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Pericarditis prophylactic therapy after sinus node–sparing hybrid ablation for inappropriate sinus tachycardia/postural orthostatic sinus tachycardia

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BACKGROUND Pericarditis is the most common complication following hybrid sinus node–sparing ablation for inappropriate sinus tachycardia (IST)/postural orthostatic tachycardia syndrome (POTS).

OBJECTIVE The study sought to evaluate the association of prophylaxis therapy on the risk of symptomatic pericarditis following hybrid IST/POTS ablation.

METHODS All consecutive patients undergoing to hybrid ablation of symptomatic IST/POTS refractory or intolerant to drugs were retrospectively analyzed. Pharmacological prophylaxis therapy was based on acetylsalicylic acid and colchicine started on the day of the ablation and continued for at least 3 months. The primary endpoint was occurrence of symptomatic pericarditis. The secondary endpoint was occurrence of pericarditis-related complications, including the following: duration of pericarditis >3 months, hospitalization for pericarditis, postpericardiectomy pleuro-pericarditis, and pericardiectomy.

RESULTS A total of 220 patients undergone to hybrid IST/POTS ablation were included and 44 (20%) underwent prophylaxis therapy. Pericarditis occurred in 101 (45.9%) patients, with 97 (96%) in the first 5 days. At survival analysis, prophylaxis was associated with higher rate of freedom from pericarditis (81.9% vs 47.2%, log-rank $P < .001$). Pericarditis-related complications were low, occurring in 7 (3.2%) patients. There was no difference in pericarditis-related complications between the patients who underwent prophylaxis therapy and patients who did not. At Cox multivariate analysis, predictors of pericarditis were IST (vs POTS) (hazard ratio 0.61, 95% confidence interval0.39-0.99, $P = .04$) and prophylaxis therapy (hazard ratio 0.27, 95% confidence interval 0.13-0.55, $P < .001$).

CONCLUSION In a large cohort of patients undergoing hybrid ablation for IST/POTS, a prophylaxis therapy with acetylsalicylic acid and colchicine was associated with a lower rate of symptomatic pericarditis.

KEYWORDS Sinus node; Inappropriate sinus node tachycardia; Postural orthostatic sinus tachycardia; Hybrid ablation; Pericarditis

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KEY FINDINGS

- After hybrid sinus node–sparing inappropriate sinus node tachycardia ablation, a symptomatic pericarditis can be diagnosed in 18.1% of patients receiving prophylaxis treatment vs 52.8% of patients not receiving prophylaxis treatment (73% risk reduction);
- Patients undergoing prophylaxis therapy demonstrated a significantly lower heart rate post–hybrid ablation compared with patients not receiving prophylaxis therapy.
- Prophylaxis therapy was well tolerated, and none of the patients discontinued it prematurely.

Introduction

Inappropriate sinus node tachycardia (IST) and postural orthostatic tachycardia syndrome (POTS) are characterized by a nonphysiological increase in resting heart rate.[1–3] Symptoms are various, including the following: palpitations, dyspnea, fatigue, syncope, exercise intolerance, chest pain, anxiety, and depression.[3,4] A novel sinus node–sparing hybrid ablation for IST/POTS has been demonstrated to be an effective and safe therapeutic option in patients with symptomatic drug-resistant IST and POTS.[5–7] Pericarditis is the most common complication following hybrid ablation for IST/POTS; its rate is up to 78% in the first 3 months and up to 4% between 3 and 6 months.[5] Similar findings were observed in a multicenter prospective registry, demonstrating acute pericarditis as the most common complication after hybrid ablation.[7] However, a recent multicenter study documented a rate of 47% of pericarditis following hybrid sinus node–sparing procedure, and only in 9% of patients the symptoms continued up to 6 months.[6] All symptoms of pericarditis were responsive to medical treatment, including administration of nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine[8] and less frequently corticosteroids.[5,6]

To date, no studies evaluated the benefits of a prophylactic pharmacological therapy for pericarditis in patients undergoing novel hybrid IST/POTS ablation.

