

2024-2025

THÈSE
pour le
DIPLÔME D'ÉTAT DE DOCTEUR EN MÉDECINE
CARDIOVASCULAIRE

Long-term Anticoagulation After New-Onset Atrial Fibrillation Following Cardiac Surgery: Efficacy and Safety at 2 Years.

Anticoagulation au long cours après fibrillation atriale de novo en postopératoire de chirurgie cardiaque : efficacité et sécurité à 2 ans.

Étude rétrospective monocentrique

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Né le 13/05/1997 à Sarreguemines (57)

Sous la direction du Dr POIRIER Antoine et du Dr DANG VAN Simon

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SERMENT D'HIPPOCRATE

« Au moment d'être admis(e) à exercer la médecine, je promets et je jure d'être fidèle aux lois de l'honneur et de la probité. Mon premier souci sera de rétablir, de préserver ou de promouvoir la santé dans tous ses éléments, physiques et mentaux, individuels et sociaux. Je respecterai toutes les personnes, leur autonomie et leur volonté, sans aucune discrimination selon leur état ou leurs convictions. J'interviendrai pour les protéger si elles sont affaiblies, vulnérables ou menacées dans leur intégrité ou leur dignité. Même sous la contrainte, je ne ferai pas usage de mes connaissances contre les lois de l'humanité. J'informerai les patients des décisions envisagées, de leurs raisons et de leurs conséquences. Je ne tromperai jamais leur confiance et n'exploiterai pas le pouvoir hérité des circonstances pour forcer les consciences. Je donnerai mes soins à l'indigent et à quiconque me les demandera. Je ne me laisserai pas influencer par la soif du gain ou la recherche de la gloire.

Admis(e) dans l'intimité des personnes, je tairai les secrets qui me seront confiés. Reçu (e) à l'intérieur des maisons, je respecterai les secrets des foyers et ma conduite ne servira pas à corrompre les mœurs. Je ferai tout pour soulager les souffrances. Je ne prolongerai pas abusivement les agonies. Je ne provoquerai jamais la mort délibérément.

Je préserverai l'indépendance nécessaire à l'accomplissement de ma mission. Je n'entreprendrai rien qui dépasse mes compétences. Je les entretiendrai et les perfectionnerai pour assurer au mieux les services qui me seront demandés.

J'apporterai mon aide à mes confrères ainsi qu'à leurs familles dans l'adversité. Que les hommes et mes confrères m'accordent leur estime si je suis fidèle à mes promesses ; que je sois déshonoré (e) et méprisé(e) si j'y manque ».

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List of abbreviations

AC	Anticoagulation
ACC	American College of Cardiology
ACS	Acute coronary syndrome
AF	Atrial fibrillation
AHA	American Heart Association
BPM	Body mass index
CKD	Chronic kidney disease
CPB	Cardiopulmonary bypass
DOAC	Direct oral anticoagulant
EACTS	European Association for Cardio-Thoracic Surgery
ESC	European Society of Cardiology
LVEF	Left ventricular ejection fonction
OAC	Oral anticoagulation
POAF	Postoperative atrial fibrillation
PVD	Peripheral vascular disease
TIA	Transient ischemic attack
VKA	Vitamin K antagonist

Plan

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INTRODUCTION

Postoperative atrial fibrillation (POAF) is the most common atrial arrhythmia and the leading medical complication after cardiac surgery with cardiopulmonary bypass (CPB), occurring in 20% to 50% of patients depending on the series and type of procedure^{1,2}.

New-onset POAF typically occurs between the 2nd and 4th postoperative day and is most often transient². The pathophysiology is complex and involves various mechanisms including acute hemodynamic and mechanical stress, autonomic imbalance, ischemia-reperfusion injury, pericardial irritation, and the release of inflammatory cytokines in the immediate postoperative period³. Together, these factors lead to transient atrial electrophysiological disorganization and structural remodeling, creating a substrate for atrial fibrillation in the perioperative setting.

POAF is associated with an increased occurrence of both short- and long-term cardiovascular adverse events. Beyond hospital-related complications such as acute heart failure, prolonged length of stay, and in-hospital mortality, it is also linked to higher risks of ischemic stroke and major bleeding^{4,5,6}. Over the long term, POAF markedly increases the atrial fibrillation recurrence and its related complications^{4,5,6,7}.

The management of oral anticoagulant (OAC), both in the short and long term, remains a clinical challenge, as it requires balancing thromboembolic prevention against the significantly increased post operative bleeding risk. The latest guidelines do not provide clear recommendations regarding long-term anticoagulation due to the lack of controlled trials. In this regard, European Society of Cardiology (ESC 2024)⁸ suggests considering

anticoagulation based on the individual risk profile. The American Heart Association/American College of Cardiology (AHA/ACC 2023)^{9,10} recommends considering OAC initiation for at least 60 days when POAF lasts more than 48 hours provided that surgical bleeding risk is controlled and with subsequent reassessment of the need for long-term therapy. Finally, the European Association for Cardio-Thoracic Surgery (EACTS 2024)¹¹ recommends OAC should be initiated for at least 4 weeks in patients with POAF at hospital discharged but even in those discharged in sinus rhythm, OAC may be considered depending on thromboembolic and bleeding risks with subsequent reassessment in both cases.

Several observational studies have investigated the use of curative-dose oral anticoagulation in FAPO after cardiac surgery and found no evidence of reduction in thromboembolic risk with low incidence of them but a substantial increase in bleeding events^{5,12,13,14,15,16}. In the absence of randomized trials and with guidelines providing no precise guidance, clinical practice regarding the long-term continuation of anticoagulation in POAF remains highly heterogeneous^{17,18,19,20}.

The primary objective of this retrospective monocentric study was to compare the incidence of thromboembolic events, mortality, and major bleeding within 2 years after surgery in patients with new-onset POAF, according to whether curative OAC was continued at the first postoperative visit.

METHODS

Study population

We conducted a retrospective, observational, single-center study including all adult patients who developed new-onset POAF after cardiac surgery with CPB at Angers University Hospital between January 1, 2019, and July 1, 2023. POAF was defined as any episode of atrial fibrillation, regardless of its duration, documented by electrocardiogram or detected through continuous telemetry monitoring, and reported by the treating physician in the patient's medical record. Patients with history of documented preoperative supraventricular arrhythmias were excluded from the analysis.

