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Original Research

Using the C_2HEST Score for Predicting Postoperative Atrial Fibrillation After Cardiac Surgery: A Report From the Western Denmark Heart Registry, the Danish National Patient Registry, and the Danish National Prescription Registry

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Objectives: New-onset postoperative atrial fibrillation (POAF) is a common complication after cardiac surgery. A targeted approach is necessary for prophylactic handling of the complication. The authors tested the performance of the C_2HEST score to predict POAF in patients undergoing cardiac surgery.
Design: Register-based cohort study.
Setting: Three cardiothoracic centers.
Participants: All adult patients undergoing cardiac surgery in Western Denmark between January 1, 2010, and December 31, 2018, were included. Data on patient comorbidities before surgery were obtained from the Western Denmark Heart Registry, the Danish National Patient Registry, and the Danish National Prescription Registry.
Interventions: The C_2HEST score (C_2: Coronary Artery Disease/Chronic Obstructive Pulmonary Disease [1 point each]; H: Hypertension; E: Elderly [Age ≥75, 2 points]; S: Systolic Heart Failure [2 points]; T: Thyroid disease [hyperthyroidism]) was calculated for each patient. The primary outcome was POAF within the primary hospital stay. The C_2HEST score's discriminative ability was evaluated and compared with an age-stratified version (mC_2HEST) as well as 2 validated clinical risk models ($CHADS_2$ and CHA_2DS_2-VASc).
Measurements and Main Results: Among the 14,279 patients included, 4,298 (30.1%) developed POAF. The C_2HEST score's performance was not significantly better than the $CHADS_2$ and CHA_2DS_2-VASc scores (area under the curve [AUC] 0.553 [95% confidence interval {CI} 0.543; 0.563] *v* 0.543 [95% CI 0.535; 0.552] and 0.565 [95% CI 0.555; 0.574], respectively). The age-modified (mC_2HEST) score showed only modest improvement in the risk model, with an AUC of 0.580 (95% CI 0.570; 0.590).
Conclusion: The discriminative ability of the C_2HEST score, measured by the AUC, was limited in this population, and was not proven to be superior to the $CHADS_2$, CHA_2DS_2-VASc, and mC_2HEST scores in predicting POAF after cardiac surgery.

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Key Words: Postoperative atrial fibrillation; Cardiac surgery; Risk prediction model

NEW-ONSET postoperative atrial fibrillation (POAF) is the most common arrhythmia after cardiac surgery. This complication is associated with longer hospital stay and intensive care unit stays and higher healthcare costs.[1] Furthermore, patients with POAF have a higher morbidity and mortality than patients not experiencing the complication.[2,3] Recent meta-analyses and reviews have shown a reduced risk of POAF after prophylactic treatment with beta-blockers, sotalol, amiodarone, or atrial pacing on the risk of POAF.[4,5] Other preventive measures that have shown promising results include posterior pericardiotomy and epicardial fat Botox injections.[6,7] Meanwhile, possible adverse side effects from prophylactic drugs and restricted healthcare budgets make individual risk assessment necessary, and an early detection of patients at risk who may benefit from an early prophylactic strategy and a more intensive surveillance could potentially be an effective strategy for improving patient outcomes. Earlier studies investigating predictors of POAF reflect the multifaceted complication that are most likely a result of predisposing factors in the cardiac tissue, patient comorbidities, type of surgery, and inflammatory response. Overall, among the factors with the strongest association with POAF are age, type of surgery, and atrial remodeling.[8,9]