The aims of this study were (1) to evaluate the incidence of symptomatic pericarditis in a large cohort of patients undergoing hybrid sinus node–sparing IST/POTS procedure and (2) to evaluate the efficacy and safety of a prophylactic therapy for pericarditis on symptoms and postprocedural heart rate.

Methods

Study design and patient population

All consecutive patients diagnosed with IST/POTS from June 2015 to May 2023 were prospectively enrolled in the UZ Brussel monocentric IST/POTS registry. They were included in this study if the following inclusion criteria were fulfilled: (1) diagnosis of IST or POTS following current guidelines[9]; (2) symptomatic IST/POTS refractory or intolerant to drugs (eg, beta-blocker, calcium-channel blockers, ivabradine), thus refractory to conservative treatment; and (3) hybrid sinus node–sparing IST ablation performed following our described approach.[5–7] A cardiologist together with a neurologist, both experts in IST and POTS, evaluated all patients. Other causes of sinus tachycardia or any supraventricular tachycardia were ruled out with clinical data, laboratory data, and an invasive electrophysiological study. All patients underwent a 12-lead electrocardiogram (ECG) to confirm normal P-wave morphology and a Holter 24-hour ECG to evaluate mean heart rate and the circadian variation. Additional evaluations included blood testing (complete blood count, thyroid function, renal function and electrolytes, metabolic panel, drug testing, and serum and urine catecholamines). Hybrid sinus node–sparing ablation treatment was offered to patients who were refractory to or intolerant to pharmacologic treatment. Three patients refused hybrid ablation treatment and opted for conventional sinus node ablation and pacemaker implantation and were therefore excluded from the current study. All patients signed an informed consent that had been approved by our institutional review board. The study complied with the Declaration of Helsinki as revised in 2013; the ethics committee approved the study.

Hybrid ablation procedure

Hybrid sinus node–sparing IST ablation approach has been previously described.[5–7] Briefly, three 5-mm working ports are placed in the right chest with a camera port in the fifth intercostal space at the mid-axillary line. Two other working ports are added: (1) in the third intercostal space at the anterior axillary line, a 5-mm port for instruments; and (2) in the seventh intercostal space at the anterior axillary line, a 5-mm port for instruments. After placement of the camera port, CO_2 is used to increase the working space and displacing the diaphragm down. In women, the lateral mammary fold is usually used. The pericardium is opened with an endoscopic coagulation hook and/or scissors longitudinally, anterior to the phrenic nerve until visualization of the superior vena cava (SVC) and inferior vena cava (IVC). The pericardial reflection of the IVC is then bluntly dissected until the oblique sinus. Endocardial mapping of the sinus node is performed and the position of the endocardial catheter is observed using the thoracoscopic video system. Sinus node location is marked by the surgeon with methylene blue based on the position of the endocardial catheter (sinus node–sparing approach). A bipolar bidirectional radiofrequency clamping device (EMR2; AtriCure Inc, Mason, OH) is positioned over the SVC at the junction with the right atrium to isolate the SVC. The same approach is performed to isolate the IVC. IVC isolation is performed to avoid macro–re-entrant tachycardias. To complete the hybrid IST ablation set, the crista terminalis line is performed with the clamp positioned in the oblique sinus and the anterior jaw over Waterston's groove, covering the crista terminalis. Epicardial right pulmonary vein isolation is routinely

performed in POTS patients. Then, to confirm ablation line block, further endocardial mapping is performed. If lines are not blocked, additional epicardial and/or endocardial ablations are added. The pericardium is closed and the right lung inflated. Acute endpoint of the ablation is considered a reduction of at least 25% of the heart rate or accelerated junctional rhythm.

