Impact of Oral Anticoagulation on Clinical Outcomes in Postoperative Atrial Fibrillation

G. Hossein Almassi MD, Jacquelyn A. Quin MD MPH, Eileen M. Stock PhD, Ellen Dematt MA, Kousick Biswas PhD, Brack Hattler MD, Marco A. Zenati MD Msc

INTRODUCTION

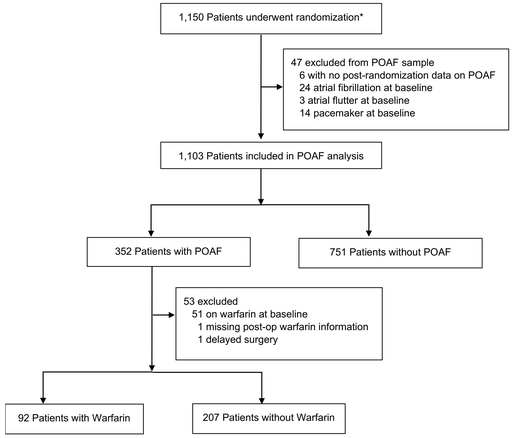
New-onset postoperative atrial fibrillation (POAF) remains the most common complication following coronary artery bypass grafting (CABG). Its adverse impact on clinical outcomes is well known. While the use of oral anticoagulation (OAC), usually with warfarin, for risk-reduction of thromboembolic stroke has been well documented in the nonsurgical population, there are few prospective studies that examine the impact of OAC on stroke and clinical outcomes in CABG patients with POAF. To address this knowledge gap, we examined the impact of OAC/warfarin on clinical outcomes in CABG patients with POAF enrolled in the REGROUP trial.

METHODS

Study Population

- Based on Cooperative Studies Program (CSP) Study #588, also known as the Randomized Endovein Graft Prospective (REGROUP) trial.
- Patients undergoing elective CABG-only surgery from Mar 2014-Apr 2017 at 16 participating VA Medical Centers
- New-onset POAF definition: any atrial-based irregular rhythm with a duration of at least 30 minutes that did not exist prior to the CABG procedure.
- Patients with a history of preoperative atrial fibrillation (AF) were excluded from this sub-analysis.
- Patients who developed POAF (or postoperative atrial flutter) were compared based on whether they were newly started on oral anticoagulation/warfarin (OAC group) vs. not (non-OAC group).

Consort Diagram of Study population:



Data Collection and Analysis

- Patient demographics, intraoperative processes of care, and postoperative outcome data were gathered by dedicated research nurses at each participating center.
- Data collected at six weeks and every three months included date of POAF, oral anticoagulant use, and POAF status.
- Clinical endpoints included all-cause death, cardiac-related death, MACE (all-cause death, repeat revascularization, acute myocardial infarction) and stroke.
- POAF vs. non-POAF groups were compared using chi-square analysis or Fisher's Exact test for categorical variables and two-sample t-tests or Wilcoxon rank-sum test for continuous variables.
- Cox proportional-hazards regression was performed to investigate the association of OAC among POAF patients with outcomes of all-cause and cardiac-related mortality, MACE, and stroke
- A p-value of 0.05 was used as the threshold for statistical significance.

RESULTS

Patient Characteristics

- POAF developed in 352/1103 (32%) patients
- Median time to POAF was on POD2 (IQR POD 2-3) with the majority of patients developing POAF within the first 5 days after surgery (Figure 1).
- Oral anticoagulation (OAC) in the form of warfarin was prescribed in 31% (92/299) of POAF patients.
- No significant patient differences were seen between the warfarin vs. no warfarin comparative groups (Table 1).

Figure 1 CSP 588 Randomized Endo-Vein Graft Prospective REGROUP Trial Days to POAF

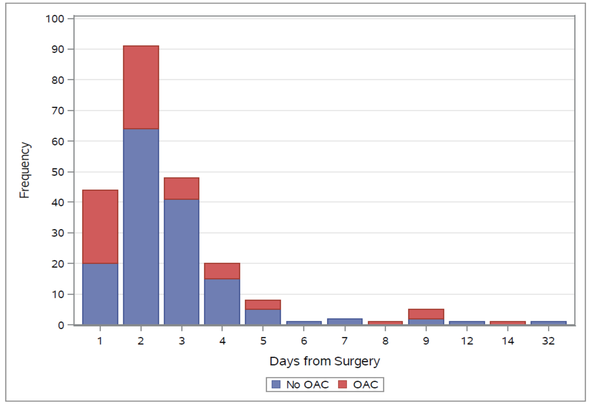


Table 1: Patient Characteristics comparing Warfarin vs. no Warfarin for POAF after CABG