Data Collection

Initial data were extracted from the local database, prospectively maintained by medical teams throughout hospitalization. Medical records were reviewed to complement missing information. Post-discharge follow-up was obtained through data collected from regional hospitals, cardiology practices, and clinics, ensuring comprehensive two-year postoperative follow-up.

Variables Collected

Preoperative data included age, sex, body mass index (BMI), and history of hypertension, diabetes, ischemic heart disease, peripheral artery disease, chronic kidney disease (defined as estimated glomerular filtration rate <60 mL/min/1.73 m²), significant carotid stenosis, and a history of ischemic stroke or transient ischemic attack (TIA). Left atrial size, preoperative medications (antiplatelet agents, anticoagulants, antiarrhythmic drugs), type of surgery (valvular or non-valvular), left ventricular ejection fraction (LVEF), EuroSCORE II, and CHA₂DS₂-VASc score were also recorded.

Perioperative and immediate postoperative data included CBP time, occurrence and timing of POAF, duration of POAF episodes (>48 h), need for cardioversion, timing of curative anticoagulation initiation, and the occurrence of thromboembolic or bleeding complications during hospitalization. Cardiac rhythm (sinusal vs atrial fibrillation or atrial flutter atrial) at hospital discharge was also documented.

Follow-up data at two years included recurrence of atrial fibrillation (paroxysmal or persistent), thromboembolic events (ischemic stroke, peripheral ischemia, or other peripheral embolism), major bleeding (BARC classification ≥ 3), and anticoagulation status.

Definitions of the treatment group

The study population was divided into two groups according to anticoagulation status at the time of the first cardiology follow-up visit, which occurred at a median of 3 months after surgery (IQR 2–4). Patients who were prescribed to continue or initiate curative anticoagulation therapy (vitamin K antagonist (VKA) or direct oral anticoagulants (DOACs)) were classified into the anticoagulation group, whereas those without such treatment were classified into the no-anticoagulation group.

Study Endpoints

The primary endpoint was defined as a composite outcome of thromboembolic events or cardiovascular death at 2 years.

The safety endpoint was defined as a composite outcome of major bleeding or all-cause death at 2 years.

Thromboembolic events included ischemic strokes, transient ischemic attacks, limb ischemia, and peripheral embolism, when mentioned or radiologically documented.

A major bleeding event was defined by grade ≥ 3 according to the BARC classification (Appendix Table AI).

Statistical Analysis

Continuous variables were expressed as mean $\pm$ standard deviation or median according to their distribution and compared using Student's t-test. Categorical variables were presented as frequencies and percentages and compared using χ^2 test.

Propensity score analysis

A propensity score was estimated using a logistic regression model including preoperative variables considered clinically relevant. The variables used for the propensity score were those assumed to influence the continuation of anticoagulant therapy beyond the first cardiology visit, and are listed in Appendix Table AV. This propensity score was then used for inverse probability weighting (IPW) to adjust comparisons between groups. Covariate balance before and after weighting was assessed using standardized mean differences (SMD), with an SMD <0.1 considered indicative of acceptable balance. Statistical significance was set at $p < 0.05$ for all analyses.

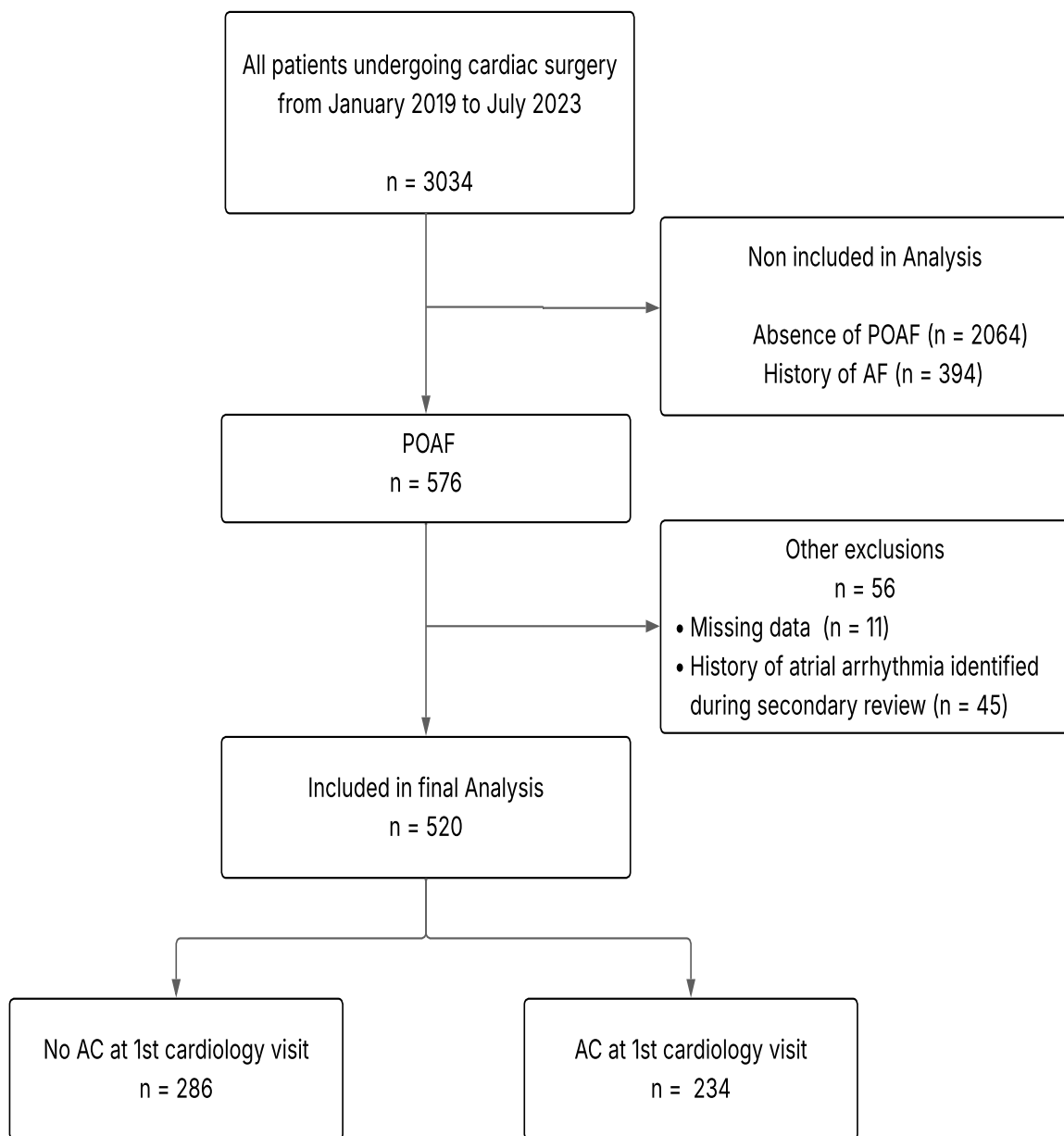


Figure 1 : Flow diagram of study inclusions and exclusions.

