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ORIGINAL ARTICLE

Long-term outcomes of electrical storm patients listed for urgent heart transplantation but not transplanted acutely

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Abstract

Aims Refractory electrical storm (ES) is a life-threatening condition in which heart transplantation (HTx) can be proposed. Nevertheless, the shortage of donors and subsequent outcomes question its place as a rescue strategy. We aim to describe the prognosis of ES patients listed for HTx but not transplanted.

Methods and results Patients registered on urgent HTx waiting list for refractory ES without being transplanted during initial hospitalization were retrospectively included in five French centres from 2010 to 2022. The primary endpoint was 1-year all-cause mortality. Forty patients were included [90% men; 56.5 (50.0–61.3) years old; 63.6% and 24.2% dilated and ischaemic cardiomyopathies]. Among them, 84.6% received amiodarone, 64.1% received beta-blockers; 50.0% required deep sedation, 35.0% mechanical circulatory support, 10.0% stellate ganglion block; and 57.5% underwent catheter ablation. At 1 year, 20 patients (50.0%) died, including 14 in-hospital deaths (35.0%). Within six patients who died post-discharge, four previously underwent HTx, and one received VAD implantation. Twenty patients (50.0%) were still alive at 1 year: 10 underwent HTx, 1 received VAD implantation followed by subsequent HTx, while another underwent VAD implantation as destination therapy. Finally, five (12.5%) were removed from the HTx waiting list due to functional improvement, distinguished by a median LVEF of 45.0% (20.0%–45.0%). The remaining three patients (7.5%) were still registered on HTx waiting list.

Conclusions Refractory ES is a critical condition with high short- and long-term mortality. While HTx serves as a rescue strategy, rhythm management can sometimes overcome the critical phase, facilitating subsequent HTx under more favourable conditions or even allowing removal from the HTx waiting list.

Keywords Advanced heart failure; Electrical storm; Heart transplantation; Mortality; Prognosis

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Introduction

Electrical storm (ES) is defined by the occurrence of ventricular arrhythmia (VA) that occurs three or more times within 24 h (separated by at least 5 min), each requiring termination by an intervention like antiarrhythmic drugs, anti-tachycardia pacing (ATP) or cardioversion/defibrillation.[1] In patients with implantable cardioverter defibrillators (ICDs), ESs have been reported to occur in 4% to 7% of patients with a primary prevention indication,[2,3] and 10% to 28% in those for secondary

prevention,[4,5] associated with a decline in quality of life and an increased combined risk of death, heart transplantation (HTx) and hospitalization for heart failure (HF).[6]

ES severity can range from recurrent asymptomatic VA episodes terminated by ATP to a life-threatening haemodynamic instability. The management may involve addressing acute triggers (myocardial ischaemia and electrolyte disorders), administering antiarrhythmics, catheter ablation, and, in refractory cases, deep sedation, sympathetic modulation and/or acute mechanical circulatory support (aMCS).[1]

For patients with persistent rhythm and haemodynamic instability despite optimal treatment, HTx stands out as a potential rescue strategy, albeit with substantial post-operative mortality.[7] Besides, the occurrence of an ES embodies a crucial turning point in the progression of HF,[8] indicating the depletion of cardiac physiological reserves.[9,10] In these cases, even if rhythm normalization is achieved, the concomitant progression of advanced HF inevitably overtakes the patient. Conversely, in certain instances, ES constitutes the main issue, triggering haemodynamic instability.[11] Cases of this nature may exhibit favourable outcomes concerning HF progression, contingent upon effective rhythm control. Anticipating the reoccurrence of rhythmic disturbances and the pace of consecutive myocardial decline is essential to reserve HTx only for refractory ES patients in whom there is no hope of myocardial recovery.

HTx remains the treatment of choice for eligible patients with advanced HF[12]; however, its role as a rescue strategy in refractory ES remains unclear and is limited by the shortage of donors[13] and the associated organ failures or haemodynamic instability impacting prognosis. Therefore, a significant proportion of refractory ES patients may remain ineligible for transplantation, either due to the unavailability of a suitable donor or due to death before donor availability. As very few data exist on this subject, the aim of this multicentre study was to determine prognosis and outcomes of patients managed for ES, listed for HTx, and ultimately not receiving cardiac graft during the acute phase.

Materials and methods

Patient population

This is an observational, retrospective, multicentre study assessing the profile and prognosis of consecutive patients who experienced a refractory ES leading to HTx listing in five French tertiary centres from 2010 to 2022. Refractory ES was defined as the recurrence of ventricular arrhythmias despite optimal multimodal treatment (antiarrhythmics, deep sedation, stellate ganglion blockade and aMCS) carried out according to the usual practices of local Heart Teams. Patients were included if they experienced a refractory ES and were subsequently listed for HTx in super-urgent status whether they were or not already registered before ES on regular HTx list. Exclusion criteria comprised adults under legal protection or those aged $<$18 years old.

