BMJ Open Atrial fibrillation after cardiac surgery: identifying candidate predictors through a Delphi process

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ABSTRACT

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Dr Jonathan Bedford; Jonathan.Bedford@ndcn.ox. ac.uk **Objectives** This study was undertaken to identify potential predictors of atrial fibrillation after cardiac surgery (AFACS) through a modified Delphi process and expert consensus. These will supplement predictors identified through a systematic review and cohort study to inform the development of two AFACS prediction models as part of the PARADISE project (NCT05255224). Atrial fibrillation is a common complication after cardiac surgery. It is associated with worse postoperative outcomes. Reliable prediction of AFACS would enable risk stratification and targeted prevention. Systematic identification of candidate predictors is important to improve validity of AFACS prediction tools.

Design This study is a Delphi consensus exercise. **Setting** This study was undertaken through remote participation.

Participants The participants are an international multidisciplinary panel of experts selected through national research networks.

Interventions This is a two-stage consensus exercise consisting of generating a long list of variables, followed by refinement by voting and retaining variables selected by at least 40% of panel members.

Results The panel comprised 15 experts who participated in both stages, comprising cardiac intensive care physicians (n=3), cardiac anaesthetists (n=2), cardiac surgeons (n=1), cardiologists (n=4), cardiac pharmacists (n=1), critical care nurses (n=1), cardiac nurses (n=1) and patient representatives (n=2). Our Delphi process highlighted candidate AFACS predictors, including both patient factors and those related to the surgical intervention. We generated a final list of 72 candidate predictors. The final list comprised 3 demographic, 29 comorbidity, 4 vital sign, 13 intraoperative, 10 postoperative investigation and 13 postoperative intervention predictors.

Conclusions A Delphi consensus exercise has the potential to highlight predictors beyond the scope of existing literature. This method proved effective in identifying a range of candidate AFACS predictors. Our findings will inform the development of future AFACS prediction tools as part of the larger PARADISE project.

Trial registration number NCT05255224.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Engagement of an international, multidisciplinary expert panel ensured a range of perspectives on predictors of atrial fibrillation after cardiac surgery (AFACS), informing the larger PARADISE Project (NCT05255224).
- ⇒ Remote participation allowed for efficient engagement across different geographical regions.
- ⇒ The relatively small panel may not have captured the full diversity of expertise, opinions and experiences found in the broader community of professionals managing patients with AFACS.
- ⇒ Inclusion of patient and public representatives in the Delphi panel added valuable perspectives to the consensus process.

INTRODUCTION

Atrial fibrillation (AF) is a common cardiac arrhythmia resulting in an irregular and often rapid heart rhythm. AF affects 30–40% of patients after cardiac surgery.¹ AF after cardiac surgery (AFACS) is strongly associated with worse outcomes, including longer hospital and intensive care unit (ICU) stays and increased risks of stroke, persistent AF and mortality.^{2–4}

Prophylactic treatments administered during the perioperative period have proven effective at lowering the incidence of AFACS.⁵ However, these treatments are not risk-free. Consequently, it is important to identify highrisk patients to target prophylaxis at those most likely to benefit. However, prediction of AFACS remains challenging. The pathophysiology of AFACS is multifactorial, involving comorbidity factors, surgical stress and the postoperative inflammatory response.⁶ Accurate AFACS prediction therefore requires consideration of a range of patient and intervention factors.

There are no reliable AFACS prediction models in widespread use despite multiple models being developed in recent years.^{7–10}

The lack of effective tools for estimating AFACS risk has prevented the implementation of targeted prophylaxis protocols. Interventions to prevent AFACS may lead to improved outcomes.

The systematic identification of candidate AFACS predictors is important for the validity of any prediction model.¹¹ While systematic reviews can identify candidate predictors from existing literature, a Delphi consensus exercise has the potential to highlight additional untested predictors based on mechanistic understanding or through clinical experience.