POAF = postoperative atrial fibrillation ; AF = Atrial Fibrillation ; AC = Anticoagulation

RESULTS

1. STUDY POPULATION AND FOLLOW-UP

1.1. Demographics

A total of 3.034 patients underwent cardiac surgery with CPB during the study period. Among them, 394 had a history of supraventricular arrhythmia and were excluded, leaving 2.640 eligible patients. Of these, 576 (21.8%) developed POAF during hospitalization. After excluding an additional patients (due to missing data or arrhythmia history identified during secondary review), 520 patients were finally included in the analysis (**Figure 1**).

At the first 3-month cardiology follow-up visit, 234 patients (45%) continued oral anticoagulation. Baseline clinical characteristics are presented in **Table I**. The mean age was 69.7 ± 9.1 years, and 80% were male, with no significant differences between groups. The CHA₂DS₂-VASc score was generally high across the cohort (47.5% >3) but did not differ between anticoagulated and non-anticoagulated patients (46.5% vs 48.3%, $p=0.856$).

Among patients who continued curative anticoagulation, antiplatelet therapy was used significantly less often, with a higher proportion receiving no antiplatelet treatment (41.0% vs. 29.4%) and a lower proportion on dual antiplatelet therapy (14.9% vs. 25.2%, $p=0.003$).

In contrast, anticoagulated patients more frequently underwent valvular surgery (64.9% vs 51.8%, $p=0.0024$), had longer mean CPB times (119.6 vs 102.4 minutes, $p=0.006$), and more often presented with left atrial dilatation (38.9% vs 27.6%, $p=0.0207$).

Table I. Baseline characteristics according to anticoagulation status

Variable	Overall (N = 520)	No Anticoagulation (N = 286)	Anticoagulation (N = 234)	P value
Clinical data				
Male sex - no (%)	416 (80.00%)	231 (80.77%)	185 (79.06%)	0.627
Age	69.67 +/-9.14	69.17 +/-8.36	70.27 +/-10.00	0.172
BMI	27.55 +/-4.56	27.40 +/-4.18	27.74 +/-5.00	0.409
Diabetes mellitus	119 (22.88%)	68 (23.78%)	51 (21.79%)	0.592
Hypertension	346 (66.54%)	186 (65.03%)	160 (68.38%)	0.421
Sleep apnea	39 (7.5%)	19 (6.64%)	20 (8.54%)	0.348
CKD	21 (4.04%)	9 (3.15%)	12 (5.13%)	0.253
History of stroke or TIA	38 (7.31%)	23 (8.04%)	15 (6.41%)	0.476
PVD	54 (10.38%)	26 (9.09%)	28 (11.97%)	0.285
Preoperative carotid stenosis	8 (1.61%)	3 (1.09%)	5 (2.26%)	0.303
EuroSCORE II (%)	2.38 +/-3.01	2.13 +/-3.13	2.69 +/-2.84	0.034
CHA ₂ DS ₂ -VASc score (>3)	247 (47.5%)	138 (48.2%)	109 (46.5%)	0.836
ACS	78 (15.00%)	48 (16.78%)	30 (12.82%)	0.208
Antiarrhythmic drug	6 (1.15%)	3 (1.05%)	3 (1.28%)	0.200
Anticoagulant therapy	32 (6.15%)	12 (4.20%)	20 (8.55%)	0.040
Antiplatelet therapy				0.003
• None	180 (34.62%)	84 (29.37%)	96 (41.03%)	
• Single antiplatelet therapy	233 (44.81%)	130 (45.45%)	103 (44.02%)	
• Dual antiplatelet therapy	107 (20.58%)	72 (25.17%)	35 (14.96%)	
Préoperative LVEF				0.760
• Preserved (>50%)	456 (87.69%)	251 (87.76%)	205 (87.61%)	
• Mildly reduced (41–49%)	47 (9.04%)	27 (9.44%)	20 (8.55%)	
• Reduced (<41%)	17 (3.27%)	8 (2.80%)	9 (3.85%)	
LAVi (> 34 mL/m ²)	122 (32.88%)	54 (27.55%)	68 (38.86%)	0.020
Surgery data				
CPB (minutes)	110.19 +/-56.39	102.35 +/-50.45	119.58 +/-61.58	0.006
Valvular surgery	300 (57.69%)	148 (51.75%)	152 (64.96%)	0.002
Valve type				0.003
• Aortic	215 (41.35%)	113 (39.51%)	102 (43.59%)	
• Mitral	70 (13.46%)	28 (9.79%)	42 (17.95%)	
Left atrial appendage closure	31 (5.96%)	13 (4.55%)	18 (7.69%)	0.131

Values are n (%) for categorical variables or median (interquartile range) for continuous variables.

TIA = transient ischemic attack; LVEF = left ventricle ejection fraction

PVD = peripheral vascular disease; ; ACS : acute coronary syndrome; CPB = cardiopulmonary bypass

LAVi = left atrial volume index; CKD = chronic kidney disease; BMI = body mass index

1.2. In hospital and early events (<3 months)

Perioperative and early postoperative data are summarized in **Table II**. The majority of first POAF episodes occurred within the first postoperative week (95% before day 7). In the group with continuation of anticoagulation at 3 months, AF burden was significantly higher, with more frequent episodes lasting >48h (71.8% vs 25.5%, $p<0.0001$) and greater persistence of AF at hospital discharge (55.1% vs 14.3%, $p<0.0001$).

In-hospital thromboembolic events were more frequent among patients who were subsequently anticoagulated at 3 months (6.4% vs 1.4%, $p=0.0024$), while no significant difference was observed regarding major bleeding events or tamponade.

