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Prognosis of Transient New-Onset Atrial Fibrillation During Vascular Surgery

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Abstract *Background:* Chronic atrial fibrillation (AF) in a non-surgical setting is associated with cardiovascular events. However, the prognosis of transient new-onset AF during vascular surgery is unknown.
Objective: The purpose of this study is to investigate the prognosis of new-onset AF during vascular surgery using continuous electrocardiographic monitoring (continuous-ECG).
Methods: In this study, 317 patients, all in sinus rhythm, scheduled for major vascular surgery were screened for cardiac risk factors. Continuous-ECG recordings for 72 h and standard ECG on days 3, 7 and 30 were used to identify new-onset AF. Cardiac troponin T (cTnT) was measured routinely after surgery. Study endpoint was a composite of cardiac death, myocardial infarction, unstable angina and stroke (cardiovascular events) at 30 days after surgery and during late follow-up. Median follow-up was 12 (interquartile range 2–28) months.
Results: New-onset AF was noted in 15 (4.7%) patients. All but three patients returned spontaneously to sinus rhythm. The composite endpoint of cardiovascular events within 30 days and during late follow-up occurred in 34 (11%) and 62 (20%) patients, respectively. Multivariate regression analysis showed that new-onset AF was associated with perioperative (hazard ratio (HR) 6.0; 95% CI: 2.4–15) and late cardiovascular events (HR 4.2, 95% CI: 2.1–8.8).
Conclusion: New-onset AF during vascular surgery is associated with an increased incidence of 30-day and late cardiovascular events.

Cardiovascular complications are a major cause for morbidity and mortality in patients undergoing non-cardiac vascular surgery.[1] It is estimated that after non-cardiac surgery, 2–10% of patients develop cardiac arrhythmias, of which atrial fibrillation (AF) is the most common form.[2–5] AF is facilitated by electrolyte disturbances, hypoxia and acidosis. Postoperative AF is associated with a prolonged

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hospital stay, as well as neurological and cardiac complications and increased health-care costs. It was estimated that after cardiac surgery atrial tachyarrhythmias increased costs by $6356 per patient.[6] Patients with recurrent episodes of preoperative AF are probably at the greatest risk for this adverse outcome.

The impact of new-onset AF in the perioperative period after vascular surgery is ill defined. Importantly, the incidence of postoperative AF is closely related to the extensiveness of cardiac rhythm monitoring. Till date, detection of cardiac arrhythmias was most frequently performed with intermittent and/or daily electrocardiographic (ECG) monitoring and based on patients' complaints. However, this might be insufficient to detect the true incidence of new-onset AF and its impact on perioperative and long-term outcome after vascular surgery. It must be considered that perioperative new-onset AF is often short lived and asymptomatic, making detection difficult.

Therefore, the purpose of this study was to assess the incidence and impact of perioperative new-onset AF in vascular surgery patients using continuous-ECG registration for the first 48 h after surgery.

Methods

Study population

The study population consisted of 409 patients undergoing elective abdominal aortic aneurysm repair or peripheral artery bypass surgery at the Erasmus Medical Center in Rotterdam, the Netherlands, during the period 2004–2009. Patients with a history of cardiac arrhythmias ($n = 28$), cardiac pacemaker ($n = 6$), left ventricular hypertrophy ($n = 33$) and left or right bundle branch block ($n = 25$) were excluded. The hospital's ethical committee approved the study.

Preoperative cardiovascular screening

We determined the cardiac risk score for each patient in our data set, and a point was assigned to each of the following characteristics: advanced age (>70 years), history of myocardial infarction (MI), angina pectoris, congestive heart failure, stroke, diabetes mellitus (fasting glucose level $\geq 7.0\ \mathrm{mmol\,l^{-1}}$ or use of insulin or oral glucose-lowering medication) and renal insufficiency (serum creatinine $> 170\ \mu\mathrm{mol\,l^{-1}}$). Based on the number of these risk factors, patients were stratified into low- (no risk factors), intermediate- (one or two risk factors) and high-risk (at least three risk factors) categories.[7] Furthermore, all patients were screened for hypertension (blood pressure $\geq 140/90$ mmHg or blood-pressure-lowering medication), hypercholesterolaemia (plasma cholesterol level $\geq 5.5\ \mathrm{mmol\,l^{-1}}$ or use of cholesterol-lowering medication), smoking status and chronic obstructive pulmonary disease (defined as a forced expiratory volume in 1 s (FEV1) $< 70\%$ of age- and gender-predictive value or medication use).[8]