The Delphi method involves a structured communication technique to gather consensus among experts.¹² This iterative process involves rounds of surveys where experts provide their independent opinions which are then collated by a facilitator and fed back to the panel.¹³ Delphi processes have previously been used to inform critical care practice, including management of COVID-19¹⁴ and identification of core outcome measures after respiratory failure.¹⁵

This study aimed to identify candidate AFACS predictors through expert consensus. These variables will supplement those identified through a systematic review of existing literature¹⁶ and a national cohort study.¹⁷ The final consolidated list of variables will inform two AFACS prediction models as part of the larger National Institute of Health Research-funded 'Predicting AF after Cardiac Surgery–the PARADISE Score' project (NCT05255224). The PARADISE project aims to develop two validated clinical prediction models to determine the risk of a patient developing AFACS: one in the preoperative assessment clinic or on admission for surgery (PARADISE-1) and another for the postoperative period (PARADISE-2).

METHODS

We undertook a Delphi consensus exercise to identify candidate AFACS predictors as part of the larger PARADISE project. We used the ACcurate COnsensus Reporting Document (ACCORD) guidance to report our Delphi process.¹⁸ We used an online survey tool (Survey Monkey) for data collection and analysis.

Panel selection

We identified potential expert participants through national research networks. We selected participants to reflect a multidisciplinary group of health professionals and patient representatives. Participants were invited via email and were not known to each other. We conducted this Delphi study entirely through electronic contact and data capture. We aimed for a panel size of 10–15 participants to achieve content validity.^{19 20}

Stage 1

Panel members were asked to spontaneously list factors that affect AFACS risk in critically ill patients. We permitted potential protective factors as suggestions. We offered panel members six categories (demographics, comorbidities, vital signs, intraoperative variables, postoperative interventions and postoperative investigation results) to provide structure to responses.

Stage 2

The variables generated in stage 1 were re-presented to the panel. We asked each panel member to select variables that they felt affect AFACS risk. We refined the list by only retaining variables selected by at least 40% of panel members, which was consistent with previous work identifying candidate risk factors.²¹ The facilitating study team



Figure 1 Demographic predictors identified by the Delphi panel in round 1. Light grey bars represent predictors not selected by 40% of the panel in round 2 and therefore not selected for the final list.



Figure 2 Vital sign predictors identified by the Delphi panel in round 1. Light grey bars represent predictors not selected by 40% of the panel in round 2 and therefore not selected for the final list.

had no voting rights nor influence over panel responses. The Delphi exercise was facilitated by a member of the study team with domain knowledge and consensus exercise experience.

Patient and public involvement

Patient and public representatives were included in the Delphi panel.

RESULTS

Participants

We approached 32 experts located in the UK, Germany, Belgium, Canada and North America. Of these, 15 (47%) agreed to participate in the Delphi process. The final panel included cardiac intensive care physicians (n=3), cardiac anaesthetists (n=2), cardiac surgeons (n=1), cardiologists (n=4), cardiac pharmacists (n=1), critical



Figure 3 Intraoperative predictors identified by the Delphi panel in round 1. Light grey bars represent predictors not selected by 40% of the panel in round 2 and therefore not selected for the final list. AF, atrial fibrillation; IABP, intra-aortic balloon pump; SVT, supraventricular tachycardia.



Figure 4 Postoperative investigation predictors identified by the Delphi panel in round 1. Light grey bars represent predictors not selected by 40% of the panel in round 2 and therefore not selected for the final list. ABG, arterial blood gas; CK-MB, creatine kinase-myocardial band; CRP, C-reactive protein; Echo, echocardiogram; LVEF, left ventricular ejection fraction; pCO2, partial pressure of carbon dioxide; pH, potential of hydrogen; pO2, partial pressure of oxygen.

care nurses (n=1), cardiac nurses (n=1) and patient representatives (n=2).

Stage 1

Over the six domains of demographics, comorbidities, vital signs, intraoperative factors, postoperative interventions and postoperative investigation results, the panel generated 122 distinct candidate variables.