The C_2HEST score (C_2: Coronary Artery Disease/Chronic Obstructive Pulmonary Disease [1 point each]; H: Hypertension; E: Elderly [Age ≥75, 2 points]; S: Systolic Heart Failure [2 points]; T: Thyroid disease [hyperthyroidism]) was developed to predict incident atrial fibrillation (AF) and has since been tested and validated in different subgroups of patients with good predictive performance.[10,11] Recently, an age-stratified criterion was added to the C_2HEST score (mC_2HEST, m: Age ≥65, 1 point), taking into account the increased risk of incident AF with increasing age, and improving the prediction model's area under the curve (AUC), at least statistically.[12] Many attempts have been made to provide surgeons with a risk model to assess the patient's risk of POAF, but most rely on advanced techniques (eg, echocardiography, electrocardiogram) or biomarkers not routinely collected in a surgical setting. Furthermore, several studies have tested the ability of the $CHADS_2$ (congestive heart failure, hypertension, 75 years of age or older, diabetes mellitus, and previous stroke or transient ischemic attack) and CHA_2DS_2-VASc (congestive heart failure, hypertension, 75 years of age and older, diabetes mellitus, previous stroke or transient ischemic attack, vascular disease, 65 to 74 years of age, female) scores to predict POAF after cardiac surgery and found they had good performance,[13-15] although these scores were initially introduced to predict the risk of embolic stroke in patients with AF.[16] The usefulness of these risk scores has been proven in different study populations, and an easy-to-remember bedside tool is especially needed in a busy clinical setting. Recently, the C_2HEST score has proven valid and with high performance in predicting AF in multiple larger populations.[17,18] Because of the overlap between predictors and risk factors in AF/POAF patients, the authors thought it interesting if the score would show similar good results in a cardiac surgery population, where an easy clinical tool for prediction of POAF is still warranted.

The aim of this study was to investigate the performance of the C_2HEST score in predicting POAF after cardiac surgery and to compare its performance to the mC_2HEST, $CHADS_2$, and CHA_2DS_2-VASc scores. The authors hypothesized that the simple clinical C_2HEST score would show similar predictive abilities for POAF as previously shown in other subgroups of patients.

Methods

This study followed the proposed checklist for Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD): the TRIPOD statement, prediction model validation.[19]

This study was approved by the institutional review board at Aalborg University Hospital (id-number 2020-022). Ethical approval is not required for registry-based studies in Denmark.

Data Sources

The data used for this study were retrieved from 3 registers: the Western Denmark Heart Registry (WDHR), The National Patient Registry (NPR), and the Danish National Prescription Registry (DNPR). The WDHR contains data on all patients referred for diagnostic, invasive, and cardiac procedures in Western Denmark since 1999 (approximately 3.5 million inhabitants).[20] This clinical database contains data on the clinical characteristics of patients and cardiac procedures. Patient demographics, perioperative data, and postoperative data were collected at the time of the patient's surgery and entered by the responsible physicians and secretaries. The reliability of the WDHR data has previously been assessed,[21] and the positive predictive value of the diagnosis of POAF has been proven valid.[22] Using the unique person identification number, which is given to all Danish citizens at birth or immigration, the authors linked the patients to the NPR and the DNPR for complete preoperative data on all cardiac surgical patients. The NPR holds information on all admissions from all Danish hospitals with one primary discharge diagnosis code and possibly one or more secondary discharge diagnoses according to the ICD-10 (International Classification of Diseases, 10th revision). Information regarding all redeemed prescriptions, date of dispensation, strength, and quantity of medications is registered in the DNPR. This database has been shown to be valid and the degree of completeness is exceptional.[23] The specific ICD and ATC (Anatomic

Therapeutic Chemical) codes used in the study can be seen in Supplemental Table 1.

Study Population

The study population consisted of all patients ≥18 years of age who underwent cardiac surgery in Western Denmark between January 1, 2010, and December 31, 2018. If patients had undergone multiple cardiac surgeries during the study period, only the first procedure was included.

Patients with preoperative ongoing AF or a history of AF before the surgery and patients who underwent cardiac transplants performed were excluded.

Variables

Patients were considered to have coronary artery disease (CAD) if they were registered with a previous acute myocardial infarct and/or percutaneous coronary intervention or scheduled for a coronary artery bypass grafting either isolated or in combination with other procedures registered in the WDHR. Likewise, the diagnosis of chronic obstructive pulmonary disease (COPD) was accepted if registered in WDHR and/or in the NPR.

