


# Perioperative Amiodarone to Prevent Atrial fibrillation after Septal Myectomy in obstructive hypertrophic cardiomyopathy

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## Abstract

**Aims** Amiodarone reduces the incidence of atrial fibrillation (AF) following coronary artery bypass surgery; however, the benefit of perioperative amiodarone in patients undergoing septal myectomy (SM) for obstructive hypertrophic cardiomyopathy (oHCM) has not been studied. We hypothesized that prophylactic amiodarone would reduce the incidence of postoperative AF (POAF) following SM for oHCM.

**Methods and Results** A single-centre, pre-post intervention open-label study of oral amiodarone (200 mg twice daily starting 7 days preoperatively and 200 mg once daily continuing for 30 days postoperatively) in patients without prior AF undergoing SM for oHCM from 2014 to 2018. The primary outcome was incident AF within 30 days. Secondary outcomes were unplanned readmission, AF treatment, total and intensive care unit (ICU) length of stay (LOS), and pacemaker implantation for high-grade atrioventricular (AV) block. 61 patients met inclusion criteria with 34 (55.8%) in the pre-intervention (control) group and 27 (44.2%) in the post-intervention (amiodarone) group. The incidence of POAF was 11.0% in the amiodarone group compared with 38.2% in the control group ( $P = 0.017$ ). After adjusting for age, amiodarone was associated with less POAF [adjusted odds ratio (aOR) 0.21; 95% confidence interval (CI) 0.05, 0.76;  $P = 0.016$ ]. ICU (2 days [IQR 1, 4] vs. 3 days [IQR 2, 4];  $P = 0.165$ ) and total (6 days [IQR 5, 6] vs. 6 days [IQR 5, 7];  $P = 0.165$ ) LOS were similar, as was the rate of pacemaker implantation (7.4% vs. 8.3%,  $P > 0.999$ ). There were no adverse events associated with amiodarone.

**Conclusions** Perioperative oral amiodarone is safe and was associated with lower incidence of POAF following SM for oHCM.

**Keywords** Hypertrophic cardiomyopathy; Septal myectomy; Postoperative atrial fibrillation; Amiodarone

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## Introduction

Hypertrophic cardiomyopathy (HCM) is the most common monogenic cardiomyopathy, with an estimated population prevalence of 0.2–1.4%.<sup>1,2</sup> HCM is strongly associated with atrial fibrillation (AF), with a reported prevalence of approximately 20% and annual incidence of 2.0–2.5% in this population.<sup>3,4</sup> Patients with HCM and AF have high rates of thromboembolic disease, leading to the current recommen-

dation for systemic anticoagulation in all patients with coexistent HCM and AF, regardless of commonly used risk models.<sup>5</sup> AF has also been associated with increased rates of cardiovascular mortality in patients with HCM.<sup>6,7</sup>

Patients with symptomatic obstructive HCM (oHCM) refractory to medical therapy who are not at prohibitively high risk are often referred for surgical septal reduction via septal myectomy (SM). AF is common after cardiac surgery, although the incidence of new postoperative AF (POAF)

following SM is not well described. POAF is associated with worse clinical outcomes and increased hospital LOS following non-HCM related cardiac surgery.<sup>8–10</sup> The Prophylactic Oral Amiodarone for the Prevention of Arrhythmias That Begin Early After Revascularization, Valve Replacement, or Repair (PAPA-BEAR) trial previously demonstrated that prophylactic amiodarone reduced the rate of POAF in a general cardiac surgery population, although patients with HCM were not included.<sup>11</sup> Patients with HCM represent a unique patient population with a high prevalence of AF, which is typically symptomatic, likely due to coexistent diastolic dysfunction and relative reliance on atrial function for adequate ventricular filling. We hypothesized that prophylactic perioperative amiodarone use would decrease the incidence of POAF following SM for oHCM and, in turn, decrease medical interventions, simplify the postoperative course, and decrease length of stay (LOS).

