Supraventricular Tachycardia Causing Left Ventricular Dysfunction

Denise Zaffalon[a], Linda Pagura[a], Antonio Cannatà[a,b], Giulia Barbati[c], Caterina Gregorio[c], Gherardo Finocchiaro[d], Laura Vitali Serdoz[e], Massimo Zecchin[a], Enrico Fabris[a], Marco Merlo[a,*], and Gianfranco Sinagra[a]

There is limited evidence on characterization and natural history of supraventricular tachycardia (SVT)-induced left ventricular (LV) dysfunction. The aim of this work was to characterize clinical features and long-term evolution of SVT-induced LV dysfunction. Patients consecutively admitted with sustained SVT and heart rate >100 bpm as the only known cause of a new onset LV systolic dysfunction (i.e., LV ejection fraction [EF] <50%) were analyzed. Patients were then revaluated periodically. Recovered LVEF (i.e., ≥50%) and a composite of death, heart transplant or first episode of major ventricular arrhythmias were evaluated as study end-points. We enrolled 83 patients. After SVT therapy, 56 (67%) showed a recovered LVEF at the last follow-up of median 54 (interquartile range 36 to 87) months. Seventeen (30%) of those patients had a temporary new drop in LVEF during follow-up associated to high-rate SVT relapse. At presentation, patients with recovered LVEF were younger (52 vs 67 years respectively, p <0.001) and had higher LVEF (34% vs 27% respectively, p = 0.005) compared to non-recovered LVEF patients. Finally, 4% of recovered LVEF patients vs 26% of nonrecovered LVEF patients experienced death/heart transplant/major ventricular arrhythmias during follow-up (p = 0.004). In conclusion, after almost 5 years of follow-up, two-thirds of patients with high-rate SVT causing a newly diagnosed LV systolic dysfunction recovered and maintained normal LV function after SVT control, with a subsequent benign outcome. Long term individual surveillance is required in those patients, as arrhythmic recurrences and new drops in LVEF are common in the long term. **(Am J Cardiol 2021;159:72−78)**

Arrhythmia recognition and treatment are pivotal in the management of heart failure.[1] Despite both supraventricular and ventricular arrhythmias can lead to left ventricular (LV) systolic dysfunction, sustained high-rate SVT (mainly atrial fibrillation [AF]), are the most prevalent cause.[2] Recovery of LV function within 1-6 months after proper treatment of the SVT is a clue to diagnose tachycardia-induced cardiomyopathy.[3,4] However, recurrences of tachyarrhythmias can occur, possibly associated with relapses of LV dysfunction, suggesting a possible genetic predisposition to dilated cardiomyopathy (DCM).[5,6] Studies that analyze the natural history of high rate SVT as the only cause of LV systolic dysfunction, through SVT and LV dysfunction relapses in a long-term follow-up are lacking, making the prognostication and the long-term management of those patients challenging. Therefore, the aims of this study were: (1) to characterize, among patients presenting with a newly diagnosis of LV systolic dysfunction with high rate sustained SVT as the only cause, who normalized LVEF after arrhythmia management and (2) to evaluate the natural history of those patients in terms of recurrences of arrhythmias, LV systolic dysfunction and long-term survival.

Methods

All consecutive patients admitted for new-onset LV systolic dysfunction and concomitant evidence of sustained SVT with heart rate >100 bpm from January 2005 to December 2016 in the Cardiovascular Department of the University Hospital of Trieste were analyzed. Patients included in the study presented with LVEF <50% at baseline evaluation in the absence of any other known possible causes of systolic dysfunction. Therefore, patients with significant coronary artery disease, history of uncontrolled significant hypertension (>160/90 mm Hg or under 2 antihypertension drugs), alcohol intake >80 g/day over a period of at least 5 years, treatments with cardiotoxic drugs, active myocarditis proven at biopsy or cardiac magnetic resonance, moderate to severe organic valve disease, congenital heart disease, implanted pacemakers, cardioverter defibrillator or cardiac resynchronization therapy and advanced systemic disease affecting short-term prognosis were excluded.

[a]Cardiovascular Department, "Azienda Sanitaria Universitaria Giuliano-Isontina", Trieste, Italy; [b]Department of Cardiovascular Science, Faculty of Life Science and Medicine, King's College London, London, UK; [c]Biostatistics Unit, Department of Medical Sciences, University of Trieste, Trieste, Italy; [d]Cardiothoracic Centre, Guy's and St Thomas' Hospital, King's College London, London, UK; and [e]Division of Cardiac Electrophysiology, Department of Cardiology, Klinikum Fuerth, Fuerth, Germany. Manuscript received April 24, 2021; revised manuscript received and accepted August 3, 2021.

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*Corresponding author: Tel: (39) 3476932365.

E-mail address: marco.merlo79@gmail.com (M. Merlo).

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Coronary angiography was performed in patients ≥35 years with cardiovascular risk factors or evidence of significantly elevated high-sensitive troponin levels.[7] All echocardiographic variables (conventional M-Mode, 2D and Doppler) were measured according to current international guidelines.[7,8]

If not contraindicated, patients were treated with the maximum tolerated doses of -blockers targeted on heart rate, and angiotensin converting enzyme-inhibitors/angiotensin receptor blockers, along with mineral-corticoid antagonists and diuretics if necessary. Decisions regarding implantable cardioverter defibrillator for primary prevention or cardiac resynchronization therapy during follow-up were made in selected patients with DCM according to the current guidelines.[5,9]

Regarding the SVT management during the index hospitalization, a rhythm control strategy was systematically pursued, according to the institutional policy of the Centre. A successful rhythm control strategy was considered in patients with persistent restoration of sinus rhythm, obtained with pharmacological therapy, direct-current-cardioversion and/or catheter ablation. In case of failure of rhythm control, a rate control strategy was adopted[3,10,11] with a target heart rate <100 bpm (rest heart rate <90 bpm and <130 bpm during exercise).

Medical evaluation, electrocardiographic and echocardiographic data were collected for the patients at admission, at 6 months and at the last available follow-up evaluation. Recurrences of LV dysfunction were defined if patients presented LVEF <50% after a LVEF recovery at 6-month evaluation.

The following end-points were considered:

- *prevalence of reversible tachycardia-induced LV dysfunction after management of the arrhythmias*, defined as the presence of a recovery of LVEF (i.e., >50%) at 6-month evaluation after the chosen SVT treatment,[3] and thereafter maintained at the last available follow-up evaluation;
- *major outcome events,* defined as a composite of death, heart transplant or first episode of major ventricular arrhythmias, defined as ventricular fibrillation, sustained ventricular tachycardia or appropriate implantable cardioverter defibrillator intervention on ventricular tachycardia >185 bpm.

The enrolment ended at December 31, 2016, the follow-up ended at December 31, 2020, in order to have a potential follow-up of at least 4 years for all patients.

The study was approved by the institutional review board policies of hospital administration and followed the Declaration of Helsinki.

Clinical and laboratory statistics are reported as means and standard deviations, medians and interquartile ranges, or counts and percentages, as appropriate. Cross-sectional comparisons between groups were made by the analysis of variance test on continuous variables, using the Brown-Forsythe statistic when the assumption of equal variances did not hold, or the nonparametric Mann-Whitney U test when necessary. The chi-square or Fisher exact tests were calculated for discrete variables as appropriate.

An extended Kaplan-Meier estimator[12] was used to compare survival curves stratified by patients with recovered versus non-recovered LVEF starting from the first evaluation of persistently recovered LVEF. Thus, the dataset was organized in a counting process format. Extended Kaplan-Meier curves do not correspond to a fixed cohort of patients; patients can contribute to different curves at different times during follow-up. For this reason, numbers of patients at risk cannot be provided in derived graphical curves. Results were regarded as statistically significant when $p < 0.05$. All statistical analysis was performed using SPSS Statistics 24.0 package, Prism 7 and packages "survival" and "ggplot2" from software R (R Foundation for Statistical Computing, Vienna, Austria; https://www.r-project.org/).

Results

The study population included 83 patients. The complete baseline characteristics are summarized in Table 1 and Figure 1. Eighty-seven percent (72) patients underwent to effective rhythm control (27 patients with catheter ablation, 40 with DCCV and 5 with anti-arrhythmic drugs). The remaining 11 (13%) were treated with a rate control strategy for refusal by patients, persistent left atrium appendage/endo-ventricular thrombosis, ineffective rhythm control.

Enrolled patients were revaluated for a median time of 54 (36 to 87) months. Eventually, a total of 56 (67%) patients showed a long-term recovered LVEF. Forty-two (75%) and 17 (30%) of them went through SVT recurrences and temporary new drop in LVEF during follow-up associated to high-rate SVT relapse, respectively. On the other hand, 20 patients never recovered their LVEF and 7 patients did not recover LVEF from LV dysfunction relapse despite the effective SVT therapeutic strategy (Figure 2).

Figure 3 shows in detail the recurrences of SVT, possibly associated with LV systolic dysfunction, in patients with recovered versus nonrecovered LVEF at the last available follow-up evaluation.

Differences in baseline characteristics between patients with recovered versus nonrecovered LVEF are shown in Table 1. Patients with recovered LVEF were significantly younger and had significantly smaller LV dimensions and higher LVEF. In addition, non-recovered LVEF patients had significantly more frequently a family history of sudden cardiac death and a left bundle branch block (LBBB) on baseline electrocardiogram. Of note, 12 patients performed, during follow-up, cardiac magnetic resonance (3 of the non-recovered LVEF and 9 in the recovered LVEF group). Among these, only one patient (from the nonrecovered LVEF) presented late gadolinium enhancement (mesocardial, diffuse).

Regarding treatment, no differences were present except for the choice of antiarrhythmic class and for a lower proportion of patients with recovered LVEF requiring diuretics (Table 2).

A total of 27 patients underwent a catheter ablation procedure during follow up. Catheter ablation was mostly performed among patients with recovered LVEF compared to non-recovered LVEF. Finally, 93% of patients who

Table 1
Baseline and last available follow-up characteristics of patients divided by recovered LVEF versus nonrecovered LVEF

Variable	Total (83)	Recovered LVEF (56, 67%)	Non-recovered LVEF (27, 33%)	p
Age (years)	**57 (49-67)**	52 (44-61)	67 (54-73)	<0.001
Men	**70 (84%)**	46 (82%)	24 (89%)	0.428
NYHA >2	**22 (26%)**	11 (20%)	11 (41%)	0.041
Family history of cardiomyopathy	**20 (24%)**	14 (25%)	6 (22%)	0.782
SBP (mm Hg)	**120 (110-140)**	120 (110-140)	115 (105-140)	0.356
Creatinine (mg/dl)	**1.05 (0.87-1.18)**	1.05 (0.9-1.3)	1.05 (0.9-1.1)	0.428
HR (bpm)	**138 (120-150)**	135 (116-150)	140 (120-150)	0.988
LBBB	**5 (6%)**	1 (2%)	4 (15%)	0.019
LVEDVi (ml/m^2)	**65.4 (52-81.9)**	61.5 (50.3-79.7)	71.7 (61.6-86.8)	0.025
LVEF	**32 (25-37)**	34 (26-38)	27 (20-34)	0.005
MR ≥ moderate	**26 (31%)**	14 (25%)	12 (44%)	0.074
Right ventricular dysfunction	**38 (46%)**	28 (50%)	10 (37%)	0.267
Restrictive diastolic pattern	**21 (25%)**	14 (25%)	7 (26%)	0.846
Last available revaluation (54 [36-87] months)				
HR (bpm)	**67 (56-77)**	67 (55-77)	65 (60-77)	0.397
LVEDVi (ml/m^2)	**57.3 (47.7-67.2)**	53.1 (45-60.5)	65.9 (55.1-80.5)	0.001
LVEF	**55 (48-62)**	59 (55-64)	43 (32-48)	<0.001
MR ≥ moderate	**10 (12%)**	4 (7%)	6 (22%)	0.018
Right Ventricular Dysfunction	**5 (6%)**	2 (4%)	3 (11%)	0.232
Restrictive diastolic pattern	**6 (7%)**	1 (2%)	5 (18%)	0.003

AF= atrial fibrillation; AFL = atrial flutter; AT = atrial tachycardia; BMI = body mass index; DCCV = direct current cardio version; HR = heart rate; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; LVEDVi = left ventricular end diastolic volume (indexed); MR = mitral regurgitation; NYHA = New York Heart Association; SBP = systolic blood pressure.

Values are median (interquartile range).

Bold values that refer to the total population.

underwent catheter ablation were in sinus rhythm at last available evaluation versus 71% of patients who did not undergo catheter ablation (p = 0.028).

During follow-up, only 1 patient with recovered LVEF vs 7 patients with nonrecovered LVEF (Figure 4). Only 3 major ventricular arrhythmias were recorded during follow-up. Of note, one was reported in patients with recovered LVEF, represented by a torsade de pointes degenerated in ventricular fibrillation after amiodarone-induced QT prolongation and concomitant hypokalemia. The other 2 arrhythmic events, a sudden cardiac death and an appropriate implantable cardioverter defibrillator intervention, occurred in the non-recovered LVEF group. No patient was evaluated for heart transplant. Among the 8 patients who died, 2 patients underwent autopsy, both belonging to the non-recovered LVEF group, with post-mortem diagnosis of DCM; in the first case diffuse cardiac fibrosis and adipose tissue was found, in the second case, a diffuse fibrosis pattern ventricle was found.

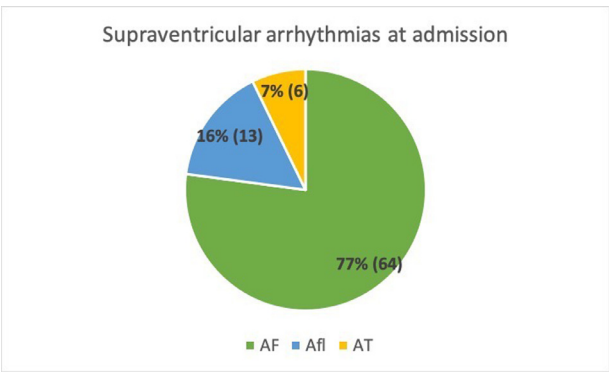

Figure 1. Supraventricular arrhythmias at admission: percentages of AF, AFL, AT. AF = atrial fibrillation; AFL = atrial flutter; AT = atrial tachycardia.

Discussion

The main results of our study are: (1) 67% of patients presenting with new-onset LV dysfunction associated to high-rate sustained SVT as the only known possible cause, showed LVEF recovery after arrhythmia management at a median follow-up of > 4 years; (2) patients with recovered LVEF showed a higher overall survival rate with respect to patients with non-recovered LVEF; (3) 42% of patients with recovered LVEF at last evaluation had experienced arrhythmic recurrences during the follow-up and 30% a new drop of LVEF subsequent to SVT relapses.

The prevalence of recovered LVEF during a long-term follow-up was not well provided before, mainly due to the lack of real-world studies that excluded important confounders that can contribute to LV dysfunction (i.e., hypertension, coronary artery disease, valve heart disease). Also, despite challenging, it appears crucial to follow these patients in the long term because SVT relapses are frequent, with potential new LVEF drops and prognostic implications.

While in tachycardia-induced cardiomyopathy, SVT are by definition the etiological trigger of LV systolic dysfunction, in DCM, SVT represent an epiphenomenon, which is associated with a poorer outcome.[13] As evident by our results, the presence of SVT associated to reduced LVEF at admission identifies DCM only in a minority of the cases. Moreover, in a population without other possible triggers of LV dysfunction, we showed, consistently with previous

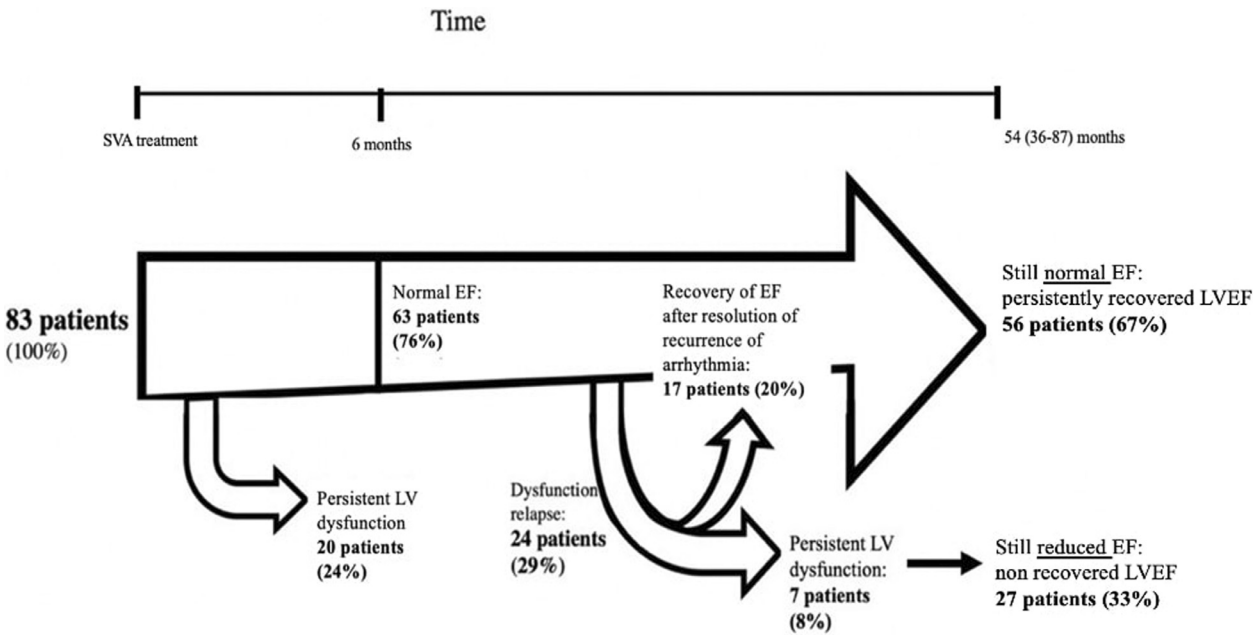

Figure 2. Time course of patients through relapses of SVT and possible new drops in LVEF. EF = ejection fraction; LV = left ventricular; SVT = supra-ventricular tachycardias.

findings,[14] that patients who persistently recovered LVEF were younger and with less remodeled LV with respect to the others. This led us to speculate that in this context, SVT might represent the pathogenic mechanism of disease inducing patients to come earlier to the attention of clinicians. On the other hand, in patients with non-recovered LVEF, SVT could be an epiphenomenon of an underlying DCM: the unlikelihood of LVEF recovery might be explained by a longer history of preclinical disease, as suggested by the older age and the more significant LV remodeling. Future studies on larger populations are needed to confirm the hypothesis here generated. Furthermore, more advanced techniques, such as strain measurements, cardiac magnetic resonance and genetic testing might be useful tools to early identify DCM from real tachycardia-induced cardiomyopathy. In fact, *TTN* truncating variants have been reported in some "secondary" forms of DCM such as alcoholic cardiomyopathy and myocarditis, raising the possibility that phenotypic expression is the result of the combination of genetic and environmental components.[15–17] SVT may be the second hit necessary for a genetically determined cardiomyopathy to reach clinical expression. Future larger cohorts are required in order to confirm those hypotheses. For now, following LVEF trajectory and SVT

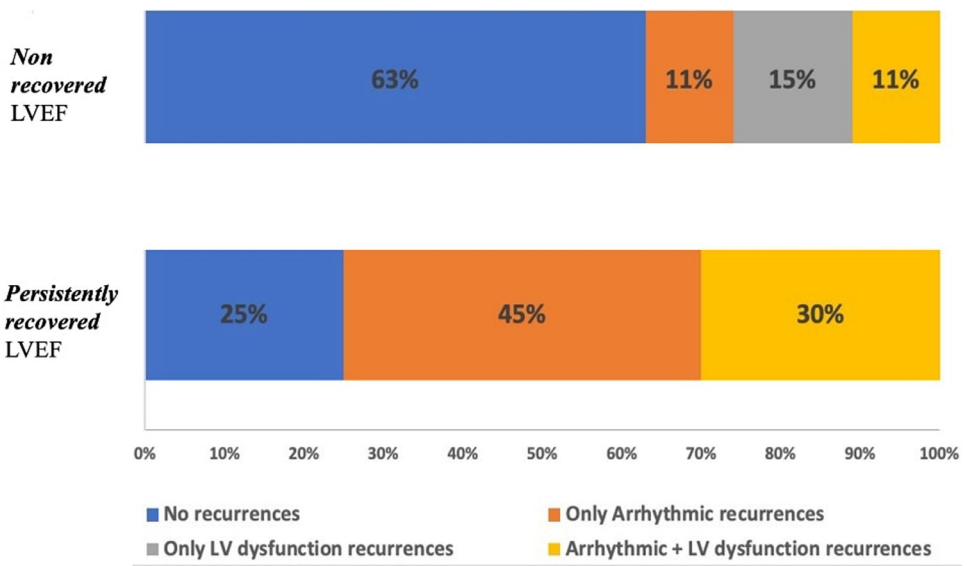

Figure 3. Arrhythmic and LV dysfunction recurrences in patients with recovered LVEF versus nonrecovered LVEF. EF = ejection fraction; LV = left ventricular.

Table 2
Baseline and last available follow-up therapy of patients divided by recovered LVEF versus non-recovered LVEF

Variable	Total (83)	Recovered LVEF (n = 56)	Non-recovered LVEF (n = 27)	p
Beta-blockers	**51 (61%)**	35 (62%)	16 (59%)	0.776
ACE-inhibitors/ARBs	**63 (76%)**	41 (6%)	22 (81%)	0.409
Calcium channel blockers	**7 (8%)**	5 (9%)	1 (4%)	0.389
Digoxin	**35 (42%)**	22 (39%)	13 (48%)	0.444
Class Ic anti-arrhythmic agents	**6 (7%)**	5 (9%)	1 (4%)	0.389
Sotalol	**9 (11%)**	7 (13%)	2 (7%)	0.485
Amiodarone	**43 (52%)**	26 (46%)	17 (63%)	0.158
Anticoagulants	**76 (93%)**	26 (46%)	17 (63%)	0.158
Diuretics	48 (58%)	27 (48)	21 (78%)	0.011
last available follow-up (54 [36-87] months)				
Beta-blockers	**48 (58%)**	29 (52%)	19 (73%)	0.069
ACE-inhibitors/ARBs	**60 (72%)**	39 (70%)	21 (78%)	0.438
Calcium channel blockers	**1 (1%)**	1 (2%)	0	0.493
Digoxin	**6 (7%)**	4 (7%)	2 (8%)	0.929
Class I anti-arrhythmic agents	**12 (15%)**	12 (21%)	0	0.011
Sotalol	**10 (12%)**	8 (14%)	2 (8%)	0.396
Amiodarone	**20 (24%)**	9 (16%)	11 (42%)	0.010
Anticoagulants	**53 (65%)**	33 (59%)	20 (77%)	0.113
Diuretics	**27 (32%)**	10 (18%)	15 (60%)	>0.001

ACE = angiotensin-converting enzyme; ARBs = angiotensin receptor blockers; LVEF = left ventricular ejection fraction.
Values are median (interquartile range).
Bold values that refer to the total population.

relapses during long-term follow-up appear pivotal in understanding the causal relationship between SVT and LV dysfunction.

The significant prevalence of recovered LVEF in the long-term that we have found supports the indication to a systematic arrhythmia management in patients admitted for new onset LV systolic dysfunction associated to high-rate SVT. It has not been completely clarified if a rhythm control rather than a rate control strategy should be preferred in patients presenting with high-rate SVT and LV dysfunction.[18] Recent data suggest that antiarrhythmic therapy and/or ablation is associated with a lower risk of cardiovascular events than usual care in patients with early atrial fibrillation.[19] Despite it was out of the aim of this study, in our

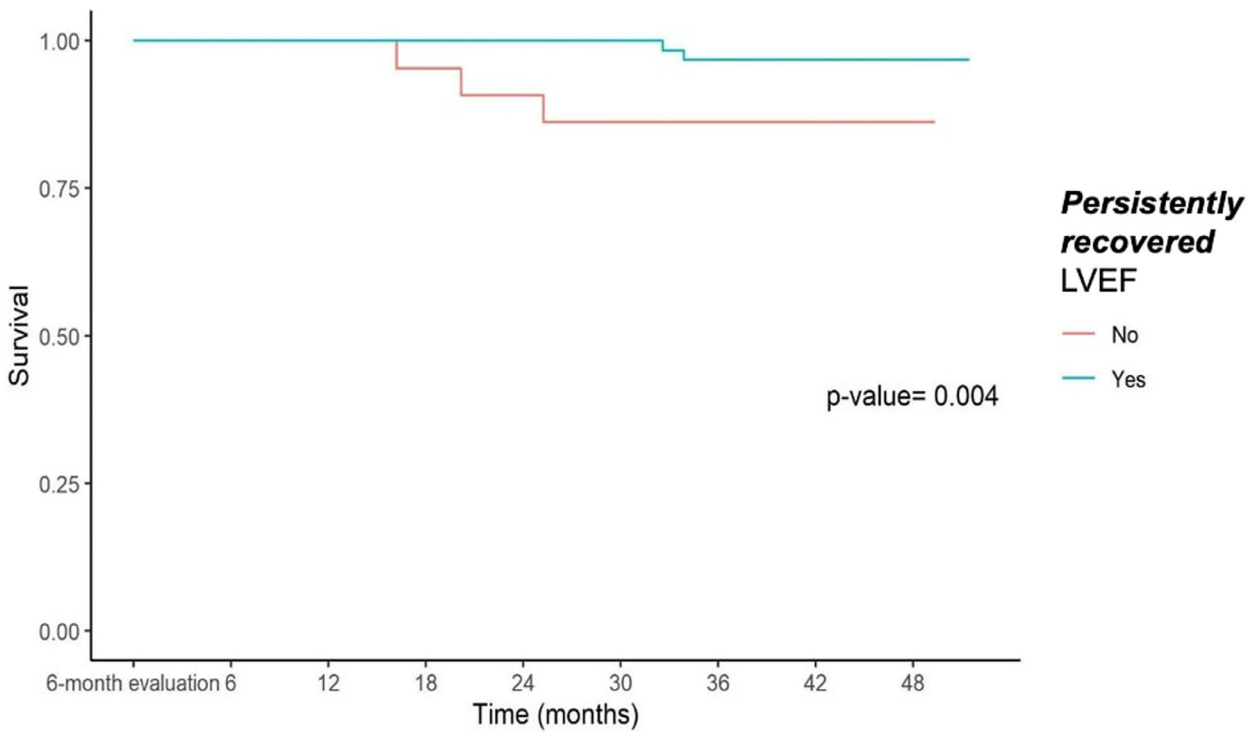

Figure 4. Extended Kaplan-Meier curves comparing death/HT/MVA in patients with recovered LVEF versus nonrecovered LVEF at last available LVEF revaluation (p = 0.007). HT = heart transplant; MVA = major ventricular arrhythmias.

population a systematic rhythm control was pursued at baseline. Moreover, patients who underwent catheter ablation were more likely to maintain sinus rhythm and to normalize their LVEF at last available follow up. Future focused prospective trials are needed in order to assess the best strategy of patients presenting with sustained, high-rate SVT as the only possible cause of new-onset LV systolic dysfunction.

Patients with recovered LVEF showed a better outcome than patients with non-recovered LVEF in our population. This further supports the systematic effort of treating SVT in patients presenting with LV systolic dysfunction, as stated above and in agreement with the recent European Society of Cardiology Guidelines for diagnosis and management of AF.[20] However, suspension of anti-arrhythmic drugs should be considered when measuring net benefit of restoration of SR, contemplating the possibility of potentially fatal adverse events, either due to drug therapy or to complications related to invasive procedures (of note, the only event in our patients with recovered LVEF was probably iatrogenic).

This study suffers from some limitations: first, it has a retrospective design. Second, the duration of the SVT was not systematically investigated. However, this reflects the daily clinical practice. Third, the small sample size with a limited number of events may have limited the statistical power: due to the limited number of events future studies on larger populations, are advocated in order to investigate the hypothesis here generated. In particular, the role of a systematic rhythm control strategy to patients with recent-onset LV dysfunction and high rate SVT, independently from LV remodeling and from optimized medical treatment should be confirmed. Fourth, echocardiography was the main tool to define dysfunction and might have led, in same patients, to artifacts due to rapid ventricular rate at the baseline evaluation. Fifth, genetic and cardiac magnetic resonance data were not systematically available.

Finally, we cannot exclude that by continuing the follow-up, some patients with recovered LVEF will experience a new recurrence of LV dysfunction, independently of recurrence of arrhythmia. However, this endorses the main message of the paper: the importance of a continuous surveillance of these patients.

In conclusion, two-thirds of patients admitted for LV systolic dysfunction in the setting of acute supraventricular tachyarrhythmias, without other apparent causes of dysfunction, showed a recovery of LVEF in the long-term structured revaluation, with a subsequent benign outcome. However, a continuous individual surveillance is required in those patients, as arrhythmic recurrences, with new drop in LVEF, are common.

Author' Contribution

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript. Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication before its appearance in the Hong Kong Journal of Occupational Therapy.

Conception and design of study: DZ, LP, AC, GB, CG, GF, LVS, MZ, MM, GS; Acquisition of data: DZ, LP, AC, GB, CG, GF, LVS, MZ, MM, GS; Analysis and/or interpretation of data: DZ, LP, AC, GB, CG, GF, LVS, MZ, MM, GS.

Drafting the manuscript: DZ, LP, AC, GB, CG, GF, LVS, MZ, MM, GS; Revising the manuscript critically for important intellectual content: DZ, LP, AC, GB, CG, GF, LVS, MZ, MM, GS.

Approval of the version of the manuscript to be published: DZ, LP, AC, GB, CG, GF, LVS, MZ, MM, GS.

Disclosures

Denise Zaffalon's reports were provided by Azienda Sanitaria Universitaria Giuliano-Isontina. Denise Zaffalon reports a relationship with Azienda Sanitaria Integrata Giuliano-Isontina that includes: nonfinancial support. Denise Zaffalon has patent pending to Not available. None.

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