The authors defined hypertension from either a registration in WDHR, treatment with at least 2 antihypertensives, or a diagnosis of hypertension registered in the NPR 10 years before the date of surgery. If patients were registered with a diagnosis of hypertension in the WDHR but not in the NPR or DNPR, the patients were categorized as not having hypertension. Likewise, if patients had a registration of a reimbursement of antihypertensive drugs, with or without a diagnosis in NPR, the patients were considered hypertensive. Congestive heart failure was defined as left ventricular ejection fraction ≤40% registered in WDHR and/or a registered diagnosis in the NPR. Thyroid disease is not registered in the WDHR; therefore, patients were considered to have thyroid disease if treated with antithyroid medicine up to 10 years before surgery or if a thyroid diagnosis was registered in the NPR. A history of peripheral vascular disease and stroke or transient ischemic attack was a composite of a registration in WDHR and NPR. Patients were considered to have a diagnosis of diabetes mellitus if they had a registration of the use of insulin and/or medically treated diabetes in the WDHR and/or by an inpatient or outpatient hospital diagnosis of type 1 or type 2 diabetes in the NPR (Supplementary Table 1).

Outcome

The study outcome POAF was defined as an episode of any length of new-onset AF recorded by continuous telemetry and/or with a standard 12-lead electrocardiogram during the postoperative period and until discharge from the surgical ward in patients who had sinus rhythm before admittance. Patients who developed POAF/incident AF after transfer to other specialist wards or hospitals later were not recorded in the WDHR.

Data Statement

Data are available as presented in this paper. According to Danish legislation, the authors' approvals to use the Danish data sources for the current study do not allow them to distribute or make patient data directly available to other parties.

Statistical Methods

Continuous variables are represented as the mean ± standard deviation when appropriate, and categorical variables are represented as frequency and percentage. Comparisons were made with Student's t test and Fisher's exact test or the Pearson's χ^2 test for continuous and categorical variables, respectively.

The associations of the respective C_2HEST score, the mC_2HEST score, $CHADS_2$ score, and the CHA_2DS_2-VASc score with the risk of POAF were evaluated by logistic regression. Furthermore, the association between the individual components of the risk scores and POAF was assessed by multivariable logistic regression analyses.

The predictive ability of the C_2HEST score, the mC_2HEST score, the $CHADS_2$ score, and the CHA_2DS_2-VASc score were estimated with receiver operating characteristic (ROC) curves and AUCs. The equality of the AUCs was tested using Delong's test.[24] The authors used bootstrapping over 1,000 samples to calculate 95% confidence intervals (CIs) for the AUCs.

For statistical analyses, STATA software version 17 (Stata Corp, StataCorp LLC, College Station, TX) was used.

Results

Of the 16,762 cardiac surgeries performed during the study period, 226 of the entries were excluded because of multiple new surgeries on the same patient. Furthermore, 2,142 patients were excluded owing to preoperative arrhythmia, 105 patients were excluded because of non-Danish citizenship, and 10 patients were under the age of 18 at the time of surgery.

A total of 14,279 patients were included in the analysis of who 4,298 (30.1%) of these developed POAF. Male patients comprised 75.9% of the population. All continuous variables appeared normally distributed. The patient clinical characteristics are presented in Table 1. Patients who developed POAF were older than those not experiencing the postoperative arrhythmia. Furthermore, when compared with patients without POAF, patients with POAF had a significantly higher prevalence of hypertension, COPD, and thyroid disease. There were no significant differences in terms of sex, diabetes, history of stroke or transient ischemic attack, previous acute myocardial infarct, or left ventricular ejection fraction.

The group of patients experiencing POAF had significantly higher mean C_2HEST scores than those with those without POAF (3.1 ± 1.5 *v* 2.75 ± 1.49, respectively; $p < 0.001$). The trend was the same for the $CHADS_2$ and CHA_2DS_2-VASc scores. Table 2 shows the univariate and multivariate regression analysis for POAF with all of the components of the