A total of 274 patients undergoing surgery (52.7%) were discharged on anticoagulation. Of these, 74 patients (27.0%) had anticoagulation discontinued, whereas 200 (73.0%) remained on anticoagulation therapy beyond 3 months.

At 3 months, atrial fibrillation recurrence was significantly more frequent in the anticoagulation continuation group (44.9% vs. 8.0%, $p < 0.0001$) and similarly, cumulative thromboembolic events were more common in this group (7.7% vs. 1.7%, $p = 0.0001$). Conversely, cumulative 3 month non tamponade major bleeding events were more common in the non-anticoagulated group (4.2% vs 0.9%, $p=0.039$), whereas overall major bleeding events did not differ significantly between the two groups (9.4% vs. 8.5%, $p = 0.421$).

Table II. Perioperative et post discharge data according to anticoagulation status

Variable	Overall (N = 520)	No Anticoagulation (N = 286)	Anticoagulation (N = 234)	P value
Postoperative data				
Day of POAF onset				
• Day 0–2	261 (50.39%)	145 (51.06%)	116 (49.57%)	0.654
• Day 3–7	231 (44.59%)	127 (44.72%)	104 (44.44%)	
• Day 7	26 (5.02%)	12 (4.23%)	14 (5.98%)	
Duration of AF > 48h	241 (46.35%)	73 (25.52%)	168 (71.79%)	0.001
Successful cardioversion	98 (18.85%)	62 (21.68%)	36 (15.38%)	0.067
In-hospital anticoagulation	274 (52.69%)	74 (25.87%)	200 (85.47%)	0.001
Time to anticoagulation initiation				0.001
• None	249 (47.88%)	212 (74.13%)	37 (15.81%)	
• Day 0–7	193 (37.1%)	50 (17.48%)	143 (61.13%)	
• >Day 7	78 (15.00%)	24 (8.39%)	54 (23.08%)	
In-hospital thromboembolic event	19 (3.65%)	4 (1.40%)	15 (6.41%)	0.002
Pericardial effusion > 5 mm	127 (24.42%)	69 (24.13%)	58 (24.79%)	0.861
Reoperation for tamponade	33 (6.35%)	16 (5.59%)	17 (7.26%)	0.436
Non-tamponade major bleeding	9	7 (2.44%)	2 (0.90%)	0.190
AF at hospital discharge	170 (32.69%)	41 (14.34%)	129 (55.13%)	0.001
Cumulative events at 3 months				
AF recurrence	128 (24.62%)	23 (8.04%)	105 (44.87%)	0.001
Persistent AF	51 (9.81%)	4 (1.40%)	47 (20.09%)	0.001
Thromboembolic events	23 (4.42%)	5 (1.74%)	18 (7.69%)	0.001
All major bleeding events	47 (9.03%)	27 (9.44%)	20 (8.54%)	0.421
Non tamponade major bleeding	14 (2.69%)	12 (4.2%)	2 (0.90%)	0.039
All cause of death	2 (0.38%)			

Values are n (%) for categorical variables

TIA = transient ischemic attack; AF = atrial fibrillation; POAF = postopérative AF

2. PRIMARY ENDPOINTS

2.1. Efficacy and security endpoints

Over the follow-up, anticoagulation was not associated with a significant reduction in the efficacy endpoint, defined as thromboembolic events or cardiovascular death (2.99%, n=7 in the anticoagulated group vs. 1.4%, n=4 in the non-anticoagulated group).

The safety endpoint occurred significantly more often in anticoagulated patients, with major bleeding observed in 6.8% (n=16) versus 0.36% (n=1), and all-cause mortality in 4.7% (n=11) versus 0.7% (n=2) (**Table III**).

Among the 4 thromboembolic events observed in the non-anticoagulated group, one patient with infective endocarditis experienced an ischemic stroke and subsequently died as a consequence of this same event. Among the 16 hemorrhagic events that occurred in anticoagulated patients, 2 patients died as a direct consequence of intracranial hemorrhage, while 4 others experienced a hemorrhagic event and subsequently died from another cause within 2 years. The characteristics of all thromboembolic, hemorrhagic, and mortality events observed between 3 months and 2 years are summarized in the Appendices (Tables AII, AIII and AIV).

After adjustment using a propensity score-weighted logistic regression, these findings were confirmed. Anticoagulation was not associated with a reduction in the efficacy endpoint (OR 3.05, 95% CI 0.94–9.87, p=0.063). Conversely, it was strongly associated with the safety endpoint, with a markedly increased risk of major bleeding or all-cause death (OR 27.6, 95% CI 8.6–88.7, p<0.001).

Table III. Clinical outcomes according to anticoagulation status

Variable	Overall (N = 520)	No Anticoagulation (N = 286)	Anticoagulation (N = 234)	Odds ratio (95% CI)	P value
Efficacy composite	11 (2.12%)	4 (1.40%)	7 (2.99%)	3.04 (0.94-9.86)	0.063
Thromboembolic event	9 (1.73%)	4 (1.40%)	5 (2.15%)		
CV death	3 (0.59%)	1 (0.36%)	2 (0.86%)		
Safety composite	24 (4.61%)	3 (1.05%)	21 (8.97%)	27.62 (8.6-88.71)	0.001
Major bleeding	17 (3.35%)	1 (0.36%)	16 (6.84%)		
All-cause death	13 (2.56%)	2 (0.73%)	11 (4.72%)		

