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RESEARCH LETTER
Interventional cardiology and cardiac surgery

Cardio-ankle vascular index predicts postoperative atrial fibrillation after cardiac surgery

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Approximately 50% of patients undergoing surgical aortic valve replacement (SAVR) develop postoperative atrial fibrillation (POAF) which is associated with poor outcome.[1] Postoperative atrial fibrillation is multifactorial and results from the interaction between pre-existing atrial fibrillation (AF), risk factors, and physiological response to surgery, including inflammation, oxidative stress, and sympathetic hyperactivity.[1] Increased arterial stiffness marks the vascular consequence of these risk factors and is inversely correlated with atrial strain which has been associated with both stroke and incident AF.[2] Indeed, high cardio-ankle vascular index (CAVI) indicating increased arterial stiffness is an AF risk factor[3] although its predictive role in POAF is unknown and is of particular interest since CAVI is underestimated in aortic valve stenosis (AVS).[4]The aim of this study was therefore to determine if arterial stiffness predicts POAF following open heart surgery.

Data were expressed as mean (± standard deviation, SD) and frequencies (%). To find independent predictors of POAF, multivariate logistic regression analysis was performed using POAF as the dependent variable. Predictors were based on clinical reasoning, missing data status and univariate correlation coefficient >0.1/<-0.1. To find the best model, variables were entered in a backward logistic regression model using Akaike Information Criteria to determine the best model. Analyses were performed using R software and $P < 0.05$ was considered statistically significant.

A total of 108 patients from the prospective Disease of the Aortic Valve Ascending Aorta and Coronary Arteries study[5] were screened for inclusion of which 88 completed measurements with carotid femoral pulse wave velocity (cfPWV) and CAVI (*Figure 1*). Patients were followed by using electronic medical record (EMR). POAF was defined as documented AF in the EMR and included immediate (during hospitalisation) and late (after hospital discharge). Also, hospitalisation due to heart failure (HF) or stroke within 30 days of surgery, and all-cause mortality was obtained. Patients were followed up to 5 years [interquartile range (IQR) 4.0–4.2] for mortality, and up to 4 years (IQR 40 days–833 days), for diagnosis of AF (latest available local EMR note). The main indication for surgery was AVS in 43 patients, aortic regurgitation in 32 patients (87% SAVR), and ascending aortic dilatation in 13 patients (no SAVR). About 10% also received concomitant coronary artery bypass grafting. The mean age of the included patients was 63.7 years (±11.2) and 71% were males.

A total of 52% of all patients developed POAF. Immediate POAF occurred in 36 patients (41.4%, of which 20 underwent SAVR due to AVS). By hospital discharge, immediate POAF had resolved in 5 patients (14%). Following discharge, 10 late POAF events (19.6%) occurred during follow-up. Baseline CAVI measured on the preoperative day was 7.8 ± 1.4 and independently associated with an increased risk for POAF (OR 1.74, 95% CI 1.15–2.79) when adjusted for confounders, in contrast to cfPWV which was not ($P = 0.7$). Baseline CAVI was not significantly associated with hospitalisation for any cause or for HF/AF/stroke, within 30 days of discharge (OR 1.73, 95% CI 0.98–3.30 and OR 1.98, 95% CI 1.00–4.61). The study was under-powered to assess the association between CAVI and postoperative mortality and/or stroke.

To the best of our knowledge, the present study is the first to establish CAVI as an independent predictive factor for POAF. The result confirms the significance of pre-existing AF risk factors associated with arterial stiffness in the initiation and likely propagation of POAF. POAF occurs when postoperative triggers act on a vulnerable preoperative atrial substrate.[3] Importantly, atrial remodelling is an important predisposing factor and shares risk factors with increased arterial stiffness, e.g. age and hypertension which are convincingly associated with AF. CAVI reflects the vascular consequence of AF-related cardiovascular risk factors and could hence explain CAVI as a predictor of POAF. Furthermore, atrial remodelling may be caused by high CAVI-mediated left ventricular overload, which places arterial stiffness upstream of the appearance of POAF and indeed, CAVI is associated with left and right atrial phasic function, prior to cardiac remodelling.[6]

In contrast to CAVI, cfPWV was not independently associated with POAF. This could indicate the importance of incorporating a more systemic arterial stiffness measurement when predicting POAF. A trend was also observed for CAVI as a predictor of all-cause hospitalisation and hospitalisation due to HF/AF/stroke although the limited number of included patients likely contributed to the non-significant result. Other limitations include follow-up via single clinic EMR, limited number

