Dosing of amiodarone for post-operative atrial fibrillation in cardiac surgery patients

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Background

- The incidence of post-operative atrial fibrillation (POAF) is high after cardiac surgery (up to 65%), and may cause hemodynamic instability, heart failure, thromboembolic events, increased length of stay and healthcare costs
- Amiodarone is recommended for the prevention and treatment of POAF when first-line beta-blockers (BB) are contraindicated or not tolerated
- However, the optimal dosing strategy for amiodarone is unknown

Objectives

To determine the optimal dosing strategy of amiodarone to prevent or treat POAF

Methods

Design

- Retrospective, cross-sectional chart review at St. Paul's Hospital

Inclusion Criteria

- Adults undergoing CABG, valve repair/replacements, or both
- On amiodarone for POAF
- In NSR pre-op (including patients with history of paroxysmal AF)

Exclusion Criteria

- Patients undergoing other cardiac surgeries, history of permanent AF, or on amiodarone for indications other than for POAF

Outcomes

Primary

- To compare the dose of amiodarone in those who develop POAF versus those who remain in NSR (for prevention of POAF)
- To compare the dose of amiodarone in those who convert to NSR versus those who remain in POAF on discharge (for treatment of POAF)

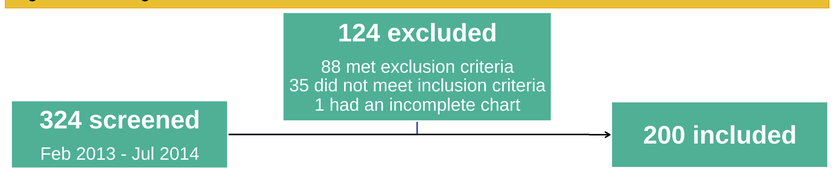
Secondary

- To compare the proportion of patients who develop POAF on IV versus PO only amiodarone regimens
- To compare time to POAF in those administered on IV versus PO only amiodarone regimens
- To compare the proportion of patients who convert to NSR within 48 hours in those administered IV vs. PO only amiodarone regimens
- To compare the dose of amiodarone in the first 2 days in those who convert to NSR within 48 hours versus those who convert after at least 48 hours

Statistics

- Convenience sample: N=200
- Statistical significance: p=0.025
- Statistical tests: descriptive, t-test, chi-squared test

Figure 1. Flow diagram



Results

Table 1. Baseline and operative characteristics

	Px* (n=67)	Tx* (n=133)
Mean age, years ± SD	67 ± 12	70 ± 9
Males, n (%)	47 (70.1)	96 (72.2)
Mean time to discharge, post-op days ± SD	10.5 ± 6.6	11.5 ± 8.4
Medical conditions, n (%)		
Hypertension	52 (77.6)	99 (74.4)
COPD	6 (9.0)	17 (12.8)
Paroxysmal AF	13 (19.4)	14 (10.5)
Heart failure or EF < 50	27 (40.3)	38 (28.6)
Diabetes mellitus	28 (41.8)	46 (34.6)
CKD or GFR < 60	20 (29.9)	36 (27)
Aortic stenosis or regurgitation	22 (32.8)	60 (45.1)
Mitral stenosis or regurgitation	13 (19.4)	27 (20.3)
Medications, n (%)		
Beta-blockers	33 (49)	71 (53)
Verapamil or diltiazem	3 (4.5)	9 (6.8)
Anticoagulants	6 (9)	7 (5.3)
Statins	35 (52.2)	83 (62.4)
Types of surgery, n (%)		
CABG alone	42 (62.7)	61 (45.9)
Valve repair or replacement	15 (22.4)	39 (29.3)
CABG & valve repair or replacement	9 (13.4)	27 (20.3)
Transapical valve replacement	1 (1.5)	6 (4.6)