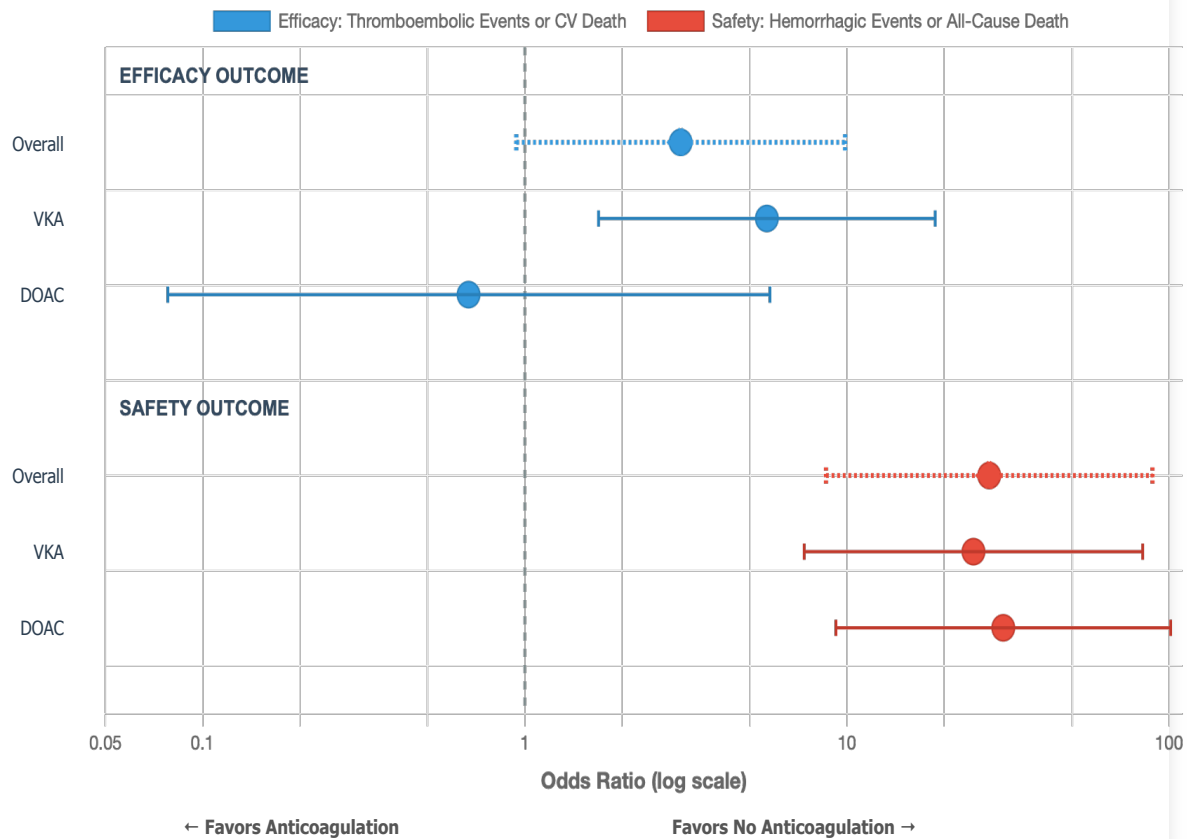
Values are n (%) for categorical variables

TE = thromboembolic; CV = cardiovascular

To further explore the impact of treatment type, outcomes were analyzed according to the class of anticoagulant used. Among anticoagulated patients (n=234), 143 (61.1%) received VKA and 91 (38.9%) DOACs. In the VKA group, thromboembolic events occurred in 4/143 (2.8%), all-cause mortality in 9/143 (6.3%), and major bleeding in 14/143 (9.8%). In the DOAC group, corresponding rates were 1/91 (1.1%), 2/91 (2.2%), and 2/91 (2.2%), respectively. After propensity score-adjusted analysis, VKA use was associated with significantly higher risks of both thromboembolic events (OR 5.64, 95% CI 1.69–18.8, $p=0.005$) and major bleeding or mortality (OR 24.7, 95% CI 7.4–82.7, $p<0.001$). DOACs were not associated with a significant reduction in thromboembolic events (OR 0.67, 95% CI 0.08–5.77, $p=0.714$) and were also associated with an increased risk of bleeding or death (OR 30.5, 95% CI 9.2–101.0, $p<0.001$).

FIGURE 2. Efficacy and Safety Primary Outcomes of Anticoagulation in Postoperative Atrial Fibrillation

Propensity Score Weighted Analysis (Inverse Probability Weighting)



Detailed Results Table

Outcome	Treatment Comparison	Events (n/N)	Odds Ratio [95% CI]	P-value
EFFICACY OUTCOME: THROMBOEMBOLIC EVENTS OR CARDIOVASCULAR DEATH				
Primary Efficacy	Any Anticoagulation vs None	7/234 vs 4/286	3.046 [0.941 - 9.865]	0.063
	VKA vs None	6/143 vs 4/286	5.640 [1.694 - 18.781]	0.005
	DOAC vs None	1/91 vs 4/286	0.669 [0.078 - 5.765]	0.714
SAFETY OUTCOME: HEMORRHAGIC EVENTS OR ALL-CAUSE DEATH				
Primary Safety	Any Anticoagulation vs None	21/234 vs 3/286	27.628 [8.604 - 88.717]	<0.001
	VKA vs None	17/143 vs 3/286	24.686 [7.365 - 82.737]	<0.001
	DOAC vs None	4/91 vs 3/286	30.547 [9.236 - 101.027]	<0.001

2.2. Impact of anticoagulation according to CHA₂DS₂-VASc and AF burden

2.2.1. CHA₂DS₂-VASc

The thromboembolic and bleeding events between 3 and 24 months according to CHA₂DS₂-VASc status are presented in **Table IV**.

Among patients with CHA₂DS₂-VASc <4, no thromboembolic events occurred in the non-anticoagulated group (0/149) versus 2 events in the continued anticoagulation group (2/124). In patients with CHA₂DS₂-VASc ≥4, thromboembolic events occurred in 4 patients in the non-anticoagulated group (4/137) compared with 3 patients in the anticoagulated group (3/110).

Major bleeding events were consistently higher in the anticoagulated groups, with 8 cases versus 1 in patients with CHA₂DS₂-VASc <4 (8/124 vs. 1/149), and 8 cases versus none in patients with CHA₂DS₂-VASc ≥4 (8/110 vs. 0/137). Finally, all-cause mortality was observed in 6 patients in the anticoagulated group versus none in patients with CHA₂DS₂-VASc <4 (6/124 vs 0/149), and in 5 versus 2 patients in the CHA₂DS₂-VASc ≥4 groups (5/110 vs. 2/137).