Stage 2

All 15 of the initial participants responded in round 2. The initial list of 122 variables was subject to a consensus



Figure 5 Postoperative intervention predictors by the Delphi panel in round 1. Light grey bars represent predictors not selected by 40% of the panel in round 2 and therefore not selected for the final list.

vote where predictors were excluded if selected by at least 40% of panel members. We generated a final list of 72 candidate variables. This process resulted in 3 demographic variables, 29 comorbidity variables, 4 vital sign variables, 13 intraoperative variables, 10 postoperative investigation variables and 13 postoperative intervention variables. These variables and their associated response percentages are shown in figures 1–5. Comorbidity variables are shown in online supplemental figure 1.

These variables were then combined with those identified in a parallel cohort study and systematic review¹⁶¹⁷ to generate a final list of candidate variables to inform the PARADISE project.

The most consistently identified demographic risk factor was patient age. Multiple comorbidities were identified. Those specific to AF risk such as prior AF and left atrial size were ranked highest. Other pre-existing conditions with demonstrable associations, including heart failure and chronic obstructive pulmonary disease, were also identified.

Many intraoperative predictors were highlighted, including cross-clamp time, the presence of intraoperative inotropic support, type of surgery, bypass time and intraoperative amiodarone administration. Echocardiographic parameters, including reduced left ventricular ejection fraction (LVEF) and left atrial dilation, ranked highest in the postoperative investigation domain. Laboratory findings felt to be important candidates included serum potassium, creatinine and lactate concentrations. White cell count was also felt to be an important predictor. Heart rate and blood pressure were highlighted as vital sign variables, along with any identified arrhythmia or ectopic beats.

Multiple postoperative interventions were identified. Beta blocker administration and beta blocker withdrawal were most consistently identified, along with amiodarone administration. Prolonged ventilation and the use of catecholaminergic medication were also highlighted.

DISCUSSION

In this consensus exercise, we aimed to identify important variables affecting AFACS risk. Highlighted variables may be used in the development of predictive models to inform future randomised trials or as covariates in prognostic studies. They will inform the development of two AFACS prediction models in the PARADISE project.

Remote participation promoted international involvement. Our approach allowed experts from different settings to contribute effectively, ensuring a comprehensive array of perspectives and maximising the advantages of the group consensus model. The expert panel identified several factors across a range of categories.

Age was the most frequently identified demographic AFACS predictor. Increasing age is associated with molecular changes in atrial tissue that drive electrical and structural changes, leading to AF initiation. These changes affect normal conduction pathways, promoting non-uniform conduction, electrical dissociation and re-entry circuits, leading to arrhythmia.^{22 23} Increasing age has been consistently identified in other studies of AFACS predictors.^{9 10 24}

Multiple comorbidities and preadmission measurements were highlighted as candidate AFACS predictors. These predominantly reflected cardiovascular, pulmonary and metabolic diseases. Left atrial size was the most consistently identified candidate predictor. Atrial dilatation is a strong predictor of AF in the community.²⁵ Many comorbidities lead to elevated atrial pressure and subsequent atrial stretch. Atrial stretch alters ion channel function and causes a decrease in atrial effective refractory period and an increase in AF inducibility.^{26 27} Increasing left atrial diameter is associated with AF risk in the general ICU and after cardiac surgery.²⁸ Obesity was highlighted as an important risk factor. This is consistent with existing literature suggesting that each 1 kg/m² increase corresponds to a 1% increase in the risk of AFACS.²⁹ This association may represent secondary changes in left atrial volume, autonomic tone and neurohormonal activation associated with obesity.