Data collection and follow-up

Usual baseline data on demographic characteristics, cardiovascular risk factors (smoking, hypertension, dyslipidaemia and diabetes mellitus), co-morbidities (chronic kidney failure, active cancer and pulmonary disorders) were recorded. HF history (type and duration of cardiomyopathy, treatments and prior transplantation listing), left ventricular ejection fraction (LVEF), history of VA prior to ES [ventricular tachycardia (VT) and ventricular fibrillation (VF)] and ICD implantation were collected. In-hospital data including ES treatment (antiarrhythmic drugs, catheter ablation, invasive ventilation, aMCS and stellate ganglion blockade), clinical presentation, biological parameters (natriuretic peptides, troponin and lactates), LVEF and ES triggers were obtained from medical files. Long-term follow-up was performed according to each local Heart Team protocol. Unfortunately, the SCAI SHOCK stage classification[14] was not yet available at the time of our study, which is why these data could not be prospectively collected. However, by relying on the method previously described by Thayer et al.,[15] we were able to retrospectively determine the maximum SCAI classification stage reached during hospitalization based on the total use of vasopressors, inotropes, and aMCS devices.

Endpoints

The primary endpoint was 1-year all-cause mortality. Secondary endpoints included the number of ventricular assist devices (VADs) implanted during the index hospitalization and at 1-year follow-up, the number of HTx performed after 1 year of follow-up (having HTx during the index hospitalization could not be an endpoint as these patients were excluded), and in-hospital all-cause mortality. Additionally, we explored the causes of mortality, HTx and VAD, when applicable.

Statistical analysis

Continuous variables are reported as medians and interquartile ranges (IQR) when appropriate. Categorical variables are described as frequencies and percentages. Comparisons were made using Mann–Whitney non-parametric test for continuous variables and chi-square test or Fisher's exact test for categorical variables. All tests were two-tailed. A value of $P \leq 0.05$ was accepted as statistically significant. Analyses were performed using R software [version 4.3.2 (2023-10-3)].

Ethics

According to French ethics and regulatory law (Public Health Code), all patients received information about anonymized data collection. Written informed consent for participation was not required for this study in accordance with the national legislation. The study was registered by the Toulouse University Hospital (registration number: RnIPH 2024-71-59) and covered by the MR-004.

Results

Baseline characteristics

A total of 40 patients were included in the study, whose characteristics are summarized in *Table 1*. During the same period, 2919 patients were listed for HTx for any reason and 2224 were finally transplanted in our five centres. In brief, the median age of the cohort was 56.5 years (50.0–61.3), with 36 male patients (90.0%). Fifteen patients (37.5%) had previously experienced an ES, and 1 (2.5%) was already registered on HTx waiting list. Only seven patients (17.5%) had no history of cardiomyopathy until the occurrence of ES. Among the underlying heart diseases, dilated cardiomyopathy (DCM) was reported in 21 patients (63.6%), while ischaemic cardiomyopathy (ICM) was observed in 8 (24.2%). Notably, within the DCM subgroup, pathogenic mutations in LMNA (four patients), DSP (two patients), and MYH7 (one patient) were identified. The remaining patients were diagnosed with either arrhythmogenic right ventricular cardiomyopathy or cardiac sarcoidosis. The median latest known LVEF was 29.0% (20.0–35.0). Of note, 29 patients (72.5%) had an ICD, of which 17 were implanted for secondary prevention (58.6%), and 26 patients (65.0%) had a history of VA.

Prior to ES onset, 25 patients (64.1%) were receiving beta-blocker therapy, and 16 patients (41.0%) were prescribed amiodarone. The additional cardiac arrhythmia history is described in *Table S1*.

As shown in *Table 2*, initial presentation of cardiogenic shock was reported for 21 patients (52.5%), with a baseline median LVEF of 21.0% (20.0–30.0).

Characteristics and management of the causal ES

Table 3 presents an overview of the characteristics and management of ES. Ten patients (25.0%) experienced a triggering event, primarily associated with ST-segment elevation myocardial infarction (STEMI). Following the onset of ES, amiodarone (administered in 84.6% of cases), beta-blockers (64.1%), magnesium sulfate (51.3%) and lidocaine (41.0%) were the primary anti-arrhythmic medications administered. Despite the use of these medications, ES management required deep sedation in 20 patients (50.0%), aMCS support in 13 patients (32.5%), predominantly ECMO (92.3%) and stellate ganglion block in four patients (10.0%). VT ablation was performed in 23 patients (57.5%).

Short and long-term outcomes

Among the 40 included patients, 20 (50.0%) died at 1 year. First, 10 patients (25.0%) experienced in-hospital mortality, including two due to refractory VA, two from end-stage HF (both with VA recurrences) and five due to other complications (sepsis and stroke) (*Figure 1*).

Additionally, six patients (15.0%) underwent in-hospital VAD implantation (five left VAD and one biventricular VAD), with only two in-hospital survivors: one as destination therapy (DT), and the other as bridge to transplantation (BTT). Therefore, a total of 26 patients (65.0%) were discharged from the hospital, among whom 25 were still registered on the transplant list (including one VAD in BTT).

After 1 year of follow-up, 15 patients (37.5%) eventually underwent HTx (nine for recurrent VA and six for end-stage HF), with four of them dying subsequently. Additionally, two patients (5%) received VAD implantation (one as a BTT strategy who was subsequently transplanted and the other resulting in immediate post-operative death). One patient died without previous HTx or VAD (unknown aetiology).