## Methods

### Study design and participants

The Perioperative Amiodarone to Prevent Atrial Fibrillation after Septal Myectomy in Obstructive Hypertrophic Cardiomyopathy Study (PAPA-SMURPH) was a single site prospective pre–post intervention study designed as a pragmatic interventional study to improve the perioperative care of patients undergoing SM. Study subjects were diagnosed with HCM by clinicians expert in the field and based on standard diagnostic criteria.<sup>12</sup> All patients who underwent SM for symptomatic oHCM at our institution after September 2014 were enrolled in a registry and followed longitudinally. The pre-intervention period extended from September 2014 to March 2017 and the post-intervention period was from April 2017 to November 2018. In this ambulatory cohort of patients undergoing elective SM, the intervention consisted of oral amiodarone 200 mg twice daily starting 7 days prior to SM, then 200 mg once daily was continued via oral or enteric access for 30 days postoperatively. Patients were included in the study if they were diagnosed with oHCM, referred for clinically indicated SM, had no prior history of AF, and were not receiving antiarrhythmic therapy. The pre-intervention group patients are referred to as controls, while the post-intervention group is referred to as the amiodarone group. Preoperative clinical use of beta blockers, calcium channel blockers, and disopyramide was allowed at the discretion of the treating physician. Exclusion criteria included patient refusal to participate and prior reported allergy to amiodarone. Baseline clinical, laboratory, and electrocardiographic characteristics were collected from the electronic medical record. The study protocol was approved by the institutional review board at Oregon Health & Science University.

### Septal myectomy

We have previously detailed our approach to SM and additional procedures on the mitral valve apparatus.<sup>13</sup> Briefly, we perform broad SM via median sternotomy and transaortic approach. When appropriate, myectomy is performed across the entire septum in the left ventricular outflow tract (LVOT), from trigone to trigone. Any associated mitral valve or sub-valvular apparatus abnormalities that contribute to LVOT obstruction, SAM, or MR are then addressed with the appropriate procedure including papillary muscle realignment, resection of accessory papillary muscles and chordae tendineae and division of apicoseptal myocardial bands. We rarely perform direct mitral valve repair, Alfieri stitch, or mitral valve replacement.

### Outcomes

The primary outcome was incident POAF within 30 days of SM. Secondary outcomes were unplanned hospitalization within 30 days after SM, need for AF treatment within 30 days after SM, and total and intensive care unit (ICU) LOS. Safety outcomes were amiodarone-related clinically confirmed adverse events, as well as postoperative implantation of a permanent pacemaker for high-grade atrioventricular (AV) block.

Patients were considered to have POAF if they had >6 min of AF over the course of any 24 h period in the 30 days following surgery. This cutoff was extrapolated from prior trials of device-detected AF.<sup>14</sup> POAF was diagnosed in hospitalized patients by continuous cardiac telemetry monitoring as is standard practice following cardiac surgery. After hospital discharge, POAF was detected by electrocardiogram as clinically indicated or by clinically indicated implanted cardiac device interrogation at a 30 day follow-up visit. AF management was at the discretion of the treating physician. LOS was defined as the number of midnights spent in the hospital following SM. ICU LOS was defined as the number of midnights spent in the ICU following SM where the patient was cared for under the rules and regulations of critical care status.

### Patient reported outcomes

The Kansas City Cardiomyopathy Questionnaire (KCCQ) and New York Heart Association Classification (NYHA class) were assessed at clinical visits before and after SM.

### Statistical analysis

Descriptive statistics were used to summarize characteristics of the study population. Frequencies with percentages were calculated for categorical variables while means with

standard deviations (SDs) or medians with inter-quartile ranges (IQRs) were calculated for continuous variables. Patient and clinical characteristics by intervention group were compared using two-sample *t*,  $\chi^2$ , Fisher's exact, and Wilcoxon rank sum tests as appropriate. Within group comparisons preoperatively and postoperatively were made with paired *t* tests or Wilcoxon signed-rank tests. Kaplan–Meier analyses and log-rank test were used to estimate and compare the proportion of patients experiencing POAF at 30 days. To assess the relationship between prophylactic amiodarone use and POAF, as well as surgical characteristics and POAF, modified Firth penalized logistic regression was performed.<sup>15</sup> This approach was used to reduce bias in maximum likelihood estimation that may result from traditional logistic regression due to small sample size and data sparsity.<sup>16</sup> As one surgeon performed a small number of cases in the control group and a second surgeon performed the remainder of control cases and all post-intervention cases, we performed additional analysis excluding the control cases performed by the first surgeon. We report odds ratios (ORs) with 95% confidence intervals (CIs) and *P* values calculated by profile likelihood for the unadjusted model as well as one adjusted *a priori* for age as a known predictor of POAF. *P* values were two-sided and evaluated at a 0.05 significance level. Complete case analyses were performed with SAS version 9.4 (SAS Institute, Inc., Cary, NC, USA) and R version 3.5.1 (R Core Team, Vienna, Austria).