Detection of atrial fibrillation

Patients were continuously monitored with a 10-electrode, 12-lead digital ECG recorder (DR180 + Digital Recorder, NorthEast Monitoring Inc., Maynard, MA, USA), starting 1 day before surgery and continuing up to 2 days after. Continuous-ECG recordings were started 1 day prior to surgery, depending on the time of admission of the patient to the vascular surgery ward. Recordings were performed in the continuous 12-lead mode with a recording length of 10 s every minute. The frequency response was 0.05–150 Hz Electrocardiographic data were initially processed by a technician and analysed by two experienced cardiologists who were blinded to the patient's clinical data. After excluding all artefacts, the ambulatory electrocardiography recordings were analysed for new-onset AF. On the ECG, AF is characterised by the replacement of consistent P waves with rapid oscillations or fibrillatory waves that vary in amplitude, shape and timing, associated with an irregular, frequently rapid, ventricular response when atrioventricular conduction is intact.[9] Continuous-ECG recordings were analysed off-line. Postoperatively standard ECGs were made routinely on day 3, 7 and 30, and/or at discharge and whenever clinically indicated by chest pain or complaints of dyspnoea.

Perioperative outcome

The perioperative endpoint was a composite of cardiac death, MI, unstable angina pectoris and stroke (cardiovascular events) within 30 days after surgery. After surgery, cardiac troponin T (cTnT) levels were routinely measured on postoperative days 1, 3, 7, 30 and/or at discharge and whenever clinically indicated by chest pain or ECG changes consistent with myocardial ischaemia or infarction. MI was defined as the presence of two out of the following three criteria: (1) characteristic ischaemic symptoms lasting >20 min, (2) electrocardiographic changes including acute ST elevation, followed by appearance of Q waves or loss of R waves, or new left bundle branch block, or new persistent T-wave inversion for at least 24 h, or new ST segment depression which persists >24 h and (3) a positive troponin T, that is, $>0.10\ \mathrm{ng\,ml^{-1}}$ with characteristic rise and fall.[10] Cardiovascular death was defined as any death with a cardiovascular cause, including those following a cardiac procedure, cardiac arrest, MI, pulmonary embolus, stroke or sudden deaths not ascribed to other causes.[11]

Long-term outcome

During follow-up, outpatient visits were scheduled every 3 months after discharge. Long-term study endpoints were cardiovascular events, that is, cardiac death, MI, unstable angina pectoris and stroke. Cardiac death was defined as death caused by acute MI, cardiac arrhythmias, congestive heart failure or sudden death. Survival status was ascertained by contacting the civil service registry.

Data analysis

Continuous data are expressed as means ± standard deviation (SD) and are compared using the Student's t test. Categorical variables are described as numbers and percentages, and analysed using the chi-square test or Fisher's exact test, as appropriate. The association of new-

onset AF with short- and long-term prognosis was assessed by multivariate Cox regression analysis. All co-variables associated with perioperative cardiovascular complications (*P*-value <0.20 in univariate analysis) were included in the multivariate model. The number of outcome events in the study was limited. Therefore, to avoid over fitting, and to enable assessment of the relation between clinical risk factors and the composite endpoint, we used the risk score described by Boersma et al.[7] In multivariate analysis, adjustments were made for risk factors, cardiac risk score, site of surgery and open or endovascular procedure. Hazard ratios (HRs) are given with 95% confidence intervals (CIs). For all tests, a *p*-value of less than 0.05 (two-sided) was considered significant. All analyses were performed using SPSS 15.0 statistical software (SPSS Inc., Chicago, IL, USA).

Results

Patient characteristics

A total of 317 patients undergoing abdominal aortic aneurysm repair ($n = 216$) or peripheral arterial bypass surgery ($n = 101$) were analysed. Their mean age was 68.6 ± 9.5 years and 79% were male. According to the cardiac risk score, 23% of patients had low cardiac risk, 54% intermediate cardiac risk and 23% high cardiac risk. The baseline clinical characteristics are listed in Table 1. Patients who developed new-onset AF were significantly older ($p = 0.02$). Except for age, there were no significant differences in baseline characteristics between the two groups.