Overall, eight patients underwent VAD implantation (six in-hospital and two after discharge), with five deaths (62.5%) occurring in the postoperative period. Two patients subsequently underwent transplantation as BTT, and the last patient was transferred to a DT strategy.

Eventually, 20 patients (50.0%) were still alive at 1 year: 10 of them had undergone HTx, 1 had undergone VAD implantation followed by subsequent HTx, while another patient underwent VAD implantation as destination therapy. Of the remaining eight patients, five (12.5%) were removed from the HTx waiting list due to significant functional improvement, while the remaining three (7.5%) remained listed and awaiting a donor graft.

Comparison between 1-year survivors and non-survivors

Non-survivors exhibited a higher prevalence of chronic kidney disease (25.0% vs. 0.0%, $P = 0.047$), presented more frequently in cardiogenic shock initially (85.0% vs. 20.0%, $P < 0.01$) and required wider use of dobutamine (70.0% vs. 30.0%, $P = 0.03$), norepinephrine (35.0% vs. 5.0%, $P = 0.04$)

Table 1 Baseline characteristics of the study population

	Overall population (n = 40)	1-year survivors (n = 20)	1-year non-survivors (n = 20)	p value
Age, years, median (IQR)	56.5 (50.0–61.3)	52.5 (49.0–59.5)	59.0 (54.0–62.5)	0.09
Male sex, n (%)	36 (90.0)	17 (85.0)	19 (95.0)	0.61
BMI, kg/m^2, median (IQR)	26.7 (24.2–29.3) (n = 38)	25.5 (22.5–28.7)	28.0 (25.0–30.5) (n = 18)	0.27
Cardiovascular risk factors, n (%)				
Current smoking	9 (22.5)	3 (15.0)	6 (30.0)	0.45
Dyslipidaemia	18 (45.0)	9 (45.0)	9 (45.0)	1
Hypertension	13 (32.5)	4 (20.0)	9 (45.0)	0.18
Diabetes mellitus	9 (22.5)	3 (15.0)	6 (30.0)	0.45
Myocardial revascularization, n (%)	8 (20.0)	3 (15.0)	5 (25.0)	0.69
PAD, n (%)	2 (5.0)	2 (10.0)	0 (0.0)	0.49
Chronic kidney disease, n (%)	5 (12.5)	0 (0.0)	5 (25.0)	0.047
COPD, n (%)	2 (5.0)	1 (5.0)	1 (5.0)	1
Stroke, n (%)	3 (7.5)	1 (5.0)	2 (10.0)	1
History of cardiomyopathy, n (%)	33 (82.5)	18 (90.0)	15 (75.0)	0.76
Ischaemic	8 (24.2)	3 (16.7)	5 (33.3)	
Non-ischaemic dilated cardiomyopathy	21 (63.6)	12 (66.7)	9 (60.0)	
Cardiac sarcoidosis	1 (3.0)	1 (5.6)	0 (0.0)	
ARVC	1 (3.0)	1 (5.6)	0 (0.0)	
Unknown	2 (6.1)	1 (5.6)	1 (6.7)	
Time from cardiomyopathy diagnosis to ES, n (%)				0.5
<6 months	3 (9.1)	1 (5.6)	2 (13.3)	
6 months–5 years	5 (15.2)	4 (22.2)	1 (6.7)	
>5 years	25 (75.8)	13 (72.2)	12 (80.0)	
Latest known LVEF, %, median (IQR)	29.0 (20.0–35.0)	30.0 (22.8–39.5)	26.0 (20.0–30.0)	0.09
Previous HTx listing, n (%)	1 (2.5)	0 (0.0)	1 (5.0)	1
Baseline NYHA status, n (%)				0.57
I	5 (15.2)	4 (22.2)	1 (6.7)	
II	8 (24.2)	5 (27.8)	3 (20.0)	
III	11 (33.3)	6 (33.3)	5 (33.3)	
IV	8 (24.2)	3 (16.7)	5 (33.3)	
Treatment prior to ES, n (%)				
Beta-blockers	25 (64.1) (n = 39)	5 (25.0)	10 (52.6) (n = 19)	0.19
Amiodarone	16 (41.0) (n = 39)	7 (35.0)	9 (47.4) (n = 19)	0.52
ACEI/ARB	16 (42.1) (n = 38)	10 (50.0)	6 (33.3) (n = 18)	0.34
Sacubitril/valsartan	10 (26.3) (n = 38)	6 (30.0)	4 (22.2) (n = 18)	0.72
MRA	21 (55.3) (n = 38)	11 (55.5)	10 (55.6) (n = 18)	1
Loop diuretics	22 (57.9) (n = 38)	11 (55.5)	11 (61.1) (n = 18)	0.75
iSGLT2	7 (18.4) (n = 38)	6 (30.0)	1 (5.6) (n = 18)	0.09
Anticoagulant	16 (41.0) (n = 39)	7 (35.0)	9 (47.4) (n = 19)	0.52
Antiplatelet agents	13 (34.2) (n = 38)	6 (30.0)	7 (38.9) (n = 18)	0.73
Statin	16 (42.1) (n = 38)	9 (45.0)	7 (38.9) (n = 18)	0.75
Ventricular arrythmias, n (%)	26 (65.0)	15 (75.0)	11 (55.5)	0.32
Ventricular tachycardia	25 (62.5)	13 (65.0)	12 (60.0)	1
Ventricular fibrillation	5 (12.5)	3 (15.0)	2 (10.0)	1
Electrical storm	15 (37.5)	8 (40.0)	7 (35.0)	1
VT ablation	16 (40.0)	7 (35.0)	9 (45.0)	0.75
ICD, n (%)	29 (72.5)	16 (80.0)	13 (62.5)	0.48
Secondary prevention	17 (58.6)	8 (50.0)	9 (69.2)	
Primary prevention	12 (41.4)	8 (50.0)	4 (30.8)	
Single chamber	6 (20.7)	3 (18.8)	3 (23.1)	
Dual chamber	11 (37.9)	5 (31.3)	6 (46.2)	
Resynchronization therapy	12 (41.4)	8 (50.0)	4 (30.8)	

ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; ARVC, arrhythmogenic right ventricular cardiomyopathy; BMI, body mass index; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DOAC, direct oral anticoagulant; HTx, heart transplantation; IQR, interquartile range; MRA, mineralocorticoid receptor antagonist; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; iSGLT2, sodium-glucose cotransporter-2 inhibitors.

and aMCS (50.0% vs. 15.0%, P = 0.04). Comparison of the distribution of SCAI SHOCK stages revealed a significant trend towards a higher proportion of stages D (64.7% vs. 25.0%, $P < 0.01$) among the 1-year non-survivors. No difference was found for other baseline characteristics or therapeutic features, as shown in *Tables 1*, *2* and *3*.

Patients removed from the HTx waiting list after 1-year follow-up

Interestingly, five patients (12.5%) were eventually removed from the HTx waiting list due to significant functional improvement (Tables S2, S3, S4 and S5). Their median age was

Table 2 Clinical, echocardiographic and biological findings at baseline

	Overall population (n = 40)	1-year survivors (n = 20)	1-year non-survivors (n = 20)	P value
Clinical profile, n (%)				
Left heart failure	18 (45.0)	6 (30.0)	12 (60.0)	0.11
Right heart failure	9 (22.5)	3 (15.0)	6 (30.0)	0.45
Cardiogenic shock	21 (52.5)	4 (20.0)	17 (85.0)	<0.01
SCAI stage B	1 (4.8)	0 (0.0)	1 (5.9)	
SCAI stage C	8 (38.1)	3 (75.0)	5 (29.4)	
SCAI stage D	12 (57.1)	1 (25.0)	11 (64.7)	
Blood tests at admission, median (IQR)				
Potassium, mmol/L	4.1 (3.8–4.5) (n = 38)	4.0 (3.8–4.5)	4.1 (3.8–4.5) (n = 18)	0.81
Creatinine, μmol/L	103.5 (80.8–132.5)	90.5 (78.5–125.3)	112.0 (95.3–137.8)	0.17
Bilirubin, mg/L	13.0 (8.0–19.6) (n = 33)	11.0 (7.6–15.1) (n = 17)	13.5 (9.8–19.7) (n = 16)	0.56
ASAT, UI/L	49.0 (33.0–70.0) (n = 37)	43.5 (33.0–63.8) (n = 18)	51.0 (40.0–108.0) (n = 19)	0.16
ALAT, UI/L	38.0 (26.0–63.0) (n = 37)	33.0 (28.0–45.0) (n = 19)	44.5 (26.8–79.3) (n = 18)	0.24
PT, %	79.5 (65.3–84.8) (n = 26)	83.5 (68.8–86.5) (n = 14)	70.0 (64.8–82.3) (n = 12)	0.08
Haemoglobin, g/dL	12.9 (11.1–13.9) (n = 39)	13.2 (12.4–14.2)	12.5 (10.5–13.4) (n = 19)	0.13
Arterial blood lactates, mmol/L	1.4 (1.0–1.8) (n = 31)	1.3 (1.0–1.8) (n = 14)	1.5 (0.9–1.9) (n = 17)	0.75
NT-proBNP, pg/mL	2812.0 (1045.5–5229.5) (n = 24)	1130 (648.0–3924.0) (n = 13)	3251.0 (2264.0–5932.5) (n = 11)	0.11
BNP, pg/mL	612.0 (534.3–1385.8) (n = 10)	559.0 (464.0–665.0) (n = 5)	830.0 (559.0–2442.0) (n = 5)	0.24
Troponin T	198.9 (28.7–1553.3) (n = 20)	149.8 (28.9–1501.0) (n = 13)	899.0 (33.9–3183.5) (n = 7)	0.7
Troponin I	0.65 (0.08–0.72) (n = 6)	0.7 (0.4–1.1) (n = 2)	0.7 (0.4–0.7) (n = 3)	1
Baseline echocardiography				
LVEF, %, median (IQR)	21.0 (20.0–30.0)	21.0 (20.0–41.3)	21.5 (18.8–30.0)	0.38
TAPSE, mm, median (IQR)	18.0 (14.0–19.0) (n = 34)	18.0 (13.5–19.0) (n = 19)	16.0 (14.5–19.0) (n = 15)	0.82
PSVtdi, cm/s, median (IQR)	9.5 (8.9–11.0) (n = 28)	9.2 (8.6–10.0) (n = 18)	10.5 (9.0–11.8) (n = 10)	0.25