Table 2. POAF & amiodarone characteristics

	Px* (n=67)	Tx* (n=133)
Amiodarone for prevention, n (%)	67 (100)	
Developed POAF, n (%)	33 (49.3)	
Mean time to POAF, post-op days ± SD	2.5 ± 1.6	
Amiodarone started post-op, n (%)	62 (92.5)	
Amiodarone for treatment		133 (100)
Mean time to POAF, post-op days ± SD		2.0 ± 1.1
POAF duration < 48 hours, n (%)		88 (66.2)
AF at discharge, n (%)		17 (12.8)
Mean time to NSR, post-op days ± SD		3.75 ± 3.1
Route of amiodarone, n (%)		
IV only	1 (1.5)	0
PO only	37 (55.2)	74 (55.6)
IV & PO	29 (43.3)	59 (44.4)
Taking BB when POAF developed, n (%)	18 (54.5)	74 (55.6)
Mean time to discharge, post-op days ± SD	10.5 ± 6.6	11.5 ± 8.4

** Px: Amiodarone for prevention*
** Tx: Amiodarone for treatment*

Figure 2. Primary Outcome: Total dose of amiodarone for POAF prevention and treatment

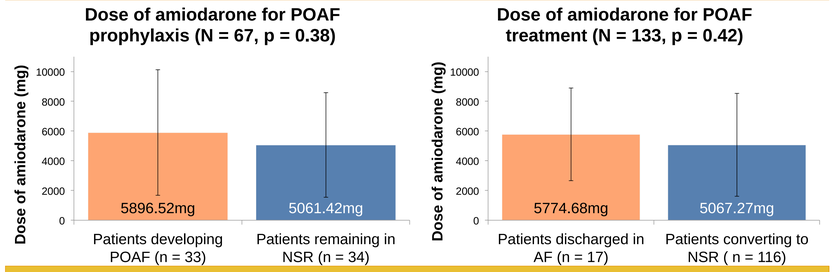


Figure 3. Efficacy of IV regimens versus oral-only amiodarone regimens for POAF

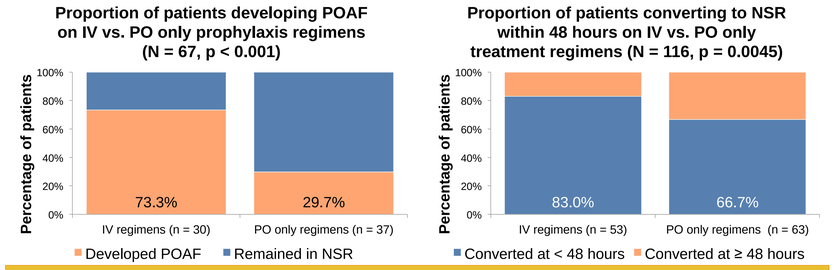
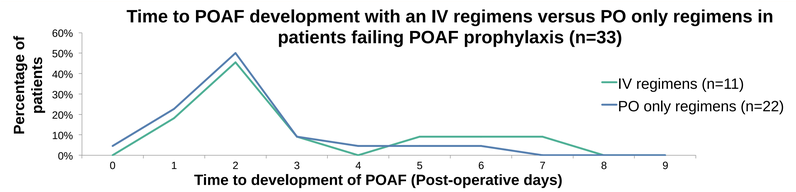


Figure 4. Difference in time to POAF development with IV versus oral-only amiodarone regimens



Other Results

- 166 (83%) developed POAF with mean time to POAF of 2.1 ± 1.2 post-op days
- No difference in dose of amiodarone in the first 2 days for POAF treatment in those who convert within 48 hours vs. those who convert after 48 hours

Limitations

- Retrospective study with small sample size
- Results are confounded by length of stay and concomitant beta-blockers
- IV amiodarone converted to PO equivalents based on 48% oral bioavailability
- POAF is very heterogeneous in its presentation

Conclusions

- Rate of POAF is high (83%) in cardiac surgery patients on amiodarone for prevention or treatment with no difference in dosing of amiodarone in those who receive successful prevention or treatment of POAF
- Approximately 5000mg (oral equivalent) of amiodarone over the index hospitalization (~11 days) was associated with high rates of NSR at discharge (89%). To achieve this, we suggest the following dosing strategies:
  - IV regimen: 150mg IV bolus, then 60mg/h x6h, then 30mg/h x18h, then 400mg PO BID x3d, then 200mg PO daily
  - PO only regimen: 400mg PO TID x2d, then BID x3d, then 200mg PO daily
- Larger studies with statistical adjustment of confounders for POAF are required to fully elicit the optimal dosing strategy