New-onset AF

Continuous-ECG monitoring was started 12.1 ± 7.2 h prior to surgery. During 20 775 patient-hours of continuous 12-lead ECG monitoring (65.5 ± 20.2 h per patient), 13 (4%) patients developed new-onset AF. In all but one continuous-ECG recording, new-onset AF occurred postoperatively. In addition, in two patients, new-onset AF was noted on standard ECGs between day 3 and 7 after surgery. A vast majority of patients (80%) were without clinical symptoms. In three patients, exacerbating heart failure symptoms were present and were treated by additional diuretics and digoxin therapy. All patients were on perioperative beta-blocker therapy as well as low-molecular-weight heparins. All but three patients with new-onset AF returned to sinus rhythm at 30 days postoperatively, as confirmed by standard ECG.

There were no significant differences in the type of anaesthesia or the duration of anaesthesia between the two groups. In the group of patients with new-onset AF, 80% had general anaesthesia, as compared to 61% in those without new-onset AF ($p = 0.80$). The mean duration of anaesthesia did not differ between the two groups (4.5 vs. 4.3 h, $p = 0.63$).

Table 1 Baseline characteristics.

	All ($n = 317$)	No AF ($n = 302$)	New-onset AF ($n = 15$)
Age, years ± SD	68.6 ± 9.5	68.3 ± 9.5	74.4 ± 8.9
Males — no. (%)	250 (79)	237 (79)	13 (85)
Cardiovascular risk factors — no. (%)			
History of myocardial infarction	100 (32)	97 (32)	3 (20)
History of angina pectoris	60 (19)	59 (20)	1 (7)
History of congestive heart failure	24 (8)	22 (7)	2 (13)
Diabetes mellitus	63 (20)	61 (20)	2 (13)
Renal dysfunction	31 (10)	28 (9)	3 (20)
History of TIA or CVA	48 (15)	44 (15)	4 (27)
Hypertension	153 (48)	144 (48)	9 (60)
COPD	133 (42)	129 (43)	4 (27)
Medication — no. (%)			
Beta-blockers	305 (96)	291 (96)	14 (93)
Statins	261 (82)	249 (83)	12 (80)
Antiplatelet therapy	217 (68)	207 (69)	10 (67)
Oral anticoagulants	48 (15)	44 (15)	4 (27)
ACE-inhibitors	86 (27)	81 (27)	5 (33)
Calcium channel blocking agents	82 (26)	76 (25)	6 (40)
Site of surgery — no. (%)			
Abdominal aorta	216 (68)	205 (68)	11 (63)
Endovascular	95	91	4
Open	121	114	7
Lower extremity artery	101 (32)	97 (32)	4 (27)

AF = atrial fibrillation; TIA = transient ischaemic attack; CVA = cerebrovascular accident; COPD = chronic obstructive pulmonary disease; ACE = angiotensin converting enzyme.

Table 2 Multivariate Cox regression analysis for perioperative cerebro-cardiovascular outcome.

	Univariate			Multivariate		
	HR	95% CI	*p*-value	HR	95% CI	*p*-value
New-onset atrial fibrillation	4.9	2.0–12	<0.001	6.0	2.4–15	<0.001
Clinical cardiac risk						
Low	1					
Intermediate	2.4	0.7–8.3	0.16	3.0	0.9–10	0.08
High	5.7	1.7–20	0.006	7.7	2.2–27	0.002
Other risk factors						
Male	0.8	0.4–2.0	0.78			
Hypertension	2.1	1.0–4.2	0.04	2.0	1.0–4.0	0.06
COPD	1.4	0.7–2.8	0.31			
Surgery						
Aortic	1		0.01	1		
Peripheral	0.3	0.1–0.8		0.2	0.1–0.5	0.001
Type of surgery						
Open	1		0.11	1		
Endovascular	0.5	0.2–1.2		0.2	0.1–0.6	0.001

Cardiovascular outcome

In total, 63 (19.9%) patients experienced cTnT release within 30 days after surgery. A total of 70 patients developed myocardial ischaemia during continuous-ECG monitoring. Eight patients with perioperative new-onset AF also had signs of myocardial ischaemia. The incidence of myocardial ischaemia in patients with new-onset AF was significantly higher compared with those without new-onset AF (53% vs. 21%, $p = 0.01$). New-onset AF was preceded by myocardial ischaemia in half of the cases.

Seven patients with new-onset AF had a combination of cTnT release and myocardial ischaemia detection.