Table IV. Clinical outcomes by CHA₂DS₂-VASc and anticoagulation status

Groupe	No AC + CHADS <4 (N = 149)	AC + CHADS <4 (N = 124)	No AC + CHADS ≥4 (N = 137)	AC + CHADS ≥4 (N = 110)
Efficacy outcome	0 (0.00%)	3 (2.42%)	5 (3.65%)	3 (2.73%)
TE events	0 (0.00%)	2 (1.61%)	4 (2.92%)	3 (2.73%)
CV cause of death	0 (0.00%)	2 (1.61%)	1 (0.73%)	0 (0.00%)
Security outcome	1 (0.67%)	11 (8.87%)	2 (1.46%)	10 (9.09%)
Major bleeding events	1 (0.67%)	8 (6.45%)	0 (0.00%)	8 (7.27%)
All cause of death	0 (0.00%)	6 (4.84%)	2 (1.46%)	5 (4.55%)

Values are n (%) for categorical variables

AC = anticoagulation; TE = thromboembolic; CV = cardiovascular; CHADS = CHA₂DS₂-VASc

2.2.2. POAF burden

The thromboembolic and bleeding events between 3 and 24 months according to POAF burden are presented in **Table V**.

For patients with POAF ≤ 48 h (n=279), thromboembolic events occurred in 4/213 patients without anticoagulation and in 0/66 anticoagulated patients. Cardiovascular death was reported in 1/213 non-anticoagulated patient and in 0/66 anticoagulated patients. Major bleeding events were observed in 1/213 non-anticoagulated patients and 2/66 anticoagulated patients. All-cause mortality reached 2/213 in the non-anticoagulated group and 3/66 in the anticoagulated group.

For patients with POAF >48 h (n=241), thromboembolic events occurred in 0/73 non-anticoagulated patients versus 5/168 anticoagulated patients. Cardiovascular death was observed in 0/73 non-anticoagulated patients and 2/168 anticoagulated patients. Major bleeding events occurred in 0/73 non-anticoagulated patients compared with 14/168 anticoagulated patients. Finally, all-cause mortality was recorded in 0/73 non-anticoagulated patient and in 8/168 anticoagulated patients.

Table V. Clinical outcomes in patients with POAF burden according to anticoagulation status

Outcome	No AC + POAF ≤ 48 H (N = 213)	AC + POAF ≤ 48 H (N = 66)	No AC + POAF >48 H (N = 73)	AC + POAF >48 H (N = 168)
Efficacy outcome	4 (1.88%)	0 (0.00%)	0 (0.00%)	7 (4.20%)
TE events	4 (1.88%)	0 (0.00%)	0 (0.00%)	5 (2.98%)
CV death	1 (0.47%)	0 (0.00%)	0 (0.00%)	2 (1.19%)
Safety outcome	3 (1.41%)	4 (6.06%)	0 (0.00%)	17 (12.5%)
Major bleeding events	1 (0.47%)	2 (3.03%)	0 (0.00%)	14 (8.33%)
All cause of death	2 (0.93%)	3 (4.54%)	0 (0.00%)	8 (4.76%)

Values are n (%) for categorical variables

AC = anticoagulation; POAF = postoperative atrial fibrillation; TE = thromboembolic; CV = cardiovascular

DISCUSSION

In our retrospective monocentric study of 520 patients undergoing cardiac surgery, propensity score-adjusted analysis showed that continuation of anticoagulation beyond the 3-months visit did not significantly reduce thromboembolic events or cardiovascular mortality at 2 years (OR 3.05, 95% CI 0.94–9.87, $p=0.063$), which remained infrequent in both groups. Conversely, it was strongly associated with a marked increase in major bleeding and all-cause mortality (OR 27.6, 95% CI 8.6–88.7, $p<0.001$).

These results differ from non-surgical atrial fibrillation, where anticoagulation is firmly established as the standard of care^{8,10}. Although interpretation was limited by the low number of ischemic events and residual confounding despite adjustment, these findings could suggest that prolonged anticoagulation in the postoperative setting may represent an overly aggressive strategy with disproportionate harm relative to its uncertain benefit.

Clinical practice reflected this uncertainty. In our cohort, anticoagulation was prescribed at discharge in 53% of patients and maintained at three months in 45%, which appeared higher than what had generally been reported in the literature^{4,5,19}. The decision to continue treatment appeared driven less by CHA₂DS₂-VASc score than by the early clinical course (persistence or recurrence of AF, duration >48h, early complications). Moreover, anticoagulated patients received significantly fewer antiplatelets, suggesting that concerns about hemorrhagic risk with combined therapy prompted clinicians to discontinue anticoagulation earlier. Patients maintained on anticoagulation displayed a more complex surgical profile, with higher rates of valvular surgery, longer CPB times, and more frequent left atrial dilatation. These factors may have influenced physicians toward prolonged

anticoagulation, but they also likely reflect a greater AF burden and higher risk of recurrence, which in turn contributed to higher prescription rates.

Stratification according to the CHA₂DS₂-VASc score revealed particularly interesting results. In low-risk patients (<4), complications occurred almost exclusively in those receiving anticoagulation, with no evidence of ischemic events. Even in high-risk patients (≥4), the non-significant trend toward thromboembolic reduction was outweighed by excess bleeding. These findings suggested that the threshold for initiating anticoagulation should likely be higher in POAF than in spontaneous AF. However, the low event rates in both groups precluded firm conclusions.

Regarding drug classes, most adverse events occurred in patients treated with VKA, with higher rates of bleeding and mortality compared with DOACs. Although the DOAC subgroup was small (n=91), these findings suggested a potential safety advantage of DOACs in this setting, a hypothesis warranting confirmation in larger studies.

While understandable in the absence of clear guidelines, this empirical approach may lead to overtreatment, particularly when POAF had already resolved at discharge. In this context, thromboembolic risk may be overestimated.

Our study has several strengths. It included a relatively large cohort of 520 consecutive patients, with comprehensive follow-up extending to two years. Furthermore, the use of propensity score adjustment strengthened the robustness of our findings, despite the observational retrospective design. Finally, the study addressed a clinically relevant and unresolved question, directly reflecting real-world practice.

Nevertheless, several limitations must be acknowledged. First, the retrospective, single-center nature of the study inherently limits external validity and introduces potential biases. Second, the overall low number of thromboembolic events reduced statistical power and precludes firm conclusions, although it also highlighted the very limited incidence of ischemic complications in both groups, which may support the hypothesis of an overly aggressive anticoagulation strategy in this context. Third, asymptomatic AF recurrences were likely underestimated in the absence of systematic monitoring, and treatment adherence could not be assessed. In addition, heterogeneity in anticoagulant drug class and dosing, together with indication bias—since treatment decisions were left to the discretion of the treating physician—represent further sources of variability.