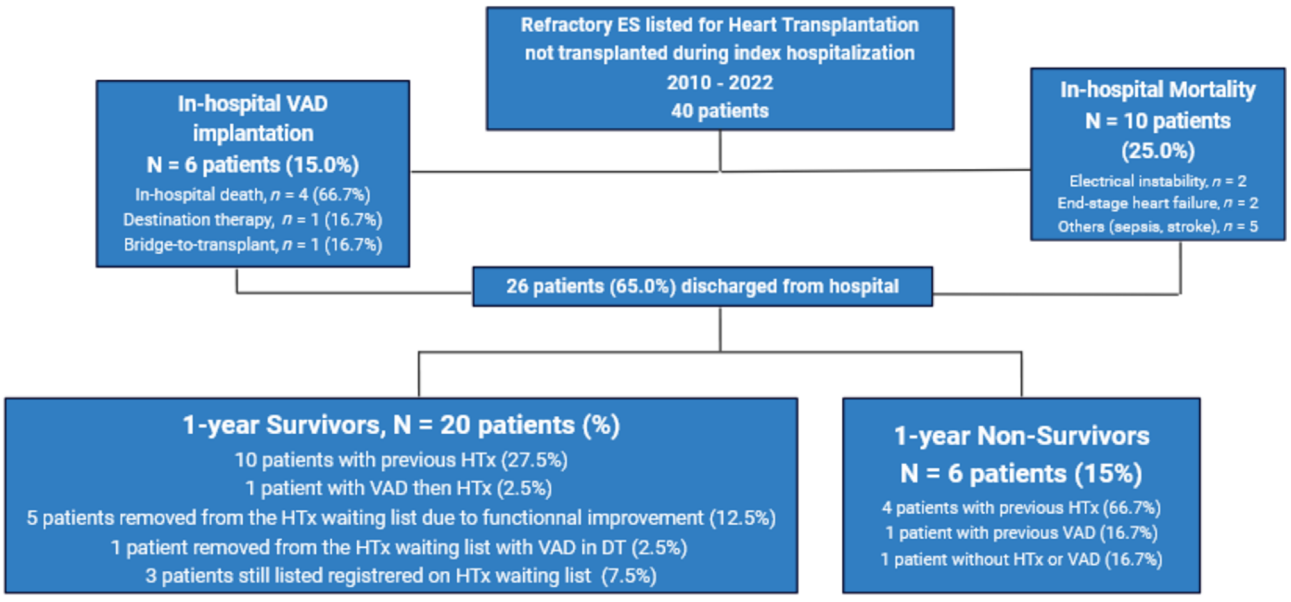
ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; BNP, brain natriuretic peptide; IQR, interquartile range, LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal-pro hormone BNP; PSVtdi = peak systolic S' wave tricuspid annular velocity; PT, prothrombin time; TAPSE, tricuspid annular plane systolic excursion.

Table 3 Electrical storm characteristics and management in the overall population

	Overall population (n = 40)	1-year survivors (n = 20)	1-year non-survivors (n = 20)	P value
Initial reason for hospitalization, *n* (%)				0.1
Ventricular arrhythmia (VT, VF, ES)	26 (65.0)	16 (80.0)	10 (50.0)	
STEMI	4 (10.0)	2 (10.0)	2 (10.0)	
NSTEMI	0 (0.0)	0 (0.0)	0 (0.0)	
Cardiogenic shock, heart failure	10 (25.0)	2 (10.0)	8 (40.0)	
Trigger factor, *n* (%)				0.2
STEMI	6 (15.0)	2 (10.0)	4 (20.0)	
NSTEMI	1 (2.5)	0 (0.0)	1 (5.0)	
Hypokalaemia	1 (2.5)	0 (0.0)	1 (5.0)	
Infection	1 (2.5)	0 (0.0)	1 (5.0)	
Hyperthyroidism	1 (2.5)	0 (0.0)	1 (5.0)	
None	30 (75.0)	18 (90.0)	12 (60.0)	
Anti-arrhythmic drugs, *n* (%)				
Beta-blocker	25 (64.1) (n = 39)	17 (85.0)	8 (42.1) (n = 19)	<0.01
Sotalol	0 (0.0) (n = 39)	0 (0.0)	0 (0.0) (n = 19)	NA
Amiodarone	33 (84.6) (n = 39)	16 (80.0)	17 (89.5) (n = 19)	0.66
Lidocaine	16 (41.0) (n = 39)	6 (30.0)	10 (52.6) (n = 19)	0.2
Mexiletine	4 (10.3) (n = 39)	2 (10.0)	2 (10.5) (n = 19)	1
Magnesium sulfate	20 (51.3) (n = 39)	8 (40.0)	12 (63.2) (n = 19)	0.2
Deep sedation, *n* (%)	20 (50.0)	8 (40.0)	12 (60.0)	0.34
Temporary external electrosystolic pacing, *n* (%)	5 (12.5)	2 (10.0)	3 (15.0)	1
Stellate ganglion blockade, *n* (%)	4 (10.0)	2 (10.0)	2 (10.0)	1
VT ablation, *n* (%)	23 (57.5)	13 (65.0)	10 (50.0)	0.52
Time from ES to VT ablation, days, median (IQR)	5.0 (2.5–12.5)	3.0 (2.0–12.0)	8.5 (3.5–14.5)	0.32
Redo VT ablation, *n* (%)	11 (27.5)	6 (30.0)	5 (25.0)	1
Vasoactive and inotrope agents, *n* (%)				
Dobutamine	20 (50.0)	6 (30.0)	14 (70.0)	0.03
Norepinephrine	8 (20.0)	1 (5.0)	7 (35.0)	0.04
Epinephrine	4 (10.0)	0 (0.0)	4 (20.0)	0.11
Levosimendan	0 (0.0)	0 (0.0)	0 (0.0)	NA
Acute mechanical circulatory support, *n* (%)	13 (32.5)	3 (15.0)	10 (50.0)	0.04
ECMO	12 (92.3)	2 (66.7)	10 (100.0)	
IABP	1 (7.7)	1 (33.3)	0 (0.0)	