A non-fatal MI and cardiac death was noted in 21 (6.6%) and 12 (3.8%) patients, respectively. One patient experienced a non-fatal perioperative stroke. The incidence of the composite perioperative outcome was noted in 34 (10.7%) patients. In univariate analysis, new-onset AF was associated with an increased risk of perioperative cardiovascular events (HR 4.9, 95% confidence interval (CI): 2.0–11.9, $p < 0.001$, Table 2). After correcting for risk factors, type and site of surgery, multivariate regression analysis showed that new-onset AF was still associated with perioperative cardiovascular events (HR 6.0, 95% CI 2.4–15.0, $p < 0.001$, Table 2).

Within a median follow-up of 12 months (interquartile range 2–28 months) after surgery, 35 (11.0%) patients experienced a non-fatal MI, nine (2.8%) unstable angina pectoris and four (1.3%) stroke, whereas 34 (10.7%) died due to a cardiac cause. In total, a combined endpoint of long-term cardiovascular events occurred in 62 (19.6%) patients. In univariate analysis, perioperative new-onset AF was associated with an increased risk of long-term cardiovascular events (HR 4.4, 95% CI: 2.1–8.8, $p < 0.001$, Fig. 1). This association between perioperative AF and long-term prognosis persisted when other cardiovascular risk factors, type and site of surgery were added to the multivariate Cox regression model (HR 4.2, 95% CI: 2.1–8.8, $p < 0.001$, Table 3).

Discussion

The current study shows that transient and predominantly asymptomatic new-onset AF during vascular surgery is associated with an increased risk for perioperative and long-term cardiovascular events. Patients with new-onset AF had an almost fivefold increased risk for perioperative cardiovascular complications. This risk persisted in the first year after surgery as patients with new-onset AF experienced a fourfold increased risk for late complications.

AF is a supraventricular tachyarrhythmia characterised by uncoordinated atrial activation with consequent deterioration of mechanical function. Factors affecting haemodynamic function during AF are loss of synchronous atrial

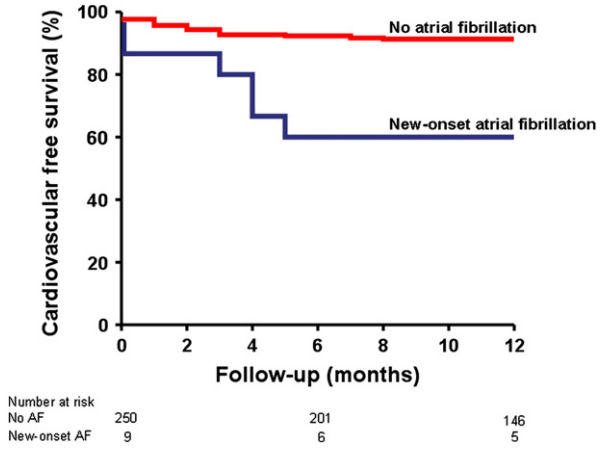

Figure 1 Long-term outcome after vascular surgery of patients with new-onset perioperative atrial fibrillation ($n = 15$) and patients without new-onset atrial fibrillation ($n = 302$). Multivariate regression analysis showed that patients with new-onset AF had a four-fold increased risk for late cardiovascular events. (HR 4.2, 95% CI 2.1–8.8).

Table 3 Multivariate Cox regression analysis for long-term cerebro-cardiovascular outcome.

	Univariate			Multivariate		
	HR	95% CI	*p*-value	HR	95% CI	*p*-value
New-onset atrial fibrillation	4.4	2.1–8.8	<0.001	4.2	2.1–8.8	<0.001
Clinical cardiac risk						
Low	1					
Intermediate	3.7	1.3–10	0.02	4.0	1.4–11	0.01
High	9.2	3.2–26	<0.001	10.7	3.7–31	<0.001
Other risk factors						
Male	1.3	0.7–2.5	0.43			
Hypertension	1.9	1.2–3.3	0.01	1.7	1.0–2.9	0.04
COPD	1.4	0.8–2.3	0.20			
Surgery						
Aortic	1		0.26	1		
Peripheral	0.7	0.4–1.3		0.5	0.3–0.8	0.01
Type of surgery						
Open	1		0.05	1		0.001
Endovascular	0.5	0.3–1.0		0.3	0.2–0.6	

mechanical activity, irregular ventricular response, tachycardia and impaired coronary arterial blood flow.[12] This may result in a decreased cardiac output, especially when diastolic ventricular filling is impaired by conditions such as hypertension and diabetes mellitus. However, most of the pathophysiological pathways and consequences of AF are investigated in the non-surgical population and after cardiac surgery.[6,12,13] The relationship between AF and impaired cardiac outcome after non-cardiac surgery is less well studied. It might be hypothesised that a sustained state of AF after vascular surgery results in a prolonged period of suboptimal left ventricular function and coronary oxygen perfusion abnormalities leading to a cardiac oxygen demand/supply mismatch, resulting in MI. Both heart failure and MI are strong predictors of adverse postoperative outcome.[14,15] In the current study there was a clear association between AF and myocardial ischaemia, as shown by an increased incidence of troponin T release. However, the relation in time could not be assessed as troponin T release can only be assessed at intervals, hence preventing the understanding of the exact time relation between AF and myocardial ischaemia. Furthermore, in our study, new-onset AF was preceded by myocardial ischaemia in half of the cases.

