<50% daily dose	45.7%	49.1%	28.6%		45.6%	46.4%	33.3%	
	≥50% daily dose	34.3%	30.2%	57.1%		35.3%	32.1%	33.3%	
P2	no BB	18.6%	13.2%	35.7%	0.127	19.1%	10.7%	33.3%	0.486
	<50% daily dose	35.7%	37.7%	21.4%		33.8%	32.1%	33.3%	
	≥50% daily dose	38.6%	43.4%	28.6%		39.7%	50.0%	33.3%	
	i.v. BB	7.1%	5.7%	14.3%		7.4%	7.1%	0.0%	
P3	no BB	13.0%	9.4%	28.6%	0.271	13.4%	3.6%	0.0%	0.532
	<50% daily dose	40.6%	39.6%	35.7%		38.8%	39.3%	50.0%	
	≥50% daily dose	43.5%	47.2%	35.7%		44.8%	53.6%	33.3%	
	i.v. BB	2.9%	3.8%	0.0%		3.0%	3.6%	16.7%	
P4	no BB	7.6%	3.8%	21.4%	0.154	7.7%	3.7%	0.0%	0.136
	<50% daily dose	43.9%	44.2%	42.9%		43.1%	37.0%	50.0%	
	≥50% daily dose	47.0%	50.0%	35.7%		47.7%	59.3%	33.3%	
	i.v. BB	1.5%	1.9%	0.0%		1.5%	0.0%	16.7%	

The table presents average daily doses of β-blockers (BB) used by subjects in certain periods: *P1* - Home (chronic dose of BB at home); *P2* – last 48 hours prior to ganglion stellate blockade; *P3* - first 48 hours after ganglion stellate blockade; and *P4* – Day 3 to ablation/discharge/Day 8 period.
The dose of β-blockers is categorized as follows: "no BB" for the group of patients who did not use BB at all; "less than 50% daily dose" as stated in the corresponding Summary of Product Characteristics (SPC, see below) for the group of patients who used less than 50% SPC recommended daily dose; and "50% and more daily dose" for the group of patients who used 50% and more SPC recommended daily dose. For the period during hospitalization, an additional category was used for the group of patients who received intravenous β-blockers instead of/on top of oral medication.
Univariate comparison, chi-square test, $p < 0.05$ (in bold) is statistically significant and expresses a significant difference in distribution of β-blocker doses between responders and non-responders for each time period and definition.
List of BBs used and their recommended daily doses according to corresponding SPCs.
Bisoprolol: max dose 10 mg, 50% dose 5 mg; *Carvedilol* max dose 50 mg, 50% dose 25 mg; *Metoprolol succinate*: max dose 200 mg, 50% dose 100 mg; *Nebivolol*: max dose 10 mg, 50% dose 5 mg.

Table 4b
Dynamics of changes in β-blocker therapy in responders and non-responders per study definitions one and two before, during the course, and after ganglion stellate blockade.