The type of surgery was identified as an important predictor. This finding is consistent with previous studies demonstrating that patients undergoing coronary artery bypass graft surgery face a 15% to 40% risk of developing AF. This risk increases up to around 50% after isolated valve surgery and up to 60% in combined procedures.¹³⁰

Furthermore, the complexity and duration of the cardiac surgery itself also play a significant role in the development of AF. Surgical trauma induces a systemic inflammatory response proportional to the degree of surgical stress, which is influenced by the duration of the surgery.^{31 32} Cardiopulmonary bypass duration was highlighted, which is consistent with existing literature. Bypass itself may increase AFACS risk sevenfold versus off-pump procedures.³³ Potential mechanisms include the duration of myocardial ischaemia, atrial cannulation, increased inflammatory response and the sequelae of cardioplegia.³⁴

Echocardiographic and laboratory measurements featured highly in the postoperative investigations domain. Consistent with preoperative findings, the presence of postoperative atrial dilatation was felt to be an important predictor of AFACS. Postoperative-reduced LVEF was also identified. Heart failure shares many common comorbidities and pathophysiological pathways with AF. As such, they are likely to coexist. Beyond common precursors, systolic heart failure itself may increase the risk of AF through many pathways, including increased atrial stretch, neurohormonal alterations and cellular remodeling.³⁵

Of the identified laboratory measurements, serum potassium had the highest level of agreement. Hypokalaemia reduces the outward repolarising current and increases intracellular calcium, thereby increasing the risk of afterdepolarisations.³⁶ Marginally lower serum potassium concentrations are associated with a higher risk of developing AF in patients in the community.³⁷ Although no causal association has been demonstrated, high-normal serum potassium concentrations are often targeted after cardiac surgery with the intention of preventing AFACS.³⁸ Routine potassium supplementation is not risk-free, and optimal target potassium levels are yet to be determined. Ongoing trials should inform this area in the future.³⁹

Postoperative factors included medications such as beta blockers (administration and withdrawal), amiodarone and catecholaminergic drugs. Perioperative beta blocker therapy has been consistently shown to reduce the incidence of AFACS.⁵ Its use as AFACS prophylaxis is recommended in national guidelines.^{40–42} However, these guidelines acknowledge the biases of existing literature and the limited evidence of improvement in patient-centred outcomes. As such, they assert that perioperative prophylaxis must be weighed against potential side effects and administered on an individualised basis. Continuation of beta blockers appears important in those patients routinely taking them preoperatively-beta blocker withdrawal was associated with a doubling of the odds of AFACS in a 2-centre study of 743 patients normally taking beta blockers undergoing cardiac surgery.⁴³ Its continuation in these patients on the first postoperative day is accordingly recommended in national guidelines.³⁸

Prolonged ventilation was identified as a candidate AFACS predictor. Ventilation lasting over 24 hours postoperatively has been found to be strongly associated with AFACS.⁸ However, its inclusion in any predictive tool postpones the tool's utility until 24 hours postoperatively. Indeed, as much of AFACS occurs early in the postoperative period,⁹ when developing any AFACS prediction model, the benefit of including any postoperative variables must be weighed against the necessary delay in prediction while these variables are being measured.

The Delphi method leverages the collective expertise and insights of a panel of experts. This can highlight novel or less-documented AFACS risk factors not evident in existing literature. It also allows for the integration of clinical experience and subjective expert opinions, which is especially valuable in areas with limited research. Panellist anonymity was maintained with consensus determined by a priori criteria. However, the findings should be interpreted in the context of certain limitations. The Delphi method relies heavily on subjective evaluations, requiring a degree of trust in the anonymous expert panel essential. This method lacks standardised guidelines for consensus or panel selection. In our study, panellists were purposively chosen to ensure diverse and relevant experience in AFACS; however, no quantitative analysis of expertise was undertaken. No sensitivity analyses were performed, and our response rate to initial response was modest, although all respondents from round 1 continued to round 2. Though international, the panel was not global, potentially biasing and limiting the generalisability of our results.

Conclusion

This international consensus exercise facilitated the generation of candidate predictors to inform the development of AFACS prediction tools as part of the larger PARADISE project. The use of a consensus exercise allowed for the incorporation of diverse expert opinions, leading to a comprehensive list of candidate predictors encompassing patient and intervention factors with a strong evidence base or biological plausibility.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants was approved by the PARADISE study and the NHS Health Research Authority (HRA) (IRAS 296508) with ethical approval by the HRA Research Ethics Committee Cambridge East (ref: 21/ EE/0166). Participants gave informed consent to participate in the study before taking part.

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