The majority of studies performed to detect the impact of AF on postoperative outcome were performed in patients undergoing cardiothoracic surgery. In these studies, the incidence of new-onset AF is as high as 40%.[6] In the non-cardiothoracic surgical setting, the risk for perioperative new-onset AF is significantly lower. As reported by Christians et al., the incidence of new-onset AF in an unselected group of 13 696 patients undergoing elective non-cardiac surgery was as low as 0.37%.[5] In specifically selected patient populations, such as surgical ICU patients, the incidence of new-onset AF might be as high as 9%, as reported by Brathwaite and Weissman.[4] Importantly, in this surgical ICU study, patients with new-onset AF also had an increased risk for mortality. Valentine et al. studied ICU patients after open aortic surgical procedure and revealed a similar incidence of 10% new-onset AF.[3] It should be noticed that these patients were followed up with continuous ECG monitoring for a mean of 6 ± 8 days. This high incidence of postoperative new-onset AF after aortic surgery has recently been reconfirmed by Noorani et al.[16] in a group of 200 patients. Those with AF (10%) had an increased risk for cardiac failure and a longer hospital stay. In the study by Noorani et al., no relation was found between AF and prognosis, but it was a retrospective study with a discontinuous fashion of ECG monitoring. In the current study, patients were followed by continuous-ECG for 72 h and a standard ECG on days 3 and 7. This might explain the lower incidence of new-onset AF observed in our study. Furthermore, intermediate-risk surgical patients, that is, endovascular aneurysm repair and peripheral bypass surgery, were included in the current study. This might have affected the incidence of new-onset AF. Another possible explanation for the lower incidence of new-onset AF might be the use of perioperative beta-blocker therapy in majority of the patients in the current study.

New-onset postoperative AF deserves attention, as it is associated with poor outcome. It warrants a specific evaluation of the cause of AF, and a more rigorous screening for postoperative AF should be considered. Advanced age was a preoperative predictor of new-onset AF. As the average age of patients scheduled for vascular surgery is increasing, the incidence of AF after vascular surgery is likely to increase. Therefore, development of easy-to-use monitoring devices, which would enable a longer continuous monitoring period, is important.

As was found in the current study, AF after non-cardiac surgery is often transient and causes little clinical complaints as only three out of 15 (20%) patients required additional medical therapy because of exacerbating heart failure symptoms. It should be appreciated that, in the current study, majority of the patients were on perioperative beta-blocker therapy and that it was continued after surgery intravenously or as a suppository when oral medication was not feasible. Current guidelines do not provide

a clear strategy for asymptomatic transient AF after non-cardiac surgery. As stated in the 2006 ACC/AHA/ESC guidelines, administration of atrioventricular (AV)-nodal blocking agents is recommended to achieve rate control in patients who develop postoperative AF.[12] Furthermore, it is considered reasonable to (1) restore sinus rhythm by pharmacological cardioversion with ibutilide or direct-current cardioversion in patients who develop post-operative AF as advised for non-surgical patients, (2) administer anti-arrhythmic medications in an attempt to maintain sinus rhythm in patients with recurrent or refractory postoperative AF, as recommended for other patients who develop AF and (3) administer antithrombotic medication in patients who develop postoperative AF, as recommended for non-surgical patients. Whether these guidelines are also applicable to patients with transient new-onset postoperative AF remains to be investigated.

Limitations

In the present study, continuous-ECG recordings were only performed for 48 h after surgery. A prolonged registration could have resulted in an increased number of patients with AF similar to prolonged registrations at the surgical ICU studies. In addition, analysis was done off-line, which prevented the assessment of a potential benefit of timely intervention.

Conclusion

New-onset AF after vascular surgery is a common, often asymptomatic, cardiac arrhythmia and is associated with a poor perioperative and long-term outcome.

Conflict of Interest

None.

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