## Results

### Study participants

Baseline characteristics are reported in *Table 1*. From September 2014 through November 2018, 84 patients underwent SM at our institution. Of these, 23 patients had pre-existing AF or a contraindication to amiodarone and were excluded. Of the 61 included patients, 34 (55.8%) were in the control group and 27 (44.2%) were in the amiodarone group. Demographic characteristics, including age and sex, were similar between the control and amiodarone groups (54.4 ± 16.3 years vs. 54.3 ± 13.8 years; *P* = 0.98, and 58.8% vs. 51.9% male; *P* = 0.59). More patients in the amiodarone group had diabetes (29.6% vs. 8.8%; *P* = 0.05). The prevalence of hypertension, coronary artery disease and obstructive sleep apnoea were similar in the amiodarone and control groups (74.1% vs. 58.8%; *P* = 0.21, 33.3% vs. 35.3%; *P* = 0.87, and 33.3% vs. 17.6%, *P* = 0.16, respectively).

Baseline, pre-SM echocardiographic characteristics are reported in *Table 2*. There were no significant differences observed between the amiodarone and control groups in left ventricular ejection fraction (LVEF), left atrial volume index, resting LVOT gradient, or lateral E/e' ratio (70% [IQR 67.5–70] vs. 72.5 [IQR 67.5–75]; *p* 0.073, 44.2 ± 15.2 mL/m<sup>2</sup> vs. 47.2 ± 20.2 mL/m<sup>2</sup>; *P* = 0.55, 60.1 ± 45.6 mmHg vs. 62.6 ± 36.8 mmHg; *P* = 0.81, and 12.5 [IQR 8.7, 14.7] vs.

**Table 1** Baseline demographic and clinical characteristics

Characteristic	Amiodarone (n = 27)		Control (n = 34)		<i>P</i> value
Age (years), mean (SD)	54.3	(13.8)	54.4	(16.3)	0.984 <sup>a</sup>
Male sex, n (%)	14	(51.9)	20	(58.8)	0.586 <sup>b</sup>
Weight (kg), mean (SD)	91.5	(19.3)	89.9	(20.2)	0.763 <sup>a</sup>
Height (cm), mean (SD)	171.1	(11)	171.1	(11.7)	0.986 <sup>a</sup>
BMI (kg/m <sup>2</sup> ), mean (SD)	31	(4.5)	30.6	(5.4)	0.730 <sup>a</sup>
Hypertension, n (%)	20	(74.1)	20	(58.8)	0.213 <sup>b</sup>
Diabetes, n (%)	8	(29.6)	3	(8.8)	0.048 <sup>c</sup>
Coronary artery disease, n (%)	9	(33.3)	12	(35.3)	0.873 <sup>b</sup>
Obstructive sleep apnoea, n (%)	9	(33.3)	6	(17.6)	0.158 <sup>b</sup>
Angina, n (%)	19	(70.4)	19	(55.9)	0.246 <sup>b</sup>
Syncope, n (%)	5	(18.5)	11	(32.4)	0.222 <sup>b</sup>
Beta blocker, n (%)	25	(92.6)	29	(85.3)	0.448 <sup>c</sup>
Calcium channel blocker, n (%)	12	(44.4)	8	(23.5)	0.084 <sup>b</sup>
Disopyramide, n (%)	9	(33.3)	15	(44.1)	0.392 <sup>b</sup>
Diuretic use, n (%)	3	(11.1)	3	(8.8)	>0.999 <sup>c</sup>
NYHA score, n (%)					0.685 <sup>d</sup>
2	10	(37)	13	(38.2)	
3	17	(63)	17	(50)	
4	0	(0)	4	(11.8)	
Preoperative KCCQ, mean (SD)	41.5	(12.5)	41.5	(12.3)	0.992 <sup>a</sup>
Preoperative creatinine, mean (SD)	0.9	(0.2)	1	(0.2)	0.236 <sup>a</sup>
Preoperative haemoglobin, mean (SD)	13.9	(1.5)	14	(1.3)	0.742 <sup>a</sup>

<sup>a</sup>*t* test.

<sup>b</sup> $\chi^2$  test.

<sup>c</sup>Fisher's exact test; and

<sup>d</sup>Exact Wilcoxon rank-sum test.

BMI, body mass index; KCCQ, Kansas City cardiomyopathy questionnaire; NYHA, New York Heart Association.