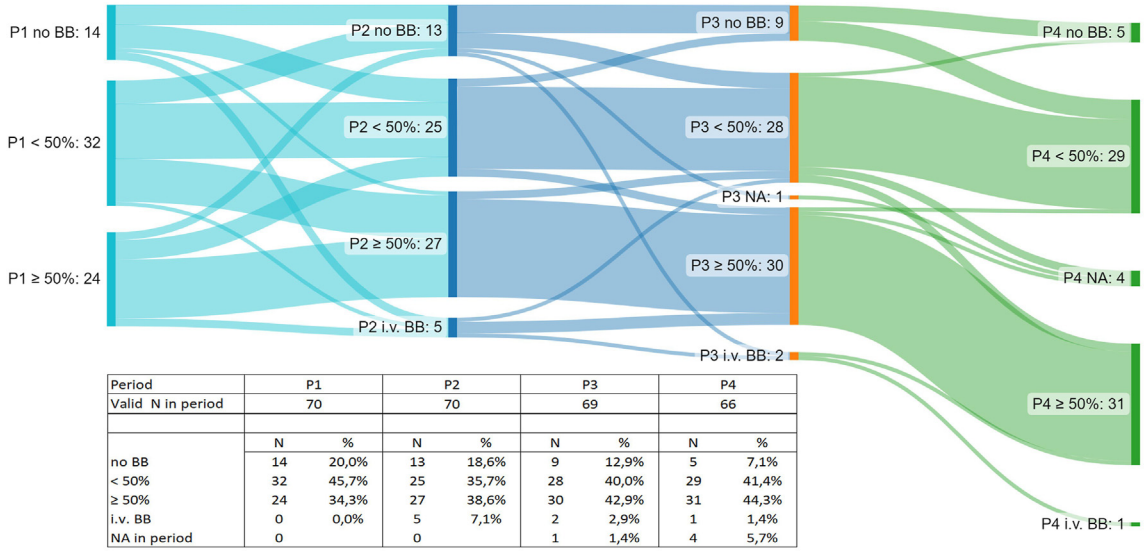
Time periods compared	β-blocker dose change	Definition ONE				Definition TWO			
		Total	Responders	NON responders	p	Total	Responders	NON responders	p
		%	%	%		%	%	%	
P1 to P2	DOSE decrease	18.6%	13.2%	42.9%	**0.027**	19.1%	7.1%	16.7%	0.401
	DOSE sustain	45.7%	43.4%	42.9%		45.6%	50.0%	33.3%	
	DOSE increase	35.7%	43.4%	14.3%		35.3%	42.9%	50.0%	
P1 to P3	DOSE decrease	18.8%	13.2%	42.9%	**0.002**	19.4%	7.1%	16.7%	0.148
	DOSE sustain	44.9%	39.6%	57.1%		44.8%	42.9%	33.3%	
	DOSE increase	36.2%	47.2%	0.0%		35.8%	50.0%	50.0%	
P2 to P3	DOSE decrease	7.2%	7.5%	6.3%	0.724	7.5%	6.4%	10.0%	0.748
	DOSE sustain	81.2%	79.2%	87.5%		80.6%	83.0%	75.0%	
	DOSE increase	11.6%	13.2%	6.3%		11.9%	10.6%	15.0%	
P1 to P4	DOSE decrease	17.9%	13.2%	35.7%	**0.006**	18.2%	10.7%	16.7%	0.321
	DOSE sustain	47.8%	43.4%	64.3%		48.5%	46.4%	33.3%	
	DOSE increase	34.3%	43.4%	0.0%		33.3%	42.9%	50.0%	

The table shows comparisons of the proportion of responders and non-responders to SGB therapy based on BB dose changes (increased, sustained, or decreased) across different time periods. The dose levels were as in Table 2a: "no BB," "less than 50% daily dose," "50% and more daily dose," and "intravenous BB," except for the two upper dose categories that were merged. Time periods, statistical methods, and BB dosing per SPCs were as in Table 4b.
An example of the classification process: A subject on 10 mg bisoprolol at home (P1), on 10 mg bisoprolol + i.v. metoprolol bolus before SGB (P2, dose sustained), on 10 mg bisoprolol with no shock/ATP within the first 48 hours (responder per definition 1, P3, dose sustained), but 5 mg bisoprolol/day and a shock after the 48-hour period (non-responder per definition two, P4, dose reduced).

we first performed a group analysis by arrhythmia burden and found a more pronounced efficacy of SGB in patients with the highest arrhythmia burden (Table 2). One explanation may be that these patients were subject to an enormous stress response, and the resulting sympathoexcitation increased the repolarization heterogeneity of cardiomyocytes via efferent sympathetic signaling, enhancing arrhythmia inducibility. β-Blockers and anti-arrhythmic drugs attenuate such neurotransmissions, and beyond this effect, SGB also mitigates non-adrenergic signaling and sensory afferent neurotransmission.[12] Of note, our exploratory analysis of arrhythmia burden reduction showed an absolute reduction of ICD shocks of 0 to 10 and/or ATPs of 0 to 20 in most ES cases (68.7%).

In the present study, the in-hospital mortality was 8.8% (6 patients), which is lower than that previously reported. The explanation for this low mortality rate may be the early application of SGB in the treatment algorithm and the selected population of patients with ICDs.

Using the ICD recordings, we detected all arrhythmias and therapies beyond 48 hours post SGB, so we could retrospectively evaluate the entire hospitalization course and ES management in terms of timing of hospital discharge and risk factors associated with non-response. In the secondary analysis of clinical response, we found that one in four patients who were closely monitored for 48 hours after SGB, regardless of the presence of sustained VAs



Period	P1		P2		P3		P4	
Valid N in period	70		70		69		66	
	N	%	N	%	N	%	N	%
no BB	14	20,0%	13	18,6%	9	12,9%	5	7,1%
< 50%	32	45,7%	25	35,7%	28	40,0%	29	41,4%
≥ 50%	24	34,3%	27	38,6%	30	42,9%	31	44,3%
i.v. BB	0	0,0%	5	7,1%	2	2,9%	1	1,4%
NA in period	0		0		1	1,4%	4	5,7%

Figure 4. Sankey chart of distribution of β-blocker (BB) dose categories across time periods.

Table 5
Comparison of anti-arrhythmic medication at discharge/day 8 between responders and non-responders per study definitions one and two.

	Definition ONE				Definition TWO			
	Total	Responders	NON responders	p	Total	Responders	NON responders	p
	%	%	%		%	%	%	
No AA	2.9%	3.8%	0.0%	0.369	2.9%	0.0%	9.5%	**0.026**
BB only	17.1%	18.9%	11.8%		16.2%	21.3%	4.8%	
Amiodarone only	4.3%	3.8%	5.9%		4.4%	2.1%	9.5%	
BB + amiodarone	74.3%	73.6%	76.5%		75.0%	76.6%	71.4%	
Sotalol	1.4%	0.0%	5.9%		1.5%	0.0%	4.8%	

AA, anti-arrhythmic therapy; BB, β-blocker therapy.
Univariate comparison, chi-square test, $p < 0.05$ (in bold) is statistically significant and expresses a significant difference in the distribution of anti-arrhythmic drugs between responders and non-responders for each definition.

during that initial window, received subsequent ICD shock therapy or ≥3 ATPs per day until the end of hospitalization/day 8/early catheter ablation. Patients with recurrent arrhythmias beyond 48 hours were mostly on catecholamine support and/or with less frequently represented β-blocker therapy (or on a low β-blocker dose), i.e., those who could not experience synergistic anti-adrenergic effects of pharmacotherapy plus SGB. These patients should be closely monitored for a long time because of the high risk of early ES recurrence. Moreover, the use of midazolam sedation showed a trend to a negative association with increased risk for clinical non-responsiveness to the algorithm-based therapy ($P = 0.068$). Opioids, propofol, and dexmedetomidine exert a much stronger anti-adrenergic effect,[27,28] and their use instead of midazolam could be beneficial in this clinical setting.

When evaluating responsiveness to therapy, as in other studies, completion of the crucial 48-hour post-SGB period without further arrhythmia was used to classify responders. This study showed, however, that even with an arrhythmia-free period of 48 hours, 8 of 53 of these patients experienced recurrence of ventricular arrhythmia requiring ICD therapy later during hospitalization. If these patients had not had ICDs, they could have been considered stabilized and no longer have been closely monitored.

A very interesting finding for clinical practice was that almost none of the patients with baseline atrial fibrillation (91.7%) undergoing SGB as part of ES treatment experienced sustained VA within 48 hours after SGB. The explanation might be the advanced autonomic dysfunction in patients with atrial fibrillation, with the prevailing effect of parasympathetic dysfunction in healthy young and sympathetic (adrenergic) dysfunction in old and those with structural heart disease.[29] A detailed investigation did not reveal significant differences between β-blocker doses applied to patients with and without atrial fibrillation within 48 h before and after SGB (Supplemental Table 2). Therefore, we consider the SGB procedure having been the major therapeutic intervention responsible for the positive response of particularly patients with atrial fibrillation to the entire treatment algorithm.

The use of amiodarone, the most widely administered anti-arrhythmic drug in ES treatment and long-term prevention (alone or in combination with β-blocker), has been supported by the international guidelines (level of recommendation I-IIb, level of evidence C).[5,9,30] Nevertheless, data to support its routine use in patients with ES not refractory to external defibrillation or with an implanted ICD are missing. In our cohort, amiodarone was administered to all patients lacking absolute contraindication to its use (LQT, allergy, hyperthyroidism), corresponding to 78% of patients undergoing the SGB procedure. Compared to patients who did not receive amiodarone, these patients did not differ in responsiveness rates in either secondary endpoint group (i.e., outcome period ≤48 h and outcome period >48 hours). These results imply that the mechanisms by which amiodarone and SGB suppress ventricular arrhythmias are different and independent.

On the contrary, the maximum use and up-titration of β-blocker therapy proved to be a crucial pharmacological intervention. The results showed that simply evaluating the representation of β-blockers at the time of SGB may provide incorrect information. In some patients, the regimen became contraindicated while others were newly introduced to β-blockers, providing misleading overall results. Having analyzed the dynamics and distribution of β-blocker doses across peri-SGB time periods, it turned out that an immediate introduction of β-blocker, or its maximum up-titration, or a switch to intravenous dosing before SGB led to a significantly higher number of acute complete responders (i.e., ≤48 hours, Table 4b). The data also showed that once the β-blocker dose was increased it then remained increased in most of the cases (Fig. 4). The positive "dynamics" of the β-blocker therapy also resulted in a higher proportion of patients taking β-blocker alone or in a combination with amiodarone at discharge/day 8. Responders per definition two (i.e., >48 hours) had a higher representation of anti-arrhythmic drugs at discharge, particularly β-blockers that could have been indicative of a better overall clinical status, and thus a better tolerance to these drugs (Table 5).

Concerning safety and tolerability of early SGB as part of the two-step algorithm, no concerns arose regarding this approach. No puncture site complications were observed despite ongoing antithrombotic therapy if indicated, although transient Horner's syndrome occurred more often than previously reported (28% vs. 67.1% in the current study).[13] According to Denby et al., and in keeping with our experience using SGB to treat refractory angina pectoris, a slight mechanical disruption of the upper and lower structures of the stellate ganglion with a needle or ganglion compression from the volume applied is associated with a greater clinical effect of the blockade but with increased incidence of transient Horner's syndrome.[31,32] For these reasons, we had anticipated that the occurrence of Horner's syndrome would predict responsiveness to SGB in suppressing ES or would be a marker of an effective block, as Amino et al. have suggested.[33] However, the results did not confirm this expectation, and neither have the findings reported by Savastano et al.[13] No other systemic complications were observed.

5. Study limitations

This study has several limitations. First, it was a single-center study with no comparator group; however, it is the largest case series to date with prospectively and systematically collected data from ES cases and SGB response in terms of immediate arrhythmia suppression and clinical success rate of the two-step algorithm. Second, we did not assess markers associated with SGB procedural success (skin temperature, heart rate variability) because doing so is difficult in acute clinical setting. Third, only a limited number of laboratory, clinical, and other relevant parameters were available for inclusion in the statistical analyses. Fourth, we did not conduct multivariate analysis because of the relatively small sample size and probable wide confidence intervals that would not support clinically relevant conclusions. For the same reasons, statistical significance values of comparisons between groups of variables do not necessarily express the clinical significance of the results. Finally, the timing of a catheter ablation procedure or dismissal from the hospital was often driven by non-medical reasons (availability, in-hospital bed occupancy), which could have affected clinical response rates.

6. Conclusions

In patients with ICDs who develop ES, the two-step institutional algorithm assessed here, including an early bedside SGB, proved to be safe and effective in suppressing malignant arrhythmias and eliminating the need for deep sedation and intubation. The reduction in ICD shocks and ATPs at 48 hours reached 87% and 65.9%, respectively, and patients with the highest arrhythmia burden experienced the highest suppression rates. A quarter of the patients required ICD therapy after 48 hours of post-SGB advanced monitoring. The need for catecholamine support, no/low-dosed β-blocker therapy, polymorphic/mixed-type VT, and baseline sinus rhythm versus atrial fibrillation were more frequent in patients with early arrhythmia recurrence. The overall results support the implementation of early SGB into routine clinical care for patients with ES.

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Conflict of interest

None declared.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.hjc.2023.04.003.

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