Table 1
Baseline Characteristics of the Patients Undergoing Cardiac Surgery

Covariates	Total N: 14279	POAF:4298 (30.1%)	No POAF: 9,981 (69.9%)	p Value
Age, y, (SD)	66.8 ±10.4	69.7 ± 9.0	65.6 ± 10.7	<0.001
Sex, male, (%)	10,844 (75.9)	3,250 (75.6)	7,594 (76.1)	0.55
Hypertension	12,601 (88.3)	3,879 (90.3)	8,722 (87.4)	<0.001
CAD	10,946 (76.7)	3,174 (73.9)	7,772 (77.9)	<0.001
COPD	1,657 (11.6)	589 (13.7)	1,068 (10.7)	<0.001
Diabetes mellitus	2,963 (20.8)	839 (19.5)	2,124 (21.3)	0.054
Thyroid disease	329 (2.3)	137 (3.2)	192 (1.9)	<0.001
Stroke/TIA	1,113 (7.8)	353 (8.2)	760 (7.6)	0.129
Vascular disease	3,489 (24.4)	1,039 (24.2)	2,450 (24.6)	0.148
Dialysis	117 (0.82)	25 (0.58)	92 (0.92)	0.11
Former AMI	2,543 (17.8)	736 (17.1)	1,807 (18.1)	0.373
Former PCI	2,079 (14.6)	578 (13.5)	1,501 (15.04)	0.044
LVEF (%), (SD)	54 ± 10.9	54 ± 10.8	53.9 ± 10.9	0.612
Previous cardiac surgery (%)				
0	13,585 (95.1)	4,111 (95.7)	9,474 (94.9)	0.302
1	520 (3.6)	144 (3.4)	376 (3.8)	
≥2	67 (0.5)	16 (0.4)	51 (0.5)	
Procedure (%)				
Aortic valve surgery	3,209 (22.5)	1,103 (25.7)	2,106 (21.1)	<0.001
CABG	8,293 (58.1)	2,195 (51.1)	6,098 (61.1)	
Mitral valve surgery	1,057 (7.4)	352 (8.2)	705 (7.1)	
Double procedure*	1,646 (11.5)	625 (14.5)	1021 (10.2)	
Triple procedure	33 (0.23)	16 (0.37)	17 (0.17)	
Other	41 (0.3)	7 (0.2)	34 (0.3)	
C_2HEST score points (%)				
0	552 (8.9)	119 (2.8)	433 (4.3)	<0.001
1	1,841 (12.9)	487 (11.3)	1,354 (13.6)	
2	4,771 (33.4)	1,165 (27.1)	3,606 (36.1)	
3	1,726 (12.1)	623 (14.5)	1,103 (11.1)	
4	3,765 (26.4)	1,279 (29.8)	2,486 (24.9)	
5	759 (5.3)	301 (7)	458 (4.6)	
6	679 (4.8)	247 (5.8)	432 (4.3)	
7	179 (1.3)	74 (1.7)	105 (1.1)	
8	7 (0.1)	3 (0.1)	4 (0.04)	
Mean C_2HEST, (SD)	2.9 ± 1.5	3.1 ± 1.5	2.8 ± 1.5	<0.001
Mean CHA_2DS_2-VASc, (SD)	2.8 ± 1.5	3 ± 1.4	2.7 ± 1.5	<0.001

Abbreviations: AMI, myocardial infarction; CABG, coronary artery bypass grafting; CAD, coronary artery disease, COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.
*Double/triple procedure: concomitant CABG and aortic/mitral valve replacement; C_2HEST, coronary artery disease or chronic obstructive pulmonary disease (1 point each), hypertension (1 point), elderly (age ≥75 years, 2 points), systolic heart failure (2 points), thyroid disease (1 point); CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, stroke or transient ischemic attack (2 points), vascular disease, age 65 to 74 years, sex category.

C_2HEST score, mC_2HEST score, $CHADS_2$, and CHA_2DS_2-VASc scores. On multivariable analysis, COPD, hypertension, and thyroid disease were shown to be independently related to the development of POAF (odds ratio [OR] 1.25 [1.12-1.40], OR 1.29 [1.13-1.47], and OR 1.55 [1.23-1.94], respectively). The variable associated with the greatest risk of POAF was age, especially age ≥65 years, and all 4 risk scores were significant predictors of POAF after cardiac surgery.

The predictive values of the C_2HEST, mC_2HEST, $CHADS_2$, and CHA_2DS-VASc scores are depicted in Figure 2 and Table 3. All AUCs were in the range of 0.55 to 0.58, with mC_2HEST reaching the highest AUC of 0.58. When calculating the AUC for C_2HEST, $CHADS_2$, and CHA_2DS_2-VASc in stratified risk groups, the authors found no differences in predictive capabilities.

Discussion

In this study, the authors tested the performance of the C_2HEST score for predicting the risk of POAF in individual patients undergoing cardiac surgery and compared this risk model with the predictive abilities of the mC_2HEST, $CHADS_2$, and CHA_2DS_2-VASc scores. Although, the mean C_2HEST score was higher in the patients who developed POAF, the C_2HEST score seems to be of a limited value as an initial screening tool for identifying patients at high risk of POAF, and the score did not perform better than the mC_2HEST, $CHADS_2$, and CHA_2DS_2-VASc scores in the present study population.