**Table 2** Baseline echocardiographic characteristics

Characteristic	Amiodarone (n = 27)		Control (n = 34)		P value
LVEF, median (IQR)	70	(67.5, 70.0)	72.5	(67.5, 75.0)	0.073 <sup>a</sup>
Left atrial volume index (mL/m <sup>2</sup> ), mean (SD)	44.2	(15.2)	47.2	(20.2)	0.548 <sup>b</sup>
Peak resting gradient (mmHg), mean (SD)	60.1	(45.6)	62.6	(36.8)	0.811 <sup>b</sup>
Maximal provoked gradient (mmHg), mean (SD)	131.7	(45.8)	129.6	(52.4)	0.873 <sup>b</sup>
Maximal LV wall thickness (mm), mean (SD)	18.5	(3.6)	19.9	(6.6)	0.297 <sup>b</sup>
RVSP at rest (mmHg), mean (SD)	33.5	(11.4)	32.1	(10.9)	0.731 <sup>b</sup>
Lateral E/e' ratio, median (IQR)	12.5	(8.7, 14.7)	11.8	(10.0, 15.2)	0.725 <sup>a</sup>
Resting MR > mild, n (%)	7	(25.9)	9	(26.5)	0.962 <sup>c</sup>
Stress MR > mild, n (%)	6	(22.2)	7	(20.6)	0.877 <sup>c</sup>
Abnormal BP response on exercise stress, n (%)	10	(37)	24	(70.6)	0.041 <sup>c</sup>

<sup>a</sup>Exact Wilcoxon rank-sum test.<sup>b</sup>t test.<sup>c</sup>χ<sup>2</sup> test.

BP, blood pressure; LV, left ventricle; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; RVSP, right ventricular systolic pressure.

**Table 3** Surgical characteristics and postoperative outcomes

Characteristic	Amiodarone (n = 27)		Control (n = 34)		P value
Procedure time, median (IQR), min	237	(201.0, 278.0)	232	(183.0, 255.0)	0.387 <sup>a</sup>
Pump time, median (IQR), min	118	(108.0, 143.0)	95	(84.0, 127.0)	0.009 <sup>a</sup>
Cross-clamp time, median (IQR), min	87	(76.0, 102.0)	67.5	(54.0, 78.0)	<0.001 <sup>a</sup>
LOS (days), median (IQR)	6	(5.0, 6.0)	6	(5.0, 7.0)	0.165 <sup>a</sup>
ICU LOS (days), median (IQR)	2	(1.0, 4.0)	3	(2.0, 4.0)	0.165 <sup>a</sup>
Postoperative KCCQ, mean (SD)	50.3	(10.7)	50.2	(12.9)	0.962 <sup>b</sup>
CABG × 1, n (%)	2	(7.4)	4	(11.8)	0.685 <sup>c</sup>
CABG × 2, n (%)	1	(3.7)	2	(5.9)	>0.999 <sup>c</sup>
MV repair by PMR, n (%)	25	(92.6)	34	(100)	0.192 <sup>c</sup>
MV repair by Alfieri stitch, n (%)	3	(11.1)	1	(2.9)	0.313 <sup>c</sup>
AV replacement, n (%)	0	(0)	1	(2.9)	>0.999 <sup>c</sup>
Postoperative NYHA class, n (%)					0.632 <sup>a</sup>
1	8	(29.6)	12	(35.3)	
2	17	(63)	20	(58.8)	
3	2	(7.4)	2	(5.9)	
Rehospitalization within 30 days, n (%)	1	(3.7)	5	(14.7)	0.214 <sup>c</sup>
Postoperative atrial fibrillation, n (%)	3	(11.1)	13	(38.2)	0.017 <sup>d</sup>
Management of POAF, n (%)					>0.999 <sup>c</sup>
None	0	(0)	1	(2.9)	
Intravenous amiodarone	3	(11.1)	6	(17.6)	
Oral amiodarone	0	(0)	1	(2.9)	
Intravenous metoprolol	0	(0)	2	(5.9)	
DCCV	0	(0)	2	(5.9)	
Transesophageal echo and DCCV	0	(0)	1	(2.9)	
Permanent pacemaker implanted, n (%)	2	(7.4)	3	(8.8)	>0.999 <sup>c</sup>

<sup>a</sup>Exact Wilcoxon rank-sum test.<sup>b</sup>t test.<sup>c</sup>Fisher's exact test.<sup>d</sup>χ<sup>2</sup> test.

AV, aortic valve; CABG, coronary artery bypass graft; DCCV, direct current cardioversion; ICU, intensive care unit; KCCQ, Kansas City cardiomyopathy questionnaire; LOS, length of stay; MV, mitral valve; NYHA, New York Heart Association; PMR, papillary muscle realignment; POAF, postoperative atrial fibrillation.

11.8 [IQR 10.0, 15.2];  $P = 0.72$ , respectively). More patients in the amiodarone group had an abnormal blood pressure response to exercise (37.0% vs. 70.6%;  $P = 0.041$ ).