Another important limitation was the imbalance between groups: patients who received anticoagulation displayed a more complex surgical profile, with higher POAF burden, greater persistence at discharge, and more thromboembolic events during the index hospitalization, whereas many non-anticoagulated patients experienced only short, self-terminating episodes. This structural difference likely influenced prescribing decisions and may have biased comparisons, despite propensity score adjustment. The quality of this adjustment was not optimal, as residual imbalances in key clinical variables persisted, limiting its ability to fully account for confounding.

These limitations underlined the need for large, multicenter, prospective studies to better define the role of anticoagulation in the management of POAF.

Our findings were consistent with several recent studies highlighting the absence of clear benefit from curative anticoagulation after POAF. Van De Kar *et al.* reported in a meta-analysis of eight studies that anticoagulation after CABG-related POAF was associated with an absolute reduction in thromboembolic risk of only 0.8% (NNT=125), at the cost of a significant increase in bleeding risk (RR=3.22, NNH=200). Similarly, Wang *et al.*, in an analysis of 254,200 patients, found a marginal thromboembolic benefit (2 events prevented per 1,000 patient-years) offset by a substantial bleeding excess (42 additional events per 1,000 patient-years). These data corroborated our observation of an unfavorable benefit-risk balance, particularly in patients at low embolic risk.

Beyond optimizing anticoagulation, several preventive strategies are emerging to reduce the incidence of POAF itself. Left posterior pericardiotomy, by facilitating postoperative pericardial fluid drainage, has shown promising results with a significant reduction in POAF in several randomized trials^{18,21,22}.

Finally, the ongoing PACES trial²³ explores a different approach, comparing anticoagulation plus antiplatelet therapy versus antiplatelet therapy alone in the early postoperative phase 3 month after CABG. Unlike our study, which evaluates the relevance of prolonged anticoagulation beyond three months, PACES addressed early management. Together, these complementary strategies should help define the optimal timing and duration of anticoagulation in this specific surgical setting.

CONCLUSION

In this retrospective monocentric study of 520 patients with transient new-onset postoperative atrial fibrillation, continuation of curative anticoagulation beyond the first 3-month visit did not reduce the incidence of thromboembolic events at two years but was associated with a significant increase in major bleeding and all-cause mortality. These findings challenge the relevance of systematic anticoagulation after cardiac surgery and emphasize the need for an individualized approach, particularly in patients at low thromboembolic risk, in whom the benefit-risk profile appears unfavorable. Larger randomized controlled trials are required to confirm these observations and establish tailored recommendations for this specific population.

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APPENDICES

Table AI. Bleeding Academic Research Consortium (BARC) Classification

BARC Type	Definition
Type 0	No bleeding
Type 1	Bleeding that is not actionable and does not cause the patient to seek medical attention (e.g., minor bruising, mild epistaxis).
Type 2	Any overt, actionable sign of hemorrhage that does not fit the criteria for Type 3, 4, or 5, but requires medical evaluation, hospitalization, or leads to a change in antithrombotic therapy.
Type 3a	Overt bleeding plus a hemoglobin drop of 3 to <5 g/dL, or any transfusion with overt bleeding.
Type 3b	Overt bleeding plus a hemoglobin drop ≥ 5 g/dL, cardiac tamponade, bleeding requiring surgical intervention (other than dental/nasal/skin/hemorrhoid), or intravenous vasoactive drugs.
Type 3c	Intracranial hemorrhage (excluding microbleeds or hemorrhagic transformation of ischemic stroke), or intraocular bleeding compromising vision.
Type 4	CABG-related bleeding (perioperative intracranial bleeding, reoperation after closure of sternotomy for bleeding, transfusion ≥ 5 units of whole blood or packed red cells within 48h, chest tube output ≥ 2 L within 24h).
Type 5a	Probable fatal bleeding (no autopsy or imaging confirmation but clinically highly suggestive).
Type 5b	Definite fatal bleeding (confirmed by autopsy or imaging).

Table AII. Thromboembolic events

Thromboembolic Event (Type)	Time to Event (months)
Ischemic stroke	12
Transient ischemic attack	11
Ischemic stroke	11
Ischemic stroke	24
Ischemic stroke	24
Ischemic stroke	12
Ischemic stroke	12
Ischemic stroke	17
Acute limb ischemia	11

Table AIII. Hemorrhagic events

Hemorrhagic Event (Type)	Time to Event (months)
Hemorrhage due to acute necrotizing pancreatitis	8
Macroscopic hematuria requiring urological management	24
Lower gastrointestinal bleeding	23
Hemothorax	24
Cranial trauma with parietal hematoma	24
Macroscopic hematuria requiring urological surgery	3
Lower gastrointestinal bleeding	24
Hemothorax	18
Lower gastrointestinal bleeding	4
Fatal hemorrhagic stroke	19
Fatal hemorrhagic stroke after AF ablation	20
Hemorrhagic shock after hysterectomy	20
Hemorrhagic stroke requiring neurosurgical shunt (EVD)	9
Lower gastrointestinal bleeding	6
Lower gastrointestinal bleeding	12
Anemia revealing colonic tumor	5
Anemia revealing colonic tumor	6

Table AIV. All-cause mortality

Cause of Death	Time to Death (months)
Neoplasia	24
Septic shock due to necrotizing pancreatitis	8
Aspiration during bowel obstruction	24
Unknown cause	17
Hemorrhagic stroke	19
Hemorrhagic stroke	20
Infective endocarditis	6
Septic shock	24
Unknown cause	7
Infective endocarditis	4
Natural death	11
Neoplasia	21
Death due to gastrointestinal bleeding	23