	Warfarin (N= 92)	No warfarin (N=207)	Total (N= 299)	P-value
Age in years - mean ± SD	68.1 ± 5.54	68.1 ± 6.53	68.1 ± 6.24	0.680
White (vs all other)	81/ 92 (88.0)	187/207 (90.3)	268/ 299 (89.6)	0.548
Smoking Last Use				0.851
Never smoked	24 (26.1)	48 (23.2)	72 (24.1)	
< 3 months prior to surgery	18 (19.6)	50 (24.2)	68 (22.7)	
≥ 3 months but < 1 year prior to surgery	1 (1.1)	3 (1.4)	4 (1.3)	
≥ 1 year prior to surgery	49 (53.3)	105 (50.7)	154 (51.5)	
Missing	0 (0.0)	1 (0.5)	1 (0.3)	
Chronic Lung Disease	20/ 92 (21.7)	38/207 (18.4)	58/ 299 (19.4)	0.495
Serum Creatinine ≥ 1.5 mg/dl	8/ 81 (9.9)	17/171 (9.9)	25/ 252 (9.9)	0.987
Cerebrovascular Accident (CVA)	6/ 92 (6.5)	16/207 (7.7)	22/ 299 (7.4)	0.712
Peripheral Vascular Disease	10/ 92 (10.9)	29/207 (14.0)	39/ 299 (13.0)	0.457
Hypertension	86/ 92 (93.5)	183/207 (88.4)	269/ 299 (90.0)	0.178
Diabetes	42/ 92 (45.7)	110/207 (53.1)	152/ 299 (50.8)	0.232
Insulin-dependent diabetes	24 (57.1)	44 (40.0)	68 (44.7)	
Non-insulin-dependent diabetes	18 (42.9)	66 (60.0)	84 (55.3)	
History of Depression	20/ 92 (21.7)	64/207 (30.9)	84/ 299 (28.1)	0.103
Ejection Fraction < 45%	16/ 92 (17.4)	22/203 (10.8)	38/ 295 (12.9)	0.120
Urgent Status	26/ 92 (28.3)	45/207 (21.7)	71/ 299 (23.7)	0.221
CHA2DS2-VASc Score - mean ± SD	2.7 ± 1.31	3.0 ± 1.57	2.9 ± 1.49	0.203
Body Surface Area (m^2) - mean ± SD	2.18 ± 0.223	2.17 ± 0.235	2.17 ± 0.231	0.590
Body Mass Index (kg/m^2) - mean ± SD	30.94 ± 4.784	30.86 ± 5.371	30.88 ± 5.190	0.740
VASQIP Patient Risk - mean ± SD	1.18 ± 1.123	1.06 ± 0.936	1.10 ± 0.997	0.581
STS Risk of Mortality - mean ± SD	0.99 ± 0.755	0.97 ± 0.845	0.97 ± 0.817	0.605
No of grafts/pt - mean ± SD	3.2 ± 0.88	3.0 ± 0.72	3.1 ± 0.78	0.215

**Data was missing for the following means: CHA2DS2-VASc Score for 18 patients in the warfarin group and 59 patients in the no warfarin group, and STS Risk of Mortality for 1 patient in the warfarin group.*

Clinical Outcomes for Warfarin vs. No Warfarin groups

- Median follow-up: 32 months (mean of 30.6 ± 10.6)
- POAF patients on OAC (warfarin) showed significantly higher rates of cardiac mortality and acute MI (Table 2).
- No significant difference in the risk adjusted MACE or stroke rate was seen between groups

Table 2: Hazard Ratio for Clinical Outcomes comparing Warfarin vs. No Warfarin

	Warfarin N=92; (%)	No Warfarin N=207 (%)	Hazard Ratio	95% CI	
MACE*	19 (21%)	29 (14%)	1.67	0.93 - 2.99	0.08
Death from any cause	12 (13%)	17 (8.2%)	1.74	0.83 - 3.65	0.14
Cardiac related death	6 (6.5%)	3 (1.4%)	4.94	1.23-19.85	0.02
Acute myocardial infarction	8 (8.7%)	5 (2.4%)	4.19	1.36-12.89	0.01
Repeat revascularization	8 (8.7%)	12 (5.8%)	1.69	0.69 - 4.15	0.25
Stroke	3 (3.3%)	10 (4.8%)	0.63	0.71 - 2.29	0.48

*MACE Composite: death, MI, and repeat revascularization

Study Limitations

- The number patients in each comparative group was small
- Information on the decision to use OAC in POAF patients vs. not was not always clear.
- Data on anti-thrombotic regimens other than warfarin, such as Plavix or direct oral anticoagulants, were not collected.
- Patients were predominantly male veterans and therefore, the results are not generalizable

CONCLUSIONS

In the REGROUP trial, a higher risk of cardiac mortality and myocardial infarction was seen with anticoagulation for POAF after CABG compared to no anticoagulation although all-cause mortality and stroke rates were not significantly different. These findings may need to be considered in shared decision-making conversations with patients on the risk-benefit ratio of using OAC to reduce the risk of thromboembolism when POAF occurs after CABG. Large randomized trials are imperative to answer the questions on the use of anticoagulation in POAF cardiac patients.

Disclosure: The views expressed are those of the authors and do not necessarily reflect the position or policy of the U.S. Department of Veterans Affairs or the United States Government.

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