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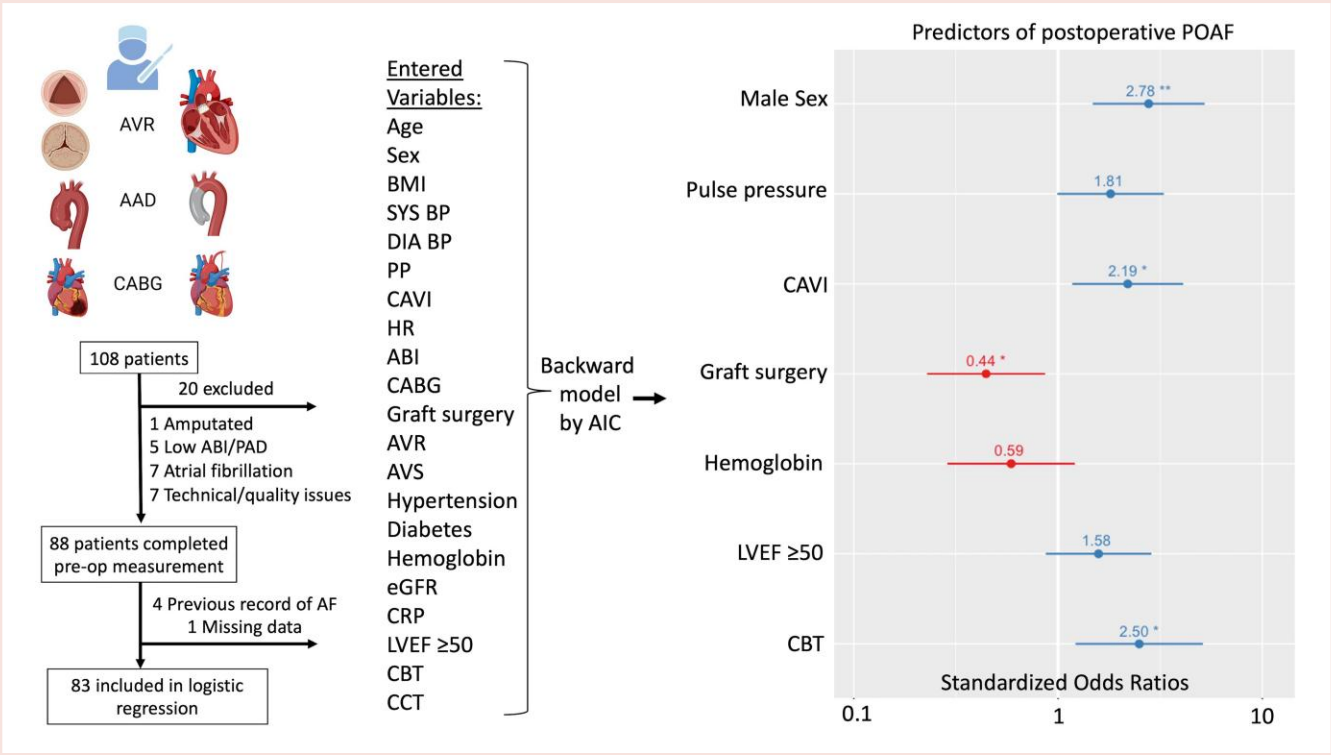

Figure 1 A total of 83 patients were included in the final logistic regression analysis, as demonstrated in the flow chart. Entered variables were based on clinical reasoning, missing data status and univariate correlation. All variables were entered in a backward stepwise logistic regression model which used Akaike Information Criteria (AIC) to ultimately yield the final model. Results from the final model are shown as plotted standardized estimates using Gelman's method, which enables comparison of the effect size of the different variables, with 95% confidence intervals. Pulse pressure, CAVI (cardio-ankle vascular index) and hemoglobin was measured 1 day before surgery. AAD; Ascending aortic dilatation, ABI; Ankle brachial index, AVR; Aortic valve replacement, AVS; Aortic valve stenosis, AF; Atrial fibrillation, BMI; body mass index (kg/m^2), CABG; Coronary artery bypass surgery, CBT; Cardio-pulmonary bypass time, CCT; Cross-clamp time, CRP; C-reactive protein, DIA BP; Diastolic blood pressure, eGFR; estimated glomerular filtration rate, HR; heart rate, LVEF; Left ventricular ejection fraction, PP; Pulse pressure, SYS BP; Systolic blood pressure. Figure created with BioRender.com.

of patients, and the use of a mixed surgical cohort. Due to a lack of active AF screening after hospital discharge, loss-to-follow-up in cases of late AF without healthcare contacts cannot be excluded.

In conclusion, the present study found that for each unit increase in CAVI, the odds of POAF after open ascending aortic/valvular surgery increased by 74%. Identification of patients at risk for POAF is of high clinical relevance and may be facilitated by measuring CAVI. Furthermore, relevant therapeutic interventions might prevent POAF through the reduction arterial stiffness which can be measured with CAVI.

Lead author biography

Oscar Plunde has a bachelor's degree in Biomedicine from Uppsala University and earned his MD degree from Karolinska Institutet in Stockholm where he also defended PhD thesis about the interplay between aortic valve stenosis and atherosclerosis. After completed internship at Karolinska University Hospital, OP joined the department of cardiology at Karolinska University Hospital as a resident physician. He later pursued an opportunity as an international medical manager at Novo Nordisk in Copenhagen. He is still active in academic research via an affiliation at Karolinska Institutet and is Review Editor for Heart Valve Disease in Frontiers in Cardiovascular Medicine.

Data availability

Individual participant data that underlie the results reported will be shared, after deidentification, with researchers who provide a methodologically sound proposal.

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Conflict of interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. O.P. was not employed by Novo Nordisk A/S when conducting the study.

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