Earlier studies have shown that age, hypertension, heart failure, COPD, and CAD were strong predictors of POAF.[25,26] However, the occurrence of CAD was more frequent in the

Table 2
Univariable and Multivariate Regression Analysis for Variables in the C_2HEST, mC_2HEST, $CHADS_2$, and CHA_2DS-VASc Scores

Component	Univariable OR (95% CI)	Multivariable OR (95% CI)
CAD	0.80 (0.74-0.87)	0.76 (0.69-0.83)
COPD	1.32 (1.19-1.48)	1.25 (1.12-1.40)
Hypertension	1.34 (1.19-1.51)	1.29 (1.13-1.47)
Age ≥75 y	1.83 (1.69-1.99)	1.78 (1.64-1.94)
Systolic heart failure	1.06 (0.96-1.16)	1.01 (0.92-1.12)
Thyroid disease	1.67 (1.34-2.09)	1.55 (1.23-1.94)
Age ≥65 y	2.21 (2.04-2.40)	2.70 (2.44-2.97)
Diabetes mellitus	0.90 (0.82-0.98)	0.90 (0.82-0.99)
Stroke/TIA/ thromboembolism	1.08 (0.95-1.24)	1.02 (0.89-1.17)
Vascular disease	0.98 (0.90-1.06)	0.95 (0.87-1.03)
Age 65-75 y	1.26 (1.17-1.35)	1.98 (1.81-2.16)
Female sex	1.03 (0.94-1.12)	0.92 (0.84-1.00)
C_2HEST		1.14 (1.11-1.17)
C_2HEST score ≥4 points		0.09 (0.01-0.16)
mC_2HEST		1.18 (1.15-1.20)
$CHADS_2$		1.14 (1.10-1.18)
CHA_2DS_2-VASc		1.16 (1.13-1.18)
CHA_2DS_2-VASc score ≥4 points		1.00 (0.93-1.08)

Abbreviations: C_2HEST, coronary artery disease or chronic obstructive pulmonary disease (1 point each), hypertension (1 point), elderly (age ≥75 years, 2 points), systolic heart failure (2 points), thyroid disease (1 point); CAD, coronary artery disease; $CHADS_2$, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, previous stroke/TIA(2 points); CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, stroke or transient ischemic attack (2 points), vascular disease, age 65 to 74 years, sex category; CI, confidence interval; COPD, chronic obstructive pulmonary disease; E, elderly (age ≥75); OR, odds ratio; S, systolic heart failure; T, thyroid disease; Vascular disease, myocardial infarction, complex aortic plaque, and peripheral artery disease.

non-POAF group in the present study population, suggesting that this variable was not a risk factor for later POAF. This was confirmed when testing using multivariable analyses.

The authors did find a strong association between the development of POAF and age, which also explains the slightly better performance of the mC_2HEST score compared with C_2HEST score. Mathew et al.[8] reported a 75% increase in the odds of developing POAF with every 10-year increase in age indicating that an age of ≥70 years places patients at high risk. However, a point to note about that study was the inclusion of patients with a history of AF.

Table 3
Comparison of Area Under the Curves for the Prediction Models

	AUC	95% CI
C_2HEST	0.553	0.543; 0.563
mC_2HEST	0.580	0.570; 0.590
$CHADS_2$	0.543	0.535; 0.552
CHA_2DS-VASc	0.565	0.555; 0.574

Abbreviations: AUC, area under the curve; C_2HEST, coronary artery disease or chronic obstructive pulmonary disease (1 point each), hypertension (1 point), elderly (age ≥75 years, 2 points), systolic heart failure (2 points), thyroid disease (1 point); $CHADS_2$, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, previous stroke/TIA(2 points); CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, stroke or transient ischemic attack (2 points), vascular disease, age 65 to 74 years, sex category; CI, confidence interval.

In accordance with the present results, most other studies reported a higher frequency of POAF in valve or double procedure surgery compared with isolated coronary artery bypass grafting. Furthermore, the authors found that the incidence of POAF in this heterogenic population was corