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Title

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Prognostic Impact of Atrial Rhythm and Dimension in Patients with Structural Heart Disease Undergoing Cardiac Sympathetic Denervation for Ventricular Arrhythmias

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Abstract

Background—Cardiac sympathetic denervation (CSD) is a promising treatment for patients with structural heart disease (SHD) and refractory ventricular tachyarrhythmias (VT). The effect of CSD on atrial rhythm, as well as the prognostic impact of atrial arrhythmias (AAs) or left atrial volume index (LAVI) on CSD outcome is unknown.

Objective—To evaluate the impact of AAs and LAVI on CSD outcome and to assess changes in AAs burden and in atrial pacing after CSD

Methods—Patients with SHD undergoing CSD for VTs were analyzed. Hazard models were built to assess predictors of sustained VT/ICD shocks recurrences and death/orthotopic heart transplant (OHT). Changes before versus after CSD were assessed on ICD, clinical and echocardiographic data. A drug index was devised to correct for medication use.

Results—Between 2009 and 2018, 91 patients (56 ± 13 years, LVEF 34 ±14%, 47% with a history of AAs) underwent left (16%) or bilateral CSD (BCSD). The median FU was 14 months (IQR 4-37). Using multivariable analysis, neither LAVI nor AAs were associated with recurrences; LAVI was an independent predictor of death/OHT. AAs burden did not change after BCSD, but

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atrial pacing increased from a median of 28% to 72% (p <0.01). LV end-diastolic diameter slightly increased; however, sustained VT/ICD shocks were reduced.

Conclusions—In patients with SHD undergoing CSD LAVI predicts death/OHT. AAs burden, already low at baseline, was unchanged after BCSD, while the need for atrial pacing increased, suggesting an impact of BCSD on sinus node chronotropism.

Keywords

cardiac sympathetic denervation; atrial arrhythmias; left atrial volume index; structural heart disease; autonomic nervous system

Introduction

Structural heart diseases (SHDs), independent of their cause, are characterized by a combination of pathological myocardial substrate and cardiac autonomic nervous system (ANS) remodeling, which promote susceptibility to both atrial arrhythmias (AAs) and ventricular tachyarrhythmias (VTs)(1). Nevertheless, patients with SHD, even at advanced stages, may present with AAs only, VTs only or a combination of both.

From a therapeutic point of view, antiarrhythmic strategies targeting the ANS, as opposed to local interventions such as catheter ablation, have the potential to prevent/treat both AAs and VTs while also affecting other pathophysiological properties of the heart (1).

Left cardiac sympathetic denervation (LCSD) is a well-established therapy for VTs in channelopathies (2). Despite a strong pathophysiological rationale and promising preclinical data, clinical experience with CSD in SHD is limited (3). Data suggest a higher efficacy of bilateral CSD (BCSD) as compared to LCSD in reducing the burden of VTs (4). Temporary unilateral stellate ganglion block (SGB) was also shown to decrease AF inducibility and AF episodes/duration (5).The prevalence and type of AAs in these patients, the correlation with clinical phenotype (cardiac geometry and function) at CSD and with outcome after CSD are unknown. The impact of CSD on AAs burden and on sinus node chronotropism in patients with SHD has not been described.

The purpose of this study was to assess the impact of pre-procedural AAs and left atrial volume index (LAVI) on CSD outcome, as well as the changes in atrial rhythm after CSD.

Methods

Patient population

A retrospective analysis of consecutive patients with SHD undergoing CSD for recurrent VTs between 2009 and 2018 at 2 centers was performed. SHD was defined as a left ventricular ejection fraction (LVEF) <55%, hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular cardiomyopathy (ARVC) or inflammatory cardiomyopathy/ sarcoidosis. Ischemic cardiomyopathy (ICM) was defined by history of myocardial infarction (MI) or myocardial perfusion defect with correlating obstructive disease on coronary angiography. Electrical storm (ES) was defined as ≥ 3 episodes of sustained or

treated VT within 24 hours. Clinical history of AAs included documented and/or treated episodes of atrial tachycardia (AT), atrial flutter (AFL) or atrial fibrillation (AF). Study approval was obtained from the institutional review board of the 2 centers.

The analysis of atrial rhythm changes after CSD based on ICD monitoring was limited to patients who received BCSD, which provides an almost complete extrinsic sympathetic denervation of atrial chambers. Patients with no atrial sensing, in permanent AF and with < 6 months of ICD monitoring after BCSD were excluded, as well as patients who received renal denervation (RDN) in the first 6 months after BCSD. For patients who received RDN 6 months after BCSD, follow up was censored at RDN. A drug index was devised to correct for medication use: beta-blockers, mexiletine, verapamil, digoxin and ranolazine were assigned 1 point, sotalol, propafenone, flecainide and dofetilide 2 points and amiodarone 3 points. Drug dosages were not incorporated in the drug index. The ICD threshold for AAs detection (automatic mode switch rate, AMS) was collected for each ICD interrogation.

Surgical procedure

CSD was performed via a minimally invasive (video- or robot-assisted) thoracoscopic surgery under general anesthesia and using single lung ventilation. The lower third to half of the left stellate ganglia, together with T2-T4 thoracic ganglia, were removed. All patients underwent either left or bilateral CSD, at discretion of the treating physician preference. Histological confirmation of neuronal cell bodies within the ganglia was obtained for all patients

Echocardiographic assessment

data was retrospectively obtained from two-dimensional transthoracic exams performed by qualified personnel as reported in supplementary table 1.

Statistical analysis

Continuous variables were assessed as mean ± standard deviation (SD) or median (interquartile range [IQRs]) and categorical variables as percentages. Cox proportional hazard models were used to assess predictors of death/orthotopic heart transplant (OHT), competing risk models for predictors of sustained VT/ICD shocks. Nine potential predictors were assessed: age, LVEF, NYHA class, chronic kidney disease (CKD), history of AAs, LAVI, left ventricular end diastolic volume index (LVEDVI), ratio between LAVI and LVEDVI (LAVI/LVEDVI). A left side procedure only (LCSD) was not included in the models because its independent impact on outcome has already been reported[3] and the majority of patients in this dataset underwent BCSD. The p values for comparing changes before versus after BCSD were computed using the Wilcoxon test for continuous variable and the Chi-Square test for categorical variables. A p value of 0.05 was considered significant. Computations were carried out using SAS 9.4 (SAS Institute, North Carolina).

Follow up

Follow up data after CSD were obtained through medical records. The primary endpoint included any ICD shock or sustained VT (30 seconds) below ICD detection, death or OHT. Secondary outcomes included AAs recurrences requiring treatment, inappropriate ICD

shocks, need for pacing upgrading, transitory ischemic attack/stroke and need of RDN for VTs. Echocardiographic, clinic and ICD data for each follow up visit were collected. For patients not followed at the institutions where CSD was performed, referring cardiologists were contacted.

Results

Between April 2009 and June 2018, 91 patients (56 ± 13 years, 15% female) with SHD underwent left (n=15, 16%) or bilateral CSD. Baseline clinical and echocardiographic characteristics at t CSD in the overall population and according to AAs history are shown in table 1 and in table 2, respectively. Mean LVEF was 34 ±14% (n=91).Most patients (84%) presented with NYHA functional class   II ; 75% had non-ischemic cardiomyopathy (NICM).Specific etiologies for cardiomyopathies are reported in supplementary table 2

A history of AAs before CSD was present in 43 patients (47%).. Except for the 4 patients with permanent AF (4%), the others were all free from ongoing AAs at the time of CSD. Most patients (n=35) had paroxysmal (n=21) or persistent (n=11) AF; in 2 patients the type of AF was unknown. Among them, 7/35 (2 paroxysmal and 5 persistent) had previously undergone AF ablation (5 transcatheter and 2 surgical) and 30/35 (85%) were on either class III (21 amiodarone, 5 sotalol and 2 dofetilide) or I AADs (propafenone, n=2) at CSD. Additionally, 4/35 (11%) patients had recently stopped amiodarone (n=3) or sotalol (n=1) because of side effects and 13/35 (37%) had an ongoing resynchronization therapy. Accordingly,, among the 46 patients (57% of which had a history of AAs) with available dual chamber ICD data before CSD and not in permanent AF (median ICD monitoring time before CSD 8 months, IQR 3–23 months), AAs burden was very low (median 0.0%, IQR 0.0–0.1%).

The only clinical difference between patients with and without a history of AAs was a higher prevalence of sleep apnea syndrome in the former (Table 1). Patients with AAs also had a higher prevalence of left atrial enlargement (LAVI>34 ml/m^2), of RV enlargement and of severe diastolic dysfunction (grade III) as well as a higher LAVI/LVEDVI ratio (Table 2). Finally, except for oral anticoagulants, ongoing drugs inthe 2 groups were similar (Supplementary table 3).

AAs and LAVI impact on CSD outcome

The median follow up after CSD was 14 months (IQR 4–37). Overall, 27 patients (30%) died before being transplanted, 17 patients underwent OHT (19%) and 53 had sustained VT/ appropriate ICD shocks (58%) during follow-up.

In the competing risk model for sustained VT/ICD shock, neither LAVI nor a history of AAs was associated with the outcome. A pre-procedural NYHA class III (HR= 7.23, 95% CI 1.50–35.39, p=0.01) and IV (HR= 9.07, 95% CI 1.18–69.5, p=0.03), as compared to class I, were the only independent predictors of sustained VT/ICD shocks, while NYHA class II had a borderline significance (HR= 3.77, 95% CI 0.85–16.64, p=0.08).

In the Cox models for death/OHT, a history of AAs was not predictive, while LAVI was statistically significant both at univariable (HR= 1.02 per unit, 95% CI 1.01–1.03, p<0.01, c stat for LAVI alone: 0.720) and at multivariable analysis. In the multivariable model controlled for age, three independent predictors for death/OHT were identified: LAVI (HR=1.02 per unit, 95% CI 1.005–1.035, p<0.01), LVEF (HR=0.95 per unit, 95% CI 0.92–0.98, p <0.01) and CKD (HR= 2.04, 95% CI 1.08–3.87, p=0.03) (c stat=0.779 for model).

Secondary outcomes after CSD

Excluding the 4 patients in permanent AF, only 3/87 patients had either episodes of AAs requiring treatment (n=2, electrical cardioversion in one case, three inappropriate ICD shocks in the other) or progression to permanent AF (n=1) after CSD (Table 3). Overall, only 1 patient who had not undergone AV node ablation before CSD (1%) suffered inappropriate ICD shocks due to AAs after CSD, as compared to 4/85 patients (5%) before; none of the 4 patients suffering inappropriate ICD shocks due AAs before CSD (mean 4 ± 2 shocks/patient) had recurrences after CSD.

Finally, 4/20 patients (20%) with a single right ventricular lead at the time of CSD, underwent ICD upgrading during follow up: 2 with the addition of an atrial lead only (respectively 110 and 123 days after BCSD), the remaining with the addition of both an atrial and a left ventricular lead (respectively 35 and 345 days after BCSD). The need for upgrading was 4/18 (22%) in patients who received BCSD and 0/2 (0%) in those undergoing LCSD (p=1.00)

Changes in atrial rhythm after BCSD (N=34)

ICD report with atrial sensing before and after BCSD were available for 34 patients (52 ± 14 years, 24% female, mean LVEF $41\pm 12\%$, 41% with a clinical history of AAs), including 2 ICM, 1 mixed CMP and 31 NICM. Specific etiologies of CMPs are reported in supplementary table 2, while figure 1 clarifies how these 34 patients were selected. The median ICD monitoring time was 8 months (IQR 5–17) before and 15 months (IQR 8–21) after BCSD (p=0.01). Among the 14 patients with a history of AAs, most (n=8) suffered paroxysmal AF, only 3 had persistent AF. Overall, 4/14 patients had previously undergone ablation for AAs (AT/AFL ablation in 2 patients, persistent AF ablation in the others) and 9/11 (82%) were either on Class III (n=7) or I (n=2) AADs. Mean LAVI in patients with AAs history was 38 ± 21 ml/m^2, as compared to 24 ± 8 ml/m^2 in patients without AAs (p=0.02).

During follow-up, 2 patients died (6%) and 6 had OHT (18%, table 3). The AT/AF burden, already low before BCSD, remained stable after the procedure; the percentage of patients with AAs episodes lasting more than 24 hours was unchanged as well. However, the percentage of atrial pacing increased from a median of 28% to 72% (p <0.01), in association with a significant increase in the programmed lower rate interval (LRI) for atrial pacing (from 59 ± 12 to 64 ± 11 bpm, p<0.01). At the same time, ventricular pacing percentages, NYHA functional class, cardiac chambers volumes and biventricular function were stable, but a mild increase in LV end diastolic diameter (from 57 to 60 mm, p <0.01) was noticed, as reported in table 4. Of note, the monthly drug index did not change, but the mean daily

dose of amiodarone/patient was significantly lower at last follow-up (from 279 ± 94 mg to 196 ± 118, p=0.04), as reported in the supplementary table 4. Finally, the number of ICD shock/patient was significantly reduced after BCSD from a median of 8 to a median of 1 (p <0.01).

Discussion

AAs and LAVI impact on CSD outcome

In our cohort of patients with SHD undergoing CSD a history of AAs (mainly AF) was common, but AAs burden was very low. AAs were not associated with outcome , while LAVI was independently associated with death/OHT occurrence.

The association between SHD, HF and AAs is well known. Yet, the prevalence and the prognostic impact of AAs in patients with SHD vary consistently across studies. A large meta-analysis (6) of patients with an ICD recently showed that AF increases the risk of mortality and ICD appropriate shocks; this association seems to be lost after VT ablation (7). but was suggested (3) after CSD. However, the potential relationship between AF and mortality/OHT after CSD was never assessed in a multivariable model. Our study is characterized by a long follow-up, a detailed characterization of AAs before CSD and an adequate power to specifically assess the impact on AAs on outcomes after CSD. Importantly, since the burden of AAs detected through the ICD was not provided in any of the abovementioned studies, the lack of association with outcomes could be partially related to a very low AT/AF burden at the time of VT ablation/CSD, as underlined by our data.

Left atrial enlargement as assessed by LAVI is strongly related to LV filling pressure independently from LVEF (8). Of note, in our population only 10% of patients presented with significant mitral valve regurgitation (MR); therefore, this variable was not included in our models, despite its established prognostic value in CMP patients (9). Potential explanations for the observed prevalence of MR include relatively preserved LV dimensions in our study population, different types of CMPs and previous successful mitral valve surgery. LAVI has been associated with an increased risk of all-cause mortality, cardiovascular mortality and HF hospitalization in a broad spectrum of cardiomyopathies (10). Yet, LAVI prognostic impact in patients with SHD and refractory VTs is largely unexplored. Our data show that in patients undergoing CSD for VTs (largely in sinus rhythm at the time of CSD) LAVI is independently associated with overall mortality and OHT but not with VT recurrences. The lack of association between LAVI and VTs in our population could be related to the ongoing antiarrhythmic interventions, including AADs, VT ablation and CSD. It is particularly tempting to speculate that the potential detrimental effect of left atrial enlargement in terms of increased sympathetic signaling and VTs susceptibility might be mitigated by CSD.

Changes in atrial rhythm after CSD

AAs burden at BCSD was very low, despite almost half of the patients had a history of AAs. The predominance of patients with paroxysmal AF and the high use of AADs because of VTs are likely to be the main responsible for these findings, together with the small % of

patients who had previously received catheter ablation for AAs. Accordingly, LAVI was largely preserved in this subgroup of patients (n=34). After BCSD there was a mild increase in LV end diastolic diameter but AAs burden stayed stable, In this setting, a protective effect of BCSD towards AAs onset/progression seems plausible, also considering that the mean doses of amiodarone were significantly reduced after BCSD.

The mechanisms involved in AAs onset and maintenance in SHDs are complex, but cardiac ANS is certainly involved (1). Pre-clinical data showed that the sympathetic neuronal sprouting that follows ventricular MI affects the entire heart and leads to an increased AF susceptibility (11). Sympathetic activation is thought to promote AAs mainly through focal mechanisms such as enhanced automaticity and triggered activity. Such mechanisms may act as trigger for AF on a susceptible substrate or as AT/AF maintaining driver in case of persistent rapid firing (1). Yet, in patients with paroxysmal AF undergoing AF ablation, temporary unilateral SGB not only reduced AF inducibility/duration, but also prolonged atrial effective refractory period, potentially suggesting additional re-entrant related functional mechanisms for sympathetic activation mediated pro-arrhythmic effects (5). The relatively small LA dimensions in the studied population underscore the potential contribution of local/functional mechanisms as opposed to mechanisms mainly related to LA enlargement/fibrosis in promoting susceptibility to AAs.

Finally, we described for the first time the impact of CSD on cardiac chronotropy in patients with SHD. In our cohort, almost one fourth of patients with a single ventricular lead before CSD underwent atrial catheter implantation after the procedure; all of them had received BCSD. Among patients who already had a dual chamber ICD before BCSD, a mild but significant increase in the programmed lower rate interval (LRI) for atrial pacing was noticed after BCSD, in association with a consistent increase in the percentage of atrial pacing over time.

Previous canine experiments (12), combined with recent optogenetic studies in mouse (13), suggest that the right stellate ganglion plays a pivotal role in the neuronal circuits that control heart rate (HR). In conscious dogs both right and bilateral stellectomy (but not left) were associated with significantly lower resting HR and peak HR during exercise (12). The impact of temporary right SGB on HR in humans is more controversial (5, 14, 15. The only available study assessing the acute effects of percutaneous stellate block on sinus node chronotropism in patients with SHD, including 9 patients, showed a significant increase in corrected sinus node recovery time after SGB (particularly right SGB) without changing in HR. Patients with SHD have detectable clinical signs of autonomic imbalance characterized by sympathetic hyperactivity and parasympathetic withdrawal. Additionally, stellate ganglia from subjects undergoing BCSD for refractory VTs showed signs of inflammation, neurochemical remodeling, and oxidative stress (16). In this setting BCSD is expected over time not only to reduce sympathetic drive to the heart, but also to improve vagal control both at the central and at the peripheral level (17). The increased parasympathetic drive to the sinus node after BCSD may contribute to explain the impact on resting HR despite ongoing polytherapy with BBs and AADs. Of note, patients are expected to be more active in the months after CSD due to an overall improvement in the quality of life related to the highly significant reduction of ICD shocks (18).

Taken all together, our findings suggest that patients with a single lead ICD and/or without ICD undergoing BCSD should be monitored for the potential need of atrial pacing, particularly in case of preexisting bradycardia. Of course, AADs down titration should be tried first, albeit the optimal timing for trying AADs down titration after BCSD has not being established yet.

Limitations—Data were collected retrospectively and are not complete for all variables; yet, the percentage of missing data is overall low. ICD programming was left to the discretion of the treating physician, therefore was not uniform. Finally, despite being performed by qualified personnel, the echocardiographic evaluations were neither centralized nor blinded.

Conclusions—A history of atrial arrhythmias was frequent in patients with SHD and refractory ventricular arrhythmias undergoing CSD, but did not affect the outcome. LAVI, on the other hand, was an independent predictor of death/orthotopic heart transplant. The burden of atrial arrhythmias, already low at baseline, stayed stable after BCSD despite a mild progression of left ventricular enlargement, suggesting a protective effect of BCSD.

Finally, a relatively high need for dual chamber upgrading was observed after BCSD, combined with a significant increase in the percentage of atrial pacing in subjects who already had an atrial catheter. These findings suggest that subjects with a single lead ICD and/or without ICD undergoing BCSD should be monitored for the potential need of atrial pacing.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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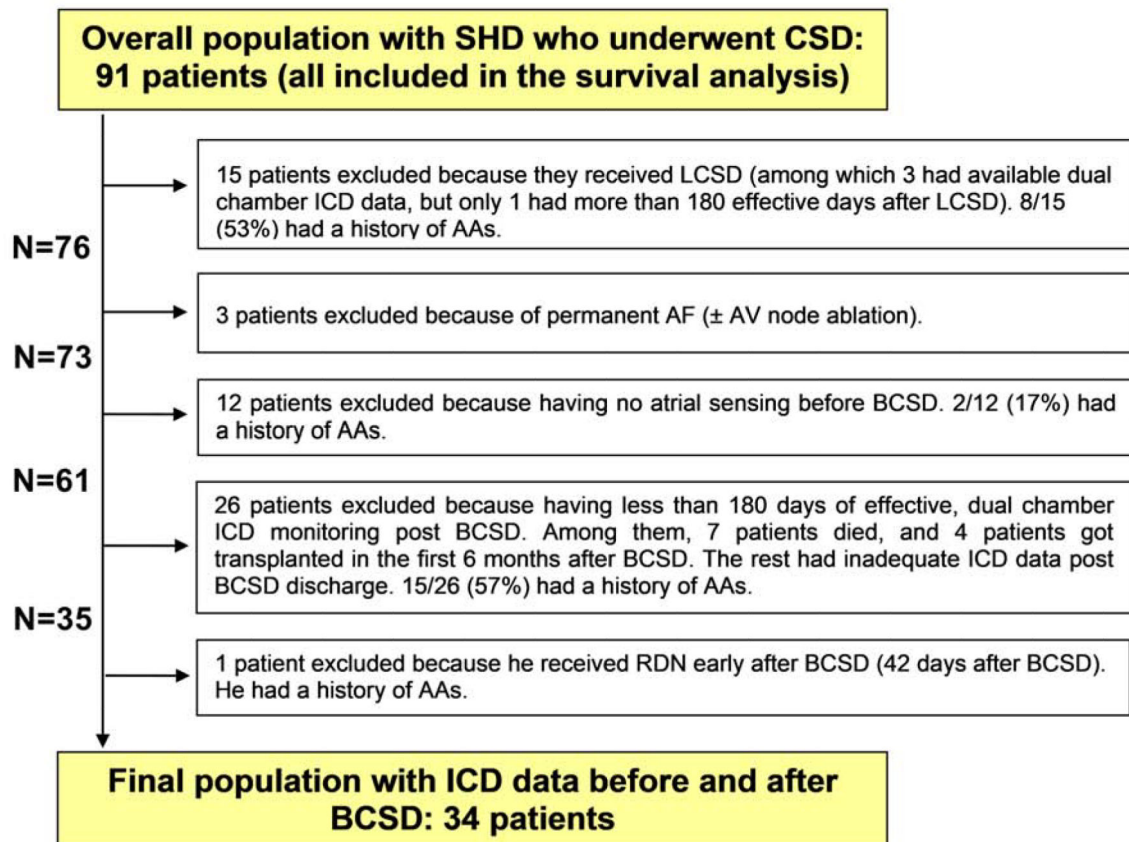
Figure 1:

flowchart of the 34 patients included in the analysis on atrial rhythm and atrial pacing. AAs= atrial arrhythmias; AF= atrial fibrillation; BCSD= bilateral cardiac sympathetic denervation; LCSD= left cardiac sympathetic denervation; SHD=structural heart disease.

Table 1:

Baseline characteristics of the study population at CSD

	All patients, N=91	History of AAs, N=43	No AAs, N=48
Age	56 ± 13	59 ± 13	54 ± 13
Body mass index	29 ± 6	29 ± 5	29 ± 6
Female gender	14 (15)	5 (12)	9 (19)
Hypertension	52 (57)	28 (65)	24 (50)
Hyperlipidemia	47 (52)	23 (54)	24 (50)
Diabetes	21 (23)	7 (16)	14 (29)
TIA/Stroke	12 (13)	7 (16)	5 (10)
Sleep Apnea Syndrome	19 (21)	13 (30)	6 (12) [**]
COPD	8 (9)	4 (9)	4 (8)
CKD (GFR <60 ml/min/m^2)	31 (34)	16 (37)	15 (31)
Creatinine (mg/dL)	1.2 ± 0.7	1.3± 0.8	1.2 ± 0.4
NICM	68 (75)	33 (77)	35 (73)
Previous heart surgery, excluding LVAD	24 (26)	11 (26)	13 (27)
- CABG	9 (10)	5 (12)	4 (8)
- Aortic valve replacement	7 (8)	3 (7)	4 (8)
- Mitral valve replacement/repair	6 (7)	2 (5)	4 (8)
ICD	89 (98)	43 (100)	46 (96)
CRT-D	30 (33)	17 (40)	13 (27)
Age from first ICD implant to CSD	5 (3–9)	5 (2–9)	5 (3–9)
Atrial lead/sensing	76 (83)	39 (91)	37 (77)
Atrial lead	71 (78)	37 (86)	34 (71)
NYHA Class I/II/III/IV	9/49/27/6 (10/54/30/6)	4/25/11/3 (9/58/26/7)	5/24/16/3 (10/50/33/6)
LVAD	3 (3)	1 (2)	2 (4)
ES history	67 (74)	32 (74)	35 (73)
Previous VT ablation	74 (81)	33 (77)	42 (85)
History of AAs	43 (47)	43 (100)	
- AT/AFL only	4 (4)	4 (9)	
- Paroxysmal/Persistent AF	35 (38)	35 (81)	
- Permanent AF	4 (4)	4 (9)	
Previous AT/AF ablation	9 (10)	9 (21)	
Previous AV node ablation	3 (3)	3 (7)	
Inappropriate ICD shocks	6 (7)	3 (7)	3 (6)
- Due to atrial arrhythmias	4 (4)	3 (7)	1 (2)
BNP at CSD admission [*]	277 (83–762)	562 (118–809)	196 (75–682)
Number of sustained VT/ICD shocks in the year before CSD	8 (4–17)	7 (4–16)	10 (5–17)

Values are reported as mean ± SD, n (%), or median (interquartile range). AAs= atrial arrhythmias; AF= atrial fibrillation; AFL= atrial flutter; AT= atrial tachycardia; AV= atrioventricular; BNP= brain natriuretic peptide; CABG= coronary artery bypass graft, CKD= chronic kidney disease;

COPD= chronic obstructive pulmonary disorder; CRT-D= cardiac resynchronization therapy-defibrillation; CSD= cardiac sympathetic denervation; ES= electrical storm; LVAD= left ventricular assist device, NICM= nonischemic cardiomyopathy; NYHA= New York Heart Association; TIA= transitory ischemic attack; VT= ventricular tachyarrhythmias.

[*]
BNP data was available for 60 of 91 patients.

[**]
= p<0.05 between the 2 groups (patients with and without AAs).

Table 2:

Echocardiographic data at CSD

	Available, n	History of AAs, n=43	No AAs, n=48
Body surface area, m²	43/48	2.1 ± 0.2	2.0 ± 0.2
LVEF, %	43/48	33 ± 15	35± 12
LVEDD, mm	38/44	61 ± 11	60 ± 9
LVEDVI, ml/m²	40/43	90 ± 53	87 ± 34
- LVEDVI> 75		19 (47)	26 (60)
LAVI, ml/ m²	40/43	50 ± 31	35 ± 18
- LAVI > 34		27 (68)	17 (35) *
LAVI/LVEDVI	40/43	0.62 ± 0.44	0.43 ± 0.19 *
RAVI, ml/m²	31/36	34 ± 20	30 ± 12
RV dilation	42/46	23 (55)	13 (28) *
RV dysfunction	41/47	21 (51)	21 (46)
Valvular stenosis/regurgitation moderate	43/47	7 (16)	5 (11)
-Mitral regurgitation moderate		5 (12)	4 (8)
Systolic PAP, mmHg	36/41	34 ± 13	30 ± 9
Severe diastolic dysfunction (grade III)	33/39	14 (42)	7 (18) *

Values are reported as mean ± SD, n (%), or median (interquartile range). AAs= atrial arrhythmias; LAVI= left atrial volume index; LVEDD= left ventricular end diastolic diameter; LVEDVI= Left ventricular end diastolic volume index; LVEF= left ventricular ejection fraction; PAP= pulmonary arterial pressure; RAVI= right atrial volume index; RV= right ventricle.

*
= p<0.05 between groups.

Table 3:

Secondary outcomes after CSD

	All patients, n=91	Subgroup of 34 with ICD data before and after BCSD
AF electrical cardioversion	1 (1)	1 (1)
ICD inappropriate shocks	1 (1)	0 (0)
- Due to AF	1 (1)	
Transition to permanent AF	1 (1)	1 (1)
ICD Upgrading	4 (4)	1 (3)
- Right atrium lead	2 (2)	0 (0)
- Right atrium + left ventricle lead	2 (2)	1 (3)
Stroke/TIA	1 (1), TIA *	1 (3)
AV node ablation	0 (0)	0 (0)
RDN for VTs	8 (9)	4 (12)

Values are reported as n (%). AF=atrial fibrillation; AV= atrioventricular; RDN=renal denervation; TIA= transitory ischemic attack; VTs= ventricular tachyarrhythmias.

*
In absence of documented AF.

Table 4:

Changes before vs after BCSD (n=34)

	n*	Before BCSD	After BCSD	p value-change
ICD data				
AAs burden, %	34	0.0 (0–0.7)	0.0 (0–0.1)	0.49
Atrial pacing, %	29	28 (9–77)	72 (27–92)	<0.01
At least one episode of AAs	34	14 (41)	12 (35)	0.80
Longest AAs 24 hours	32	2 (6)	2 (6)	1.00
AMS rate, bpm	33	174 ± 15	171 ± 14	0.13
Rate response function on	33	11 (33)	17 (52)	0.21
Lower rate interval, ppm	33	59 ± 12	64 ± 11	<0.01
Right ventricular pacing (dual chamber ICD), %	22	1.1 (1–6.7)	3 (0.7–20.3)	0.21
Biventricular pacing, %	8	95.5 (91.9–96.4)	97.1 (95.7–98.3)	0.64
Echocardiographic data				
LVEF, %	27	40 ±12	37 ± 13	0.17
LVEDVI, ml/m²	21	72 ± 26	75 ± 22	0.49
LVEDD, mm	23	57 ± 8	60 ± 9	<0.01
LAVI, ml/m²	22	30 ± 17	35 ± 22	0.51
LAVI > 34	22	8 (36)	7 (32)	0.75
RAVI, ml/ m²	19	26 ± 10	34 ± 21	0.34
RV dysfunction	24	7 (29)	7 (29)	1.00
Valvular stenosis/regurgitation moderate	25	3 (12)	7 (28)	0.16
Clinical data				
Number of sustained VT/ ICD shocks	34	8 (3–15)	1 (0–4)	<0.01
NYHA class	34	2.0 (2–2)	2.1 (2–3)	0.50
Drug Index/Month	34	91 (61–122)	91 (59–122)	0.76

Values are reported as mean ± SD, n (%), or median (interquartile range). AAs= atrial arrhythmias; AMS= automatic mode switch; LAVI= left atrial volume index; LVEDD= left ventricular end diastolic diameter; LVEDVI= left ventricular diastolic volume index; LVEF= left ventricular ejection fraction; RAVI= right atrial volume index; RV= right ventricle. n* = patients with paired data (before and after BCSD).