Table AV. Propensity score covariate balance

Variable	SMD (Raw)	SMD (Weighted)	Variance Ratio (Raw)	Variance Ratio (Weighted)
Sex – Male	0.066	-0.041	1.106	0.952
Age	0.132	0.211	1.402	1.156
Valve type – Aortic	0.103	-0.010	1.030	0.999
Valve type – Mitral	0.249	0.112	1.749	1.288
BMI	0.136	-0.056	1.542	1.743
EuroSCORE II	0.173	0.175	0.747	0.800
Hypertension	0.094	-0.023	0.933	1.019
Smoking – Active	-0.036	-0.076	0.895	0.761
Smoking – Former	-0.151	-0.285	0.867	0.770
Diabetes	-0.030	0.234	0.963	1.321
Prior ischemic stroke/TIA	-0.077	-0.067	0.770	0.758
Peripheral artery disease	0.080	0.032	1.234	1.109
Carotid stenosis	0.090	-0.004	2.005	0.976
CHA ² DS ₂ -VASc score	0.064	0.068	0.966	1.010
HAS-BLED score	0.135	0.058	0.809	0.888
Chronic kidney disease	0.082	0.046	1.463	1.277
Statin (pre-op)	-0.192	-0.133	1.116	1.089
Pre-op anticoagulant	0.171	0.013	1.907	1.046
Antiplatelet therapy – Single	0.020	0.197	1.004	1.060
Antiplatelet therapy – Dual	-0.272	-0.324	0.668	0.623
Left atrial appendage closure (perioperative)	0.139	0.025	1.767	1.111
Successful cardioversion	-0.149	-0.219	0.790	0.674
Delay before anticoagulation – 0–2 days	0.219	0.170	3.504	3.407
Delay before anticoagulation – 3–7 days	0.946	0.251	1.873	1.146
Delay before anticoagulation – >7 days	0.442	0.195	2.620	1.514
AF duration >48 h	1.135	0.268	1.079	1.001
Atrial fibrillation at discharge	1.007	0.310	2.034	1.228
In-hospital ischemic stroke/TIA	0.200	0.062	3.228	1.426
AF recurrence <3 months	1.041	0.211	3.573	1.163
In-hospital hemorrhagic event	-0.207	-0.039	0.229	0.793
Anticoagulation at discharge – VKA	1.835	0.440	1.197	0.987
Anticoagulation at discharge – DOAC	0.466	-0.067	6.596	0.850

Anticoagulation au long cours après fibrillation atriale de novo en postopératoire de chirurgie cardiaque : efficacité et sécurité à 2 ans.

RÉSUMÉ

Introduction :

La fibrillation atriale postopératoire (FAPO) est la principale complication après chirurgie cardiaque et est associée à une augmentation du risque thromboembolique et de décès à long terme. Les recommandations actuelles demeurent imprécises et reposent sur des données limitées. L'objectif de cette étude observationnelle était d'analyser l'efficacité et la sécurité d'un traitement anticoagulant à long terme en cas de FAPO de novo.

Méthodes :

Étude rétrospective monocentrique menée au CHU d'Angers, incluant 520 patients opérés entre janvier 2019 et juillet 2023 et ayant présenté une FAPO de novo durant l'hospitalisation. Le suivi débutait à la première consultation de cardiologie, réalisée dans un délai médian de 3 mois. Le critère principal d'efficacité associait événements thromboemboliques et décès cardiovasculaire à 2 ans, tandis que le critère de sécurité associait hémorragies majeures (BARC ≥ 3) et décès toutes causes à 2 ans. Les comparaisons entre patients anticoagulés et non anticoagulés à l'issue de cette consultation ont été ajustées par pondération sur score de propension.

Résultats :

Lors de la première visite de suivi, 234 patients atteints de FAPO recevaient un traitement anticoagulant (45 %). A deux ans, les événements thromboemboliques et décès cardiovasculaires restaient peu fréquents (7 patients (2,99 %) sous anticoagulants contre 4 patients (1,40 %) sans anticoagulants), sans bénéfice significatif des anticoagulants (OR ajusté 3,05 ; IC à 95 % 0,94-9,87 ; $p = 0,063$). En revanche, le critère d'évaluation de la sécurité était significativement plus élevé chez les patients sous anticoagulants (21 patients (8,97 %) sous anticoagulants contre 3 patients (1,05 %) sans anticoagulants (OR ajusté 27,6 ; IC à 95 % 8,6-88,7 ; $p < 0,001$).

Conclusion :

Dans la fibrillation atriale de novo après chirurgie cardiaque, la poursuite d'une anticoagulation curative au-delà de la première consultation de suivi (3 mois) n'a pas semblé réduire les événements thromboemboliques, mais a été associée à une augmentation significative du risque hémorragique et de la mortalité à 2 ans.

Mots-clés : Fibrillation atriale post opératoire, Anticoagulation, Arythmie, Chirurgie cardiaque

Long-term Anticoagulation After New-Onset Postoperative Atrial Fibrillation Following Cardiac Surgery: Efficacy and Safety at 2 Years.

ABSTRACT

Introduction :

Postoperative atrial fibrillation (POAF) is the most common complication after cardiac surgery and is associated with an increased risk of long-term thromboembolic events and mortality. Current guideline recommendations remain vague and are based on limited evidence. The aim of this observational study was to analyze the efficacy and safety of a long-term anticoagulation therapy for patients with de novo POAF.

Methods :

We conducted a single-center retrospective study at Angers University Hospital, including 520 patients who underwent cardiac surgery between January 2019 and July 2023 and developed new-onset POAF during hospitalization. Follow-up began at the first cardiology consultation, performed at a median of 3 months postoperatively. The primary efficacy endpoint was a composite of thromboembolic events and cardiovascular death at 2 years, while the primary safety endpoint combined major bleeding (BARC ≥ 3) and all-cause mortality at 2 years. Comparisons between patients with and without anticoagulation were adjusted using propensity score weighting.

Results :

At the first follow-up visit, 234 patients with POAF were receiving anticoagulation (45%). At 2 years, thromboembolic events and cardiovascular death remained infrequent (7 patients (2.99%) with anticoagulation vs. 4 patients (1.40%) without), with no significant benefit of anticoagulation (adjusted OR 3.05; 95% CI 0.94–9.87; $p=0.063$). In contrast, the safety endpoint was significantly increased in anticoagulated patients (21 patients (8.97%) with anticoagulation vs. 3 patients (1.05%) without ; adjusted OR 27.6; 95% CI 8.6–88.7; $p<0.001$).

Conclusion :

In new-onset atrial fibrillation after cardiac surgery, continuation of curative anticoagulation beyond the first follow-up consultation (3 months) did not seem to reduce thromboembolic events but was associated with a significant increase in major bleeding and mortality at 2 years.

Keywords: Postoperative atrial fibrillation, Anticoagulation, Arrhythmia, Cardiac surgery