Pre– and post–hybrid ablation management

Pharmacological prophylaxis therapy was based on the administration of 500 mg of acetylsalicylic acid 3 times a day and 0.5 mg of colchicine 2 times a day (once daily if the patient's weight is <70 kg), following current guidelines for the diagnosis and management of pericardial diseases.[10] Medications were started on the day of the ablation procedure and continued for at least 3 months. Acetylsalicylic acid was decreased by 500 mg every 4 weeks. In case of allergy to acetylsalicylic acid, other NSAIDs were prescribed. Prophylaxis therapy was started in all patients undergoing hybrid IST ablation after January 2021. In patients not receiving standard postprocedure prophylaxis therapy, therapy was administered if symptomatic pericarditis occurred. In particular, the same protocol was used with 500 mg of acetylsalicylic acid 3 times a day and 0.5 mg of colchicine 2 times a day. According to the European Society of Cardiology guidelines,[10] the diagnosis of acute pericarditis was made with 2 of the following criteria: (1) pericardial chest pain, (2) pericardial friction rub, (3) pericardial electrocardiogram changes, and (4) pericardial effusion. In patients experiencing symptomatic pericarditis despite receiving prophylaxis therapy, colchicine and acetylsalicylic acid were continued based on clinical judgment. In all cases of pericarditis, dose tapering of therapy was guided by symptoms and inflammatory indices.

Follow-up

Patients were followed up in the outpatient clinic every 6 months and by remote monitoring for patients with cardiac implantable electronic devices (CIEDs). CIEDs patients underwent serial device interrogations every 6 months. Patients without CIEDs underwent a 24-hour Holter ECG at 1 month, 3 months, 6 months, and every 6 months. The postprocedural heart rate was evaluated based on the average of 3 ECGs in 3 different days prior to discharge. Symptom evaluation for pericarditis was performed every day after ablation until discharge. Pericarditis symptoms triggered prompt ECG and echocardiography.

The primary endpoint was occurrence of symptomatic pericarditis. The secondary endpoint was occurrence of pericarditis-related complications, including duration of pericarditis >3 months, hospitalization for pericarditis, pleuropericarditis, and pericardiectomy. The primary efficacy endpoint for prophylactic therapy was symptomatic pericarditis in the prophylaxis group vs the no-prophylaxis group. The primary safety endpoint for prophylactic therapy was prophylaxis side effects. Prophylaxis side effects were evaluated at each outpatient clinic evaluation and with specific telephonic consultation every month (for patients on therapy). If pericarditis was clinically suspected, a 12-lead ECG was performed for pericardial changes. All ECGs were analyzed using digital calipers by 2 independent blinded physicians (L.M. and L.P.). Discrepancies were adjudicated by a third independent physician (C.d.A.).

Table 1 Baseline characteristics of the study population

Characteristic	Total	No **P**rophylaxis therapy	Prophylaxis therapy	*p* value
Sample	220 (100)	176 (80)	44 (20)	
Symptomatic pericarditis	101 (45.9)	93 (52.8)	8 (18.1)	<.001
Age, y	31.0 ± 11.7	31.3 ± 12.4	30.3 ± 10.2	.65
Female	195 (88.6)	155 (88.0)	40 (90.9)	.59
LVEF	220 (100.0)	176 (100.0)	44 (100.0)	NA
IST	185 (84.1)	147 (83.5)	38 (86.3)	.65
POTS	61 (27.7)	50 (28.4)	11 (25.0)	.71
Autoimmune disease	10 (4.5)	8 (4.5)	2 (4.5)	1.00
Thyroid disorders	3 (1.3)	1 (0.5)	2 (4.5)	.12
Inflammatory bowel disease	3 (1.3)	3 (1.7)	0 (0.0)	1.00
Systemic lupus erythematosus	2 (0.9)	2 (1.1)	0 (0.0)	1.00
Psoriasis	2 (0.9)	2 (1.1)	0 (0.0)	1.00
Redo procedure	34 (15.4)	27 (15.3)	7 (15.9)	.93
Pericarditis-related complications	7 (3.2)	6 (3.4)	1 (2.3)	1.00
Duration >3 mo	2 (0.9)	2 (1.1)	0 (0.0)	1.00
Hospitalization	2 (0.9)	2 (1.1)	0 (0.0)	1.00
Pleuro-pericarditis	2 (0.9)	1 (0.5)	1 (2.3)	.37
Pericardiectomy	1 (0.4)	1 (0.5)	0 (0.0)	1.00
Heart rate, beats/min	81.9 ± 17.9	85.9 ± 16.5	65.9 ± 13.5	<.001
Pericardial ECG changes in patients with pericarditis	86 (85.1)	8 (100)	78 (83.8)	.61

Values are n (%) or mean ± SD.

BMI = body mass index; ECG = electrocardiography; LVEF = left ventricular ejection fraction; IST = inappropriate sinus tachycardia; POTS = postural orthostatic tachycardia syndrome.

Table 2 Criteria for pericarditis occurrence in the population

Criterion	Symptomatic pericarditis (n = 101)
Pericardial chest pain	101 (100)
Pericardial friction rub	19 (18.8)
Pericardial ECG changes	86 (85.1)
Pericardial effusion	0 (0)

Values are n (%).
ECG = electrocardiography.

Statistical analysis

All variables were tested for normality with Shapiro-Wilk test. Normally distributed variables were described as mean ± SD and the groups were compared through analysis of variance, paired *t* test, or unpaired *t* test as appropriate, while the non-normally distributed variables were described as median (interquartile range) and compared by Mann-Whitney test or Wilcoxon signed rank test as appropriate. The categorical variables were described as frequency and percentage and compared by chi-square test or Fisher's exact test as appropriate. Cohen's kappa statistic was used to assess interobserver agreement in ECG analysis. Kaplan-Meier survival analysis was performed to analyze the cumulative event rates.

A Cox proportional hazards model was performed to identify risk factors for pericarditis. The covariates entered in the univariate and multivariate Cox model were chosen according to their clinical significance. Variables with $P < .10$ were then entered in the multivariate model and selected with a backward stepwise approach. The proportional hazards assumption for the Cox model was tested with the cox.zph function. Bonferroni correction was used as appropriate.

Survival analysis was performed with *survival* and *survminer* packages on R software (version 3.6.2; R Foundation for Statistical Computing, Vienna, Austria). A P value <.05 was considered statistically significant. The analysis was performed using R software and SPSS Statistics 23.0 (IBM Corporation, Armonk, NY).

Results

Study population characteristics

The study population consisted of 220 patients with drug-resistant IST/POTS who underwent hybrid IST ablation. The mean age was 31.0 ± 11.7 years, and 195 (88.6%) patients were female. A total of 185 (84.1%) patients were treated for IST and 61 (27.7%) patients were treated for POTS. A total of 10 (4.5%) patients were affected by an autoimmune disease, including the following: 3 (1.3%) with thyroid disorders, 3 (1.3%) by inflammatory bowel diseases, 2 (0.9%) by systemic lupus erythematosus, and 2 (0.9%) by psoriasis. Out of 220 patients treated with hybrid IST ablation, 101 (45.9%) experienced symptomatic pericarditis. The baseline characteristics of patients, stratified according to symptomatic pericarditis occurrence, are summarized in Tables 1, 2, and 3. Female sex was significantly higher in patients with pericarditis vs patients without pericarditis (95 [94%] patients vs 100 [84%] patients, $P = .02$) (Table 3). Patients with pericarditis had higher postprocedural heart rate compared with patients without pericarditis (86.6 ± 18.6 beats/min vs 77.9 ± 16.2 beats/min, $P = .02$). There was no difference in prophylaxis therapy

Table 3 Characteristics of study population stratified by pericarditis occurrence

	Total	No symptomatic pericarditis	Symptomatic pericarditis	*P* value
Sample	220 (100)	119 (54.1)	101 (45.9)	
Age, y	31.0 ± 11.7	32.3 ± 12.9	29.9 ± 10.9	.14
Female	195 (88.6)	100 (84)	95 (94)	.02
BMI, kg/m^2	24.1 ± 4.8	24.0 ± 5.1	23.4 ± 4.6	.35
LVEF >50%	220 (100.0)	119 (100.0)	101 (100.0)	NA
IST	185 (84.1)	108 (90.7)	77 (76.2)	.003
POTS	61 (27.7)	28 (23.5)	33 (32.6)	.14
Autoimmune disease	10 (4.5)	3 (2.5)	7 (6.9)	.19
Thyroid disorders	3 (1.3)	1 (0.8)	2 (1.9)	.59
Inflammatory bowel disease	3 (1.3)	1 (0.8)	2 (1.9)	.59
Systemic lupus erythematosus	2 (0.9)	0 (0.0)	2 (1.9)	.22
Psoriasis	2 (0.9)	0 (0.0)	2 (1.9)	.22
Endometriosis	8 (3.6)	5 (4.2)	3 (2.9)	.75
Ehlers-Danlos syndrome	10 (4.5)	5 (4.2)	5 (4.9)	1.00
Fibromyalgia	5 (2.3)	3 (2.5)	2 (1.9)	1.00
Procedure time, min	172 ± 12	173 ± 11	171 ± 13	.95
Surgical time, min	43 ± 17	44 ± 15	42 ± 19	.94
Redo procedure	34 (15.4)	15 (12.6)	19 (18.8)	.21
Prophylaxis therapy	44 (20.0)	36 (30.2)	8 (7.9)	<.001
Heart rate, beats/min	81.9 ± 17.9	77.9 ± 16.2	86.6 ± 18.6	.02

Values are n (%), mean ± SD, or median (interquartile range).
BMI = body mass index; LVEF = left ventricular ejection fraction; IST = inappropriate sinus tachycardia; POTS = postural orthostatic tachycardia syndrome.

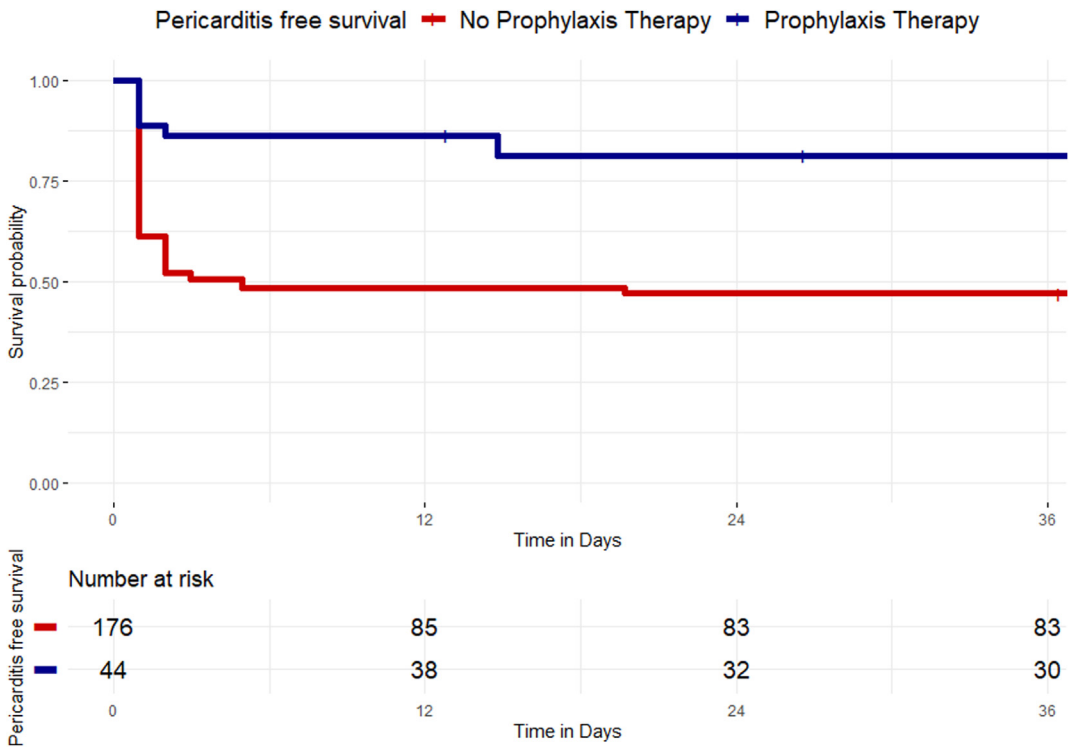

Figure 1 Kaplan-Meier curves of survival free from pericarditis stratified for prophylaxis therapy. Kaplan-Meier curves of survival free from pericarditis after hybrid inappropriate sinus node tachycardia ablation stratified for prophylaxis therapy. Freedom from pericarditis was higher in patients receiving prophylaxis therapy (blue curve), compared with patients (red curve) who did not receive it (81.9% vs 47.2%, log-rank $P < .001$).

use among patients with IST (20.5% of patients) and POTS (18.0% of patients) ($P = .65$ and $P = .71$, respectively) (Table 1).

There was no significant difference between patients suffering from symptomatic pericarditis and patients without any pericarditis in autoimmune diseases or other aforementioned comorbidities (Table 3). Criteria for pericarditis diagnosis are listed in Table 2. In particular, all 101 (100.0%) patients had chest pain, 86 (85.1%) patients had pericardial ECG changes, and 19 (18.8%) patients had pericardial friction rub. No patients had pericardial effusion. Good interobserver agreement was observed for ECG analysis ($\kappa = 0.96$).

Follow-up

After a mean follow-up of 73.3 ± 16.2 months, symptomatic pericarditis occurred in 101 (45.9%) patients. All 101 patients experienced symptomatic pericarditis within the first 20 days postablation at a mean follow-up of 2.01 ± 1.6 days: in particular, 97 (96%) patients in the first 5 days and 4 (4%) patients after the fifth day (Figure 1).

Pericarditis-related complications occurred in 7 (3.2%) patients, including the following: 2 (0.9%) patients with a duration of pericarditis >3 months, 2 (0.9%) patients with hospitalization for pericarditis, 2 (0.9%) patients with pleuro-pericarditis, and 1 (0.4%) patient developing constrictive pericarditis requiring pericardiectomy (Table 1).

The role of prophylaxis therapy in hybrid IST ablation

Out of 220 patients treated with hybrid IST ablation, 44 (20%) underwent pharmacological prophylaxis therapy. There were no differences in baseline characteristics between patients in the prophylaxis group compared with patients not receiving prophylaxis (Table 1). Among patients who received prophylaxis therapy, prophylaxis was associated with a lower rate of symptomatic pericarditis compared with patients not receiving it (8 [18.1%] patients vs 93 [52.8%] patients, $P < .001$) (Table 1).

Patients with prophylaxis therapy demonstrated significantly lower heart rate in comparison with those who did not receive prophylaxis therapy (65.9 ± 13.5 beats/min vs 85.9 ± 16.5 beats/min, $P < .001$) (Table 1).

There was no statistically significant difference in pericarditis-related complications, including duration of pericarditis >3 months, hospitalization for pericarditis, post-pericardiectomy pleuro-pericarditis, and pericardiectomy, between the patients receiving prophylaxis therapy and patients who did not receive it (Table 1).

A total of 8 (3.6%) patients receiving prophylaxis therapy developed diarrhea. None of the patients discontinued colchicine prematurely.

At survival analysis, prophylaxis was associated with higher freedom from pericarditis in patients receiving therapy compared with patients who did not receive it (81.9% vs 47.2%, log-rank $P < .001$) (Figure 1).

Table 4 Cox regression analysis for predictors of pericarditis

	Univariate analysis				Multivariate analysis			
		95% CI				95% CI		
Predictor	HR	Lower	Upper	*P* value	HR	Lower	Upper	*P* value
Age	0.99	0.97	1.01	.24				
Female	1.41	0.75	2.64	.29				
BMI	0.99	0.94	1.03	.58				
IST (vs POTS)	0.61	0.38	0.96	.04	0.61	0.39	0.99	.04
Autoimmune disease	1.68	0.78	3.64	.20				
Prophylaxis therapy	0.30	0.14	0.62	<.001	0.27	0.13	0.55	<.001

Univariate and multivariate Cox regression analysis for predictors of pericarditis recurrence after hybrid ablation.

BMI = body mass index; CI = confidence interval; HR = hazard ratio; IST = inappropriate sinus tachycardia; POTS = postural orthostatic tachycardia syndrome.

At Cox univariate analysis, predictors of pericarditis were as follows: IST (vs POTS) (hazard ratio [HR] 0.61, 95% confidence interval [CI] 0.38-0.96, $P = .04$) and prophylaxis therapy (HR 0.30, 95% CI 0.14-0.62, $P < .001$) (Table 4).

At Cox multivariate analysis, independent predictors of pericarditis were as follows: IST (vs POTS) (HR 0.61, 95% CI 0.39-0.99, $P = .04$) and prophylaxis therapy (HR 0.27, 95% CI 0.13-0.55, $P < .001$) (Table 4).

Discussion

The main findings of the current study can be summarized as follows: (1) after hybrid IST ablation, 18.1% of patients receiving prophylaxis treatment developed symptomatic pericarditis vs 52.8% of patients not receiving prophylaxis treatment; (2) patients undergoing prophylaxis therapy demonstrated a significantly lower heart rate post–hybrid ablation compared with patients not receiving prophylaxis therapy (65.9 ± 13.5 beats/min vs 85.9 ± 16.5 beats/min, $P < .001$); and (3) prophylaxis therapy was well tolerated, and none of the patients discontinued it prematurely.

Pericarditis after hybrid ablation

Sinus node hybrid ablation for IST/POTS requires the opening of the pericardium with an endoscopic coagulation hook and/or scissor. As demonstrated in the current study, the occurrence of symptomatic pericarditis is mostly in the first 5 days following the procedure, supporting the hypothesis that surgical trauma or mechanical irritation due to manipulation of the heart during surgery are primarily involved in the disease.[11,12] Symptomatic pericarditis is a known complication of both endocardial and epicardial ablation, whereas the intensity of the pericardial inflammatory reaction varies considerably.[13–15] Our data support the putative hypothesis that younger age of our population can be involved into a stronger inflammatory response. However, given the short time between thoracoscopic ablation and symptoms, inflammatory markers (eg, C-reactive protein, erythrocyte sedimentation rate) are not reliable in this clinical context. Indeed, the diagnosis is based on clinical symptoms, as recommended by current guidelines.[10] Epicardial right pulmonary vein isolation was routinely performed in all POTS patients. This might explain the higher risk of pericarditis in this subgroup.

Anti-inflammatory therapy was started immediately. Notably, no patient presented with pericardial effusion. This might be related to pericardium opening. However, postablation pericarditis has been previously described occurring after few days from endocardial ablation with chest pain and no effusion or increase in body temperature.[16]

The absence of effusion might exacerbate the pain, which was present in all patients, due to pericardial layers rubbing. Only 4% of pericarditis arise after the fifth day, some of them in a context of postpericardiectomy syndrome. This clinical syndrome usually appears after some days or weeks, having an autoimmune pathogenesis triggered by initial damage of pericardial tissue.[10] Interestingly, in 2 patients, a pleuropericarditis was diagnosed. It required hospitalization, during which a thoracentesis was performed, confirming the inflammatory origin of pleural effusion. Both patients were women of 52 and 31 years of age, respectively, without autoimmune disorders. However, in the overall cohort presented, autoimmune disorders were not associated with a higher rate of symptomatic pericarditis. A 32-year-old woman with symptomatic pericarditis occurring the day after the procedure underwent pericardiectomy due to evolution to constrictive pericarditis, despite starting corticosteroid therapy. The patient had not received prophylaxis therapy. This very rare complication has also been described after endocardial atrial fibrillation catheter ablation.[17,18] Overall, the rate of pericarditis-related complications was low (3.2%), and medical treatment resolved the pericarditis in all but 1 patient undergoing to pericardiectomy.

Prophylaxis therapy for hybrid ablation

Based on the current European Society of Cardiology recommendation for first-line therapy for acute pericarditis, we opted for a combination of acetylsalicylic acid and colchicine as prophylaxis therapy.[10] All 44 patients had no allergies or intolerance to acetylsalicylic acid, and thus no others NSAIDs were prescribed. To the best of our knowledge, this is the first study evaluating a prophylaxis approach for

hybrid ablation. The administration of prophylaxis therapy was associated with a lower rate of symptomatic pericarditis from 52.8% to 18.1% and prophylaxis therapy was independently associated with a 73% risk reduction.

Different recent studies evaluated the use of colchicine-only prophylaxis regimen after atrial fibrillation catheter ablation with radiofrequency.[19–21] Our results are in line with Mohanty and colleagues,[19] demonstrating that colchicine therapy started 7 days before to 1 month after atrial fibrillation catheter ablation was associated with a lower risk of acute pericarditis. In 2 other recent studies, colchicine did not reduce the incidence of postablation pericarditis and was associated with an increased incidence of gastrointestinal side effects. This discrepancy could be explained by different arguments. First, the incidence of postablation pericarditis is higher after hybrid ablation compared with catheter ablation of atrial fibrillation (8%–10%).[19–21] Eventually, any statistically significant difference needs a large cohort to be demonstrated with such a low event rate. Second, the prophylaxis regimen administered in the current study was colchicine associated with aspirin. In the previous studies, colchicine-only therapy was investigated. The use of aspirin might improve efficacy and clinical outcomes as per current guidelines.[10] However, after atrial fibrillation ablation, the eventual clinical benefit of aspirin should be weighed against the increased risk of bleeding in combination with anticoagulation therapy. In the positive study by Mohanty and colleagues, the prophylaxis therapy was started 1 week before ablation. The timing of the colchicine regimen initiation might play a role into clinical outcomes.

In the current study, no significant difference in the pericarditis-related complications and redo procedure rate was observed after prophylaxis therapy. Finally, no patients discontinued prophylaxis therapy, and the rate of adverse effects was limited to colchicine-related diarrhea. When compared with previous studies on colchicine after atrial fibrillation catheter ablation,[20,21] the lower side effect rate might be explained by the lower mean age in our cohort (66 years vs 31 years).[22]

Different randomized clinical trials evaluated the use of colchicine after cardiac and thoracic surgery to prevent postoperative atrial fibrillation.[23,24] A recent meta-analysis of 8 trials, comprising 1885 patients, concluded that there was a statistically significant lower risk of developing postoperative atrial fibrillation with colchicine vs. placebo.[8] Of note, there was a higher risk of adverse gastrointestinal events without difference in the risk of drug discontinuation in patients receiving colchicine vs. placebo.[8]

The Hybrid Epicardial and Endocardial Sinus Node Sparing Ablation Therapy for Inappropriate Sinus Tachycardia (HEAL-IST) trial (NCT05280093), an international, multicenter, investigational device exempt trial on hybrid sinus node–sparing ablation is currently ongoing.[25] This trial is enrolling symptomatic IST/POTS refractory or intolerant to drugs (e.g., beta-blocker, calcium-channel blockers, ivabradine), thus refractory to conservative treatment. Prophylaxis therapy for pericarditis is highly recommended in the trial.

Limitations

This is a single-center retrospective study. The diagnosis of pericarditis was performed based on the interpretation of chest pain as pericardial in origin and subsequent administration of anti-inflammatory therapy was left to the physician's discretion. The postprocedural heart rate is influenced by multiple clinical factors and its measurement with ECG is limited. The utilization of long-term recording device can improve the reliability of the measurement. We did not collect supplemental data on inflammatory biomarkers, such as C-reactive protein. However, these data can be misleading in a postsurgical clinical setting. The prophylaxis therapy was prescribed in the late cohort and was not randomized. A placebo effect cannot be ruled out. A learning effect cannot be excluded.

Conclusion

In a cohort of patients undergoing a sinus node–sparing hybrid ablation for IST/POTS, a prophylaxis therapy with acetylsalicylic acid and colchicine was associated with a lower rate of symptomatic pericarditis and postprocedural heart rate. Prophylaxis therapy was well tolerated, and none of the patients discontinued it prematurely. Prophylaxis therapy is reasonable in all patients undergoing hybrid ablation for IST/POTS.

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Data Availability: The data underlying this article will be shared on reasonable request to the corresponding author.

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