ECMO, extracorporeal membrane oxygenation; ES, electrical storm; IABP, intra-aortic balloon pump; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; VF, ventricular fibrillation; VT, ventricular tachycardia.

Figure 1 Short and long-term outcomes for patients with refractory electrical storm listed for heart transplantation and ultimately not receiving cardiac graft during the acute phase.



52.0 years (50.0–53.0), and four were known to have DCM, with a median baseline LVEF of 45.0% (20.0–45.0), consistent with less severe hepatic involvement (median total bilirubin level 7.6 vs. 15.0 mg/L, $P = 0.049$).

Three of them underwent VT ablation procedures, which required multiple attempts due to early recurrences (two patients with three procedures in total and the remaining patient with two procedures). Two patients required aMCS, while deep sedation and stellate ganglion blockade were necessary for one patient each.

Patients with history of previous ES

Among the 15 patients (37.5%) who had previously experienced an ES, 10 had history of DCM, and 4 of ICM (1 unknown). They were older (60.0 vs. 55.0 years old, $P = 0.04$), but no difference was found regarding initial presentation, LVEF (25.0% vs. 20.0%, $P = 0.37$), or in-hospital management (beta-blockers, amiodarone or aMCS), except for a less frequently use of deep sedation (26.7 vs. 64.0%, $P = 0.048$). No significant difference was found in the use of VT ablation (40.0% vs. 68.0%, $P = 0.11$) or 1-year mortality (46.7% vs. 52.0%, $P = 1.00$). Seven patients (46.7%) underwent transplantation within the year following discharge, while two (13.3%) were ultimately removed from HTx waiting list due to substantial improvement.

Discussion

In this multicentre retrospective study, we describe for the first time the prognosis and outcomes of patients managed for refractory ES who were listed for HTx but did not receive a suitable donor offer. Our main findings indicate that (1) the 1-year mortality rate is very high, reaching 50%, with 35% of in-hospital deaths; (2) a large proportion of these patients (37.5%) will eventually undergo transplantation within the year following the ES; (3) the utilization of VAD as a bailout strategy is associated with high post-operative mortality (62.5%); and (4) nonetheless, there is a relevant proportion (12.5%) of patients whose functional improvement has been sufficient to warrant removal from the HTx waiting list.

Although HTx is occasionally used in severe cases, its role in refractory ES remains unclear and is not addressed in the latest 2022 ESC guidelines on the management of VA[1] or in the latest guidelines focusing on ES management.[16] Instead, these guidelines offer general statements for patients awaiting HTx, suggesting the consideration of ICD implantation for primary prevention and discussing the use of a wearable cardiac defibrillator.

The detrimental impact of an ES on the course of HF has already been extensively demonstrated,[6,9,17] leading to a significant increase in mortality, prompting the legitimate question of the appropriateness and the timing of HTx. Yet, beyond the shortage of donors, there are several limitations related to HTx in ES, such as the associated organ failures and haemodynamic instability impacting prognosis. In a recent study,[7] Martins et al. described the outcomes of 45 patients who received high urgency HTx within 9 days due to refractory ES. In-hospital mortality rate after transplantation was 28.9%, and 1-year survival was 69%. The authors concluded that refractory ES is a rare indication for lifesaving HTx, although post-operative mortality was substantial. Our study, focused on refractory ES patients who did not receive a suitable donor offer during index hospitalization, provides additional support that HTx remains the main long-term therapeutic alternative, as 15 out of the 26 patients discharged alive eventually underwent transplantation after 1 year of follow-up (nine for recurrent VA and six for end-stage HF). Indeed, HTx offers the valuable advantage of being an effective solution for both rhythm instability and end-stage HF, whereas VADs yield rather disappointing results in refractory ES patients due to right ventricular dysfunction or recurrence of arrhythmias affecting short-term survival.[18] Our findings are consistent with this, as five out of the eight patients who underwent VAD placement died in the postoperative period. Only a minority of patients (eight) finally reached 1 year of follow-up without undergoing HTx or VAD implantation (three still registered on the HTx waiting list and five removed from it due to functional improvement).

Several interpretations and hypotheses can be drawn from these two complementary studies.

Firstly, we add further evidence that ES should be interpreted as a strong marker of current and future myocardial decline, necessitating urgent consideration of HTx for refractory cases, or the initiation of a structured pathway potentially leading to delayed HTx for ES that have been initially countered through maximal medical treatment. Indeed, given their high potential risk of progressing to end-stage HF, we can at least strongly recommend close and regular follow-up of these patients within trained and specialized expert tertiary centres to detect early signs of functional decline that should prompt the implementation of HTx, as this risk persists regardless of rhythm stabilization. These findings deserve to be underlined, as the prospect of performing HTx on an elective basis allows for better preoperative preparation/optimization, generally leading to a higher survival rate with a relatively lower and more predictable cost compared with emergent HTx.[19] Thus, it seems legitimate to initially pursue maximal treatment (including catheter ablation, deep sedation,[20] stellate ganglion block[21] and potentially aMCS), while reserving urgent HTx for cases where these interventions fail or cannot be implemented due to contraindications or intractable haemodynamic instability. These conclusions align with those reported in a 2015 study by Shivkumar et al.[11] that aimed to investigate the associa-

tion between VT recurrence after ablation and survival in patients with scar-related VT, demonstrating that catheter ablation of VT in patients with structural heart disease resulted in a 70% survival freedom from VT recurrence rate at 1 year. Interestingly, freedom from VT recurrence was associated with improved transplant-free survival, regardless of HF severity, with an overall transplant and/or mortality rate of 15% at 1 year. Furthermore, in our study, the most severe prognosis was observed for patients in whom the combination of refractory ES and end-stage HF has led to ultra-severe haemodynamic instability requiring the use of circulatory support measures, especially in the presence of overlapping pre-existing co-morbidities such as chronic kidney disease. However, these patients with co-morbid profiles also face the highest rate of HTx-related complications and post-operative mortality, reinforcing once again the notion of offering maximal treatment for all patients whenever feasible, in order to buy time to perform HTx after preoperative optimization of all co-morbidities and better anticipate potential complications.

Secondly, it should be noted that there is a small but non-negligible proportion of patients (12.5%) in whom a multimodal strategy employing all available therapeutic alternatives finally allowed to withdraw them from the HTx waiting list due to functional improvement. They were notably characterized by a high rate of redo procedures and a median initial LVEF of 45%, suggesting that their underlying heart condition primarily evolved on the arrhythmic side without end-stage HF concurrently, partly explaining the possibility to remove them from the HTx list following management of the acute refractory ES. These findings must, of course, be interpreted cautiously given the very small number of patients involved and the fact that we were unfortunately not able to precisely document the efficacy criteria for each ablation procedure, which introduces a significant risk of bias. Indeed, based on these data, we cannot exclude the possibility that the low rate of redo procedures in the subgroup of patients who remained on the HTx list is actually a consequence of a higher acute success rate of catheter ablation, although this seems unlikely given that of the 15 patients who were transplanted during the follow-up, nine were transplanted due to recurrent ventricular arrhythmias, which still indicates ineffective control of the arrhythmogenic focus. Overall, our data seem to generate the hypothesis that some cases of refractory ES may actually correspond to cardiopathies that, regardless of their phenotype (dilated, ischaemic etc.), primarily evolve in an arrhythmogenic form without significant functional impairment. For these cases, it seems appropriate to maximize antiarrhythmic treatment, possibly through repeated ablation procedures, in order to eliminate the arrhythmogenic focus, which may sometimes allow for postponing the heart transplantation plan.

Interestingly, Heart Teams involved in the study by Martins et al.[7] mainly favoured bypassing VT ablation in favour of direct HTx, as only 20% of patients underwent VT ablation, fearing associated and potentially fatal complications. Whether the initial implementation of maximalist therapy including catheter ablation will defer the need for HTx cannot be precisely predicted based on the data from our single study. However, future research should explore this topic further. Part of the answer lies in refining the stratification of the benefit–risk balance of ablation procedures, which would provide better insight into which patients stand to benefit from such interventions. In this perspective, several tools have already been developed, such as the PAINESD Score,[22] aimed at quantifying the risk of acute haemodynamic decompensation during catheter ablation considering factors such as advanced age, ICM, severe HF status (NYHA III/IV and lower LVEF), associated co-morbidities (diabetes mellitus and chronic obstructive pulmonary disease), use of general anaesthesia and presentation with VT storm. Given that ablations in the context of refractory ES are thus inherently considered high-risk procedures, these data reignite the debate on the role of prophylactic use of aMCS during ablation. Preliminary results suggest promising outcomes,[23] facilitating a more stable haemodynamic environment during the ablation procedure, enabling more reliable VT mapping, and potentially resulting in a reduction of mortality rates,[24] even though controlled randomized data are still lacking to support its widespread adoption in clinical practice. In our study, out of the 13 aMCS devices implanted, 12 were veno-arterial ECMO (the last one was IABP), which aligns with recent guidelines[1,16] where ECMO is preferred because of the level of support provided and its rapid initiation when aMCS is used as rescue therapy in acute haemodynamic decompensation due to refractory, haemodynamically intolerant VA. Besides, microaxial flow pump (Impella) could potentially serve as an alternative, particularly as prophylactic mechanical circulatory support implantation prior to catheter ablation in patients at high risk of developing haemodynamic instability. However, its use is limited by poor haemodynamic efficacy in cases of pre-existing right ventricular dysfunction, contraindication in the presence of a left ventricular thrombus, and the risk of further haemodynamic deterioration in case of recurrent VAs after its placement due to the risk of subsequent right ventricular dysfunction. As only very few observational data exist,[23] further randomized studies could focus on determining the best type of aMCS to prioritize based on each clinical scenario.

Eventually, all of these results may have been influenced by the regulations in place within the French organ allocation system,[25] operating based on several parameters: each patient's personal risk of death on waiting list (calculated with natriuretic peptide concentrations, glomerular filtration rate and total serum bilirubin levels), exceptions such as VAD-related complications or refractory ES, donor-recipient matching (morphology and blood type) and travel time between procurement and transplant hospitals. Moreover, the

score was adjusted for candidates on ECMO, with maximum points at implantation and exclusion from the heart allocation list at day 16. This framework introduces a cognitive bias in the decision-making process of Heart Teams: there might have been instances where emphasis was placed on aMCS to maximize points and facilitate faster access to HTx, at the price of increased risk of aMCS-related complications, such as sepsis and stroke, which were significant causes of mortality in our study. Additionally, the shortage of donors may have led to patients reaching the maximum duration under ECMO without receiving a suitable offer for HTx, after which they were definitively removed from HTx list. Nevertheless, our results suggest that a subset of patients benefited from aggressive rhythm management, allowing for delayed or deferred HTx, even in the most severe cases, since, for instance, two of the patients ultimately removed from HTx list had initially required ECMO support, indicating that even after HTx listing, maximizing rhythm management can improve outcomes without the need for HTx.

Limitations and futures directions

The major limitations include the retrospective nature of the study and a possible referral bias because of the recruitment from tertiary centres in France. The limited sample size of patients with refractory ES did not allow to perform multivariate analyses.

Of note, our cohort was predominantly composed of DCM, with a minority having ICM. Nevertheless, this topic warrants further exploration and refinement based on the type of cardiomyopathy, as each present with specific characteristics.[26] This includes considerations regarding the expected benefits of therapies, particularly catheter ablation, which is known to be more effective in ICM.[27] For instance, some patients had LMNA or DSP pathogenic mutations, which are known to lead to incomplete results of ablation because of extended and rapidly evolutive substrate,[28] warranting a different approach, although we do not have sufficient data to draw conclusions.

Although substantial, the utilization of catheter ablation in this cohort stands at 57.5%. Several factors may explain this relatively low rate: (1) a history of ablation in 40% of patients, for whom a repeat procedure may not have been performed due to low expected benefit; (2) the haemodynamically poorly tolerated nature of VA in the initial phase, complicating mapping and not encouraging the procedure; (3) the data collection period extending up to 2010, during which the availability and technical expertise in ablation procedures were less developed; (4) contraindications to catheter ablation, such as left ventricular thrombus and (5) a severe haemodynamic instability due to the severity of cardiogenic shock resulting in death before being able to perform ablation under stable conditions.

Lastly, while the SCAI SHOCK classification is emerging as a reference standard for cardiogenic shock phenotyping,[14,15] most studies validating the association between the SCAI SHOCK stage and mortality suffer from significant heterogeneity in the definitions used for staging (lactates and hypoperfusion) and were mainly based on cohorts of STEMI-related cardiogenic shock. Through a higher prevalence of stages D in the group of 1-year non-survivors, our study suggests the possibility to apply the SCAI classification in cardiogenic shock related to refractory ES. Nevertheless, larger studies focusing on this specific subpopulation with real-time prospective assignment of the SCAI SHOCK stage are warranted to draw formal conclusions.

Conclusions

Refractory ES represents a critical condition marked by a high 1-year mortality rate affecting half of patients. VAD implantation results in a very high mortality rate, both in the acute phase and in the long term. Long-term outcomes are challenging to predict, mainly leading to the need for subsequent transplantation or eventually functional recovery allowing removal from the transplant list. Future studies should focus on developing models to predict which patients may benefit from deferring transplantation by employing a maximalist interventional approach.

Conflict of interest

The authors declare that they have no conflict of interest.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Rhythmic history of the study population.
Table S2. Baseline characteristics of patients ultimately removed from HTx listing.
Table S3. Rhythmic history of patients ultimately removed from HTx listing.
Table S4. Clinical, echocardiographic, and biological findings of patients ultimately removed from HTx listing.
Table S5. Electrical storm characteristics and management of patients ultimately removed from HTx listing.

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