Surgical characteristics and postoperative outcomes are reported in *Table 3*. One patient in the control group

underwent concurrent aortic valve replacement. Total procedural time was similar between amiodarone and control groups (237.0 min [IQR 201.0, 278.0] vs. 232.0 min [IQR 183.0, 255.0];  $P = 0.39$ ); however, cardiopulmonary bypass time and aortic cross-clamp time were both lower in the

control group (118.0 min [IQR 108.0, 143.0] vs. 95.0 min [IQR 84.0, 127.0];  $P = 0.009$ , and 87.0 min [IQR 76.0, 102.0] vs. 67.5 min [IQR 54.0, 78.0];  $P = 0.0004$ , respectively).

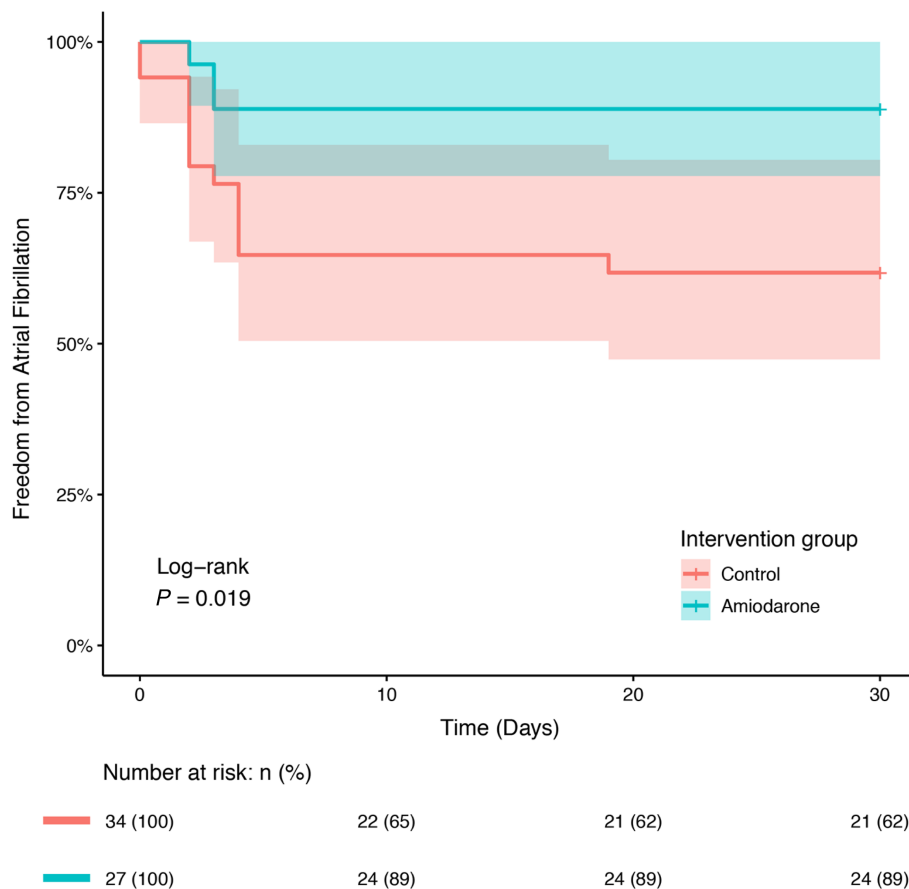
### Outcomes

Subjects in the amiodarone group demonstrated a significantly reduced incidence of POAF (11.1% vs. 38.2%;  $P = 0.017$ ) (Figure 1). In the unadjusted model, amiodarone was associated with decreased risk of POAF (OR 0.22; 95% CI 0.05, 0.76;  $P = 0.016$ ); results were similar in the age-adjusted model (adjusted OR 0.21; 95% CI 0.05, 0.76;  $P = 0.016$ ), and when the subset of patients operated on by one surgeon who performed some control cases but no amiodarone cases was excluded (OR 0.20; 95% CI 0.04, 0.83;  $P = 0.026$ ). Three patients (11.1%) in the amiodarone group received intravenous amiodarone for treatment of POAF. Twelve patients in the control group (35.3%) were treated for POAF as follows: 2 (5.9%) received intravenous metoprolol, 6 (17.6%) received intravenous amiodarone, 1 (2.9%) received oral amiodarone, 1 (2.9%)

underwent transesophageal echocardiogram and direct current cardioversion, and 2 (5.9%) patients had a total of three direct current cardioversions. We evaluated surgical factors associated with the development of POAF in a univariable regression model, and only hospital length of stay and single vessel CABG were associated with POAF (Table 4).

The median hospital length of stay was similar among amiodarone and control groups (6 days [IQR 5, 6] vs. 6 days [IQR 5, 7];  $P = 0.165$ ), as was ICU length of stay (2 days [IQR 1, 4] vs. 3 days [IQR 2, 4];  $P = 0.165$ ). No adverse events associated with amiodarone administration were reported. There was no observed difference in the rate of permanent pacemaker implantation for high-grade AV block in the amiodarone vs. control groups (7.4% vs. 8.8%,  $P > 0.999$ ). Within 30 days of SM, no readmissions occurred in the amiodarone group. Five patients in the control group (14.7%) were readmitted: 1 had acute decompensated heart failure, 1 had unrelated anaphylaxis, 2 had chest pain and palpitations (1 of these was diagnosed with pericarditis), and 1 had a pulmonary embolus. There were no deaths during the follow-up period, and no subjects were lost to follow-up.

Figure 1 Kaplan–Meier curves for incident atrial fibrillation after septal myectomy.



**Table 4** Univariable regression analysis assessing the association between surgical factors and postoperative atrial fibrillation development

Characteristic	OR (95% CI)	P value
Pump time	1.01 (0.99, 1.02)	0.347
Cross-clamp time	1.00 (0.99, 1.02)	0.670
Hospital LOS	1.75 (1.10, 2.98)	0.018
ICU LOS	1.11 (0.81, 1.51)	0.502
Postoperative KCCQ	1.00 (0.95, 1.05)	0.986
Single vessel CABG	6.01 (1.13, 39.55)	0.035
Two vessel CABG	1.35 (0.09, 12.42)	0.799
Mitral valve repair by PMR	4.02 (0.20, 1197.19)	0.419
Other mitral valve repair method	0.94 (0.07, 6.99)	0.957
Aortic valve replacement	8.87 (0.29, 2145.30)	0.209
Postoperative NYHA Class 2	1.65 (0.49, 6.38)	0.431
Postoperative NYHA Class 3	1.30 (0.10, 11.48)	0.821
Rehospitalization within 30 days	1.41 (0.21, 7.50)	0.699
Permanent pacemaker implanted	0.72 (0.06, 4.75)	0.752

LOS, length of stay; ICU, intensive care unit; KCCQ, Kansas City Cardiomyopathy Questionnaire; CABG, coronary artery bypass grafting, PMR, papillary muscle realignment; NYHA, New York Heart Association.

### Patient reported outcomes

The proportion of patients within each NYHA class at baseline and during follow-up did not significantly differ between groups ( $P = 0.445$ ); significant improvement in NYHA class was seen within amiodarone and control groups ( $P < 0.001$  for both) following SM (Figure 2). In a subgroup of patients where KCCQ score was available pre-myectomy and post-myectomy, subjects receiving amiodarone demonstrated significant improvement at 30 days (40.9 [SD 12.4] to 50.8 [SD 11.0];  $P < 0.001$ ); there was a non-significant trend towards improvement in the control group (41.9 [SD 12.9] to 47.2 [SD 12.9];  $P = 0.134$ ). Comparison between the amiodarone and control groups did not demonstrate a significant difference ( $P = 0.249$ ) (Figure 3).

### Discussion

The PAPA-SMURPH study found that prophylactic amiodarone is safe and associated with lower risk of POAF following SM for oHCM. Furthermore, our outpatient protocol is easy to administer and helps reduce the complexities and questions that arise should patients with HCM develop AF in the postoperative period.

We observed a 38.2% incidence of POAF in the control group, in line with previously published results from the non-HCM cardiac surgery literature,<sup>11,17</sup> although notably higher than a recent single-centre case series of SM for oHCM which reported an overall 21.5% incidence of POAF, with only 12.4% incidence in patients without prior AF.<sup>18</sup> We cannot explain this discrepancy. Nevertheless, POAF remains a common clinical challenge following SM, and multiple prior studies have demonstrated high rates of thromboembolism

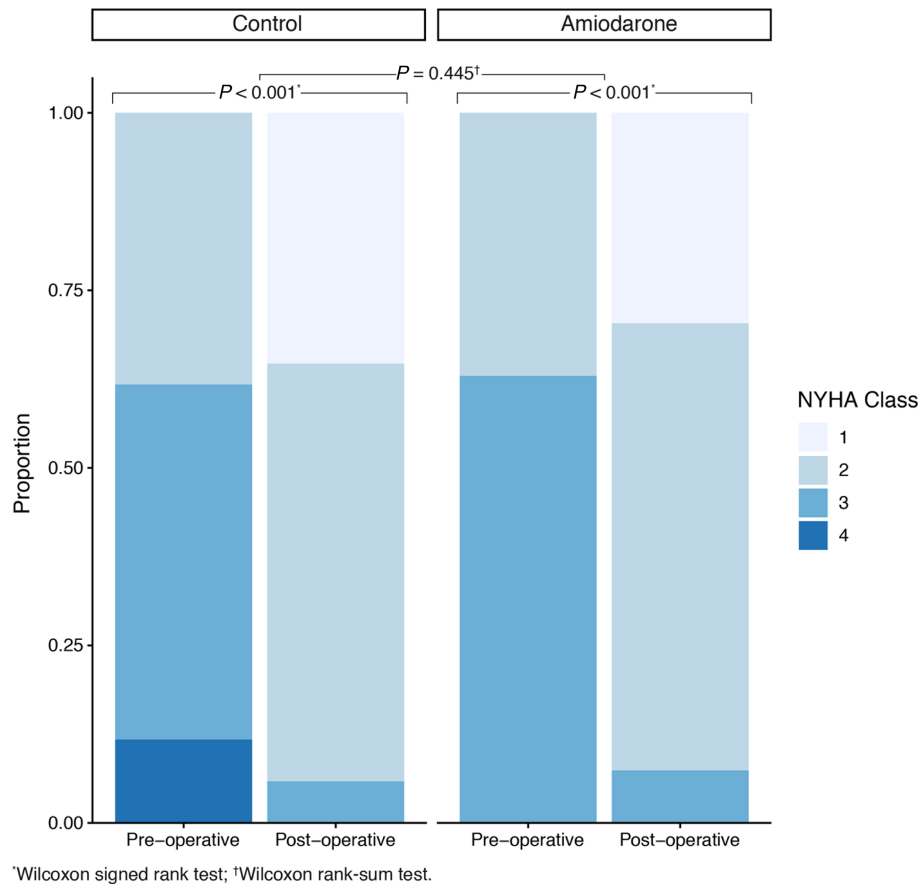
and overall increased mortality in non-surgical patients with concurrent HCM and AF.<sup>5,6,19</sup>

While there are clear guidelines as a direct result of these findings recommending anticoagulation regardless of commonly used risk models,<sup>20</sup> it is unclear what to do in the setting of HCM and POAF specifically. Our practice is to initiate systemic anticoagulation in all patients with POAF following SM in the absence of contraindication and to discontinue long-term anticoagulation only after subsequent ambulatory rhythm monitoring demonstrates consistent sinus rhythm. Recognizing that in the non-HCM population, almost half of patients with POAF developed subsequent AF, we continue to perform ambulatory ECG monitoring annually and as directed by symptoms. In a study from the Framingham cohort, the incidence of recurrent AF following a first episode of POAF after cardiac surgery was 47%,<sup>21</sup> although this did not specifically include patients with HCM.

Patients experiencing POAF tend to be discharged and maintained on higher doses of AV-nodal blocking drugs beyond the immediate 30 day postoperative period. By preventing POAF in our HCM patients, we further enable de-escalation of these drugs if appropriate, potentially leading to further symptomatic improvement due to freedom from side effects.

We opted for a low-dose oral regimen of amiodarone starting with a loading dose of 2.8 g in divided doses over 7 days, and a maintenance dose of 200 mg daily postoperatively. This was chosen based on ease of administration, minimal anticipated side effects, and after consideration of prior studies that utilized a range of amiodarone timing, route, dose and duration.<sup>22</sup> We continued amiodarone for 30 days postoperatively, longer than in most other trials, but observed only a single case of POAF beyond postoperative day 4 which occurred in a control group patient. We believe that similar results would be achieved with a shorter postoperative course of amiodarone.

**Figure 2** NYHA class before and after septal myectomy in control and amiodarone groups. NYHA, New York Heart Association.



While meta-analysis of multiple prior studies previously demonstrated that prophylactic amiodarone aimed at reduction in POAF was associated with modestly decreased hospital LOS,<sup>22</sup> we observed similar duration of total and ICU hospitalization in our control and amiodarone groups. This may be related to our relatively small sample size.

The POAF impacted the short-term clinical course of patients with HCM undergoing SM, and prophylactic amiodarone was associated with fewer interventions for POAF, with less postoperative use of intravenous amiodarone, and fewer cardioversions in the amiodarone prophylaxis group. We also evaluated patient-reported outcomes including NYHA class and KCCQ in a subgroup of patients. Both groups demonstrated significant improvements in NYHA class. There was a slightly greater increase in KCCQ score in the amiodarone group as compared with the control group; however, comparison between the groups did not demonstrate a statistically significant difference.

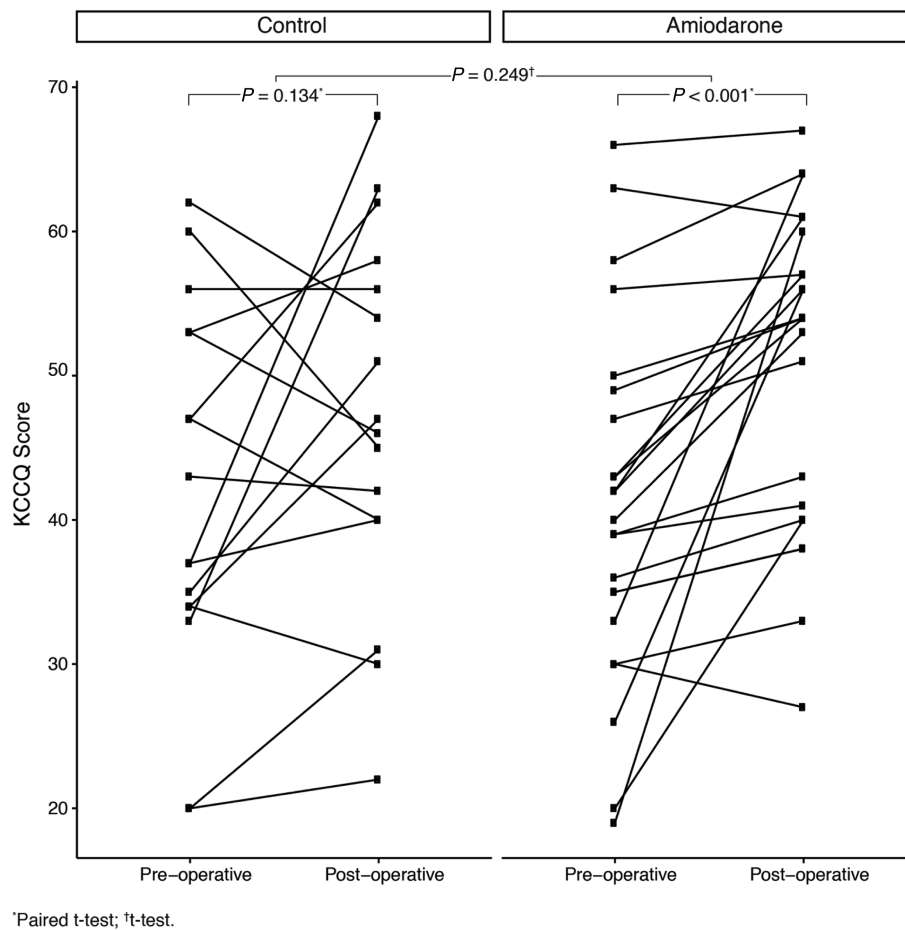
Postoperative conduction disease is a known complication of septal reduction therapy, with pacemaker placement being the cornerstone of management of postoperative high-grade AV block. Rates of 2.3–8.7% have previously been reported in operative cohorts.<sup>23,24</sup> Our observed rate of permanent pace-

maker placement for high-grade AV block was consistent with this previously reported range and similar in the control and amiodarone groups, suggesting that routine use of prophylactic amiodarone would not lead to increased rates of symptomatic bradycardia, AV block, or pacemaker implantation.

Over the duration of the study, our standard practice for SM evolved to include routine performance of papillary muscle realignment and, in eligible patients, resection of aberrant papillary muscles and secondary chordae tendineae, as well as division of apicoseptal myocardial bands. Our practice also progressed to include routine use of dobutamine stress transesophageal echo in the operating room to confirm resolution of the LVOT gradient even under pharmacologic stress, which in few cases led to return on bypass to perform additional surgery.<sup>25</sup> These changes in surgical technique may account for increased cross clamp and cardiopulmonary bypass times in the amiodarone group, and on univariable analysis, there was no association between these parameters and the development of POAF.

Our study has several important limitations including a small sample size and a non-randomized, un-blinded, and single-centre design. While inpatient monitoring for POAF was via continuous telemetry, outpatient diagnosis of POAF

**Figure 3** Connected graph of patient-reported KCCQ before and after septal myectomy in control and amiodarone groups. KCCQ: Kansas City Cardiomyopathy Questionnaire.



was via ECG and ambulatory monitoring as needed for symptoms, although ambulatory monitoring was not routinely performed in all patients. Thus, we cannot exclude that our study under-diagnosed sub-clinical POAF, but have no reason to believe that we would have detected more of this in the amiodarone group than the control group with protocol-mandated ambulatory ECG monitoring. Nevertheless, we provide data on a simple intervention associated with significantly reduced rates of clinically relevant POAF without attributable adverse events.

## Conclusions

Results from the PAPA-SMURPH study indicate that perioperative low-dose outpatient amiodarone use was associated with a significantly lower incidence of POAF in patients with oHCM undergoing surgical septal reduction.

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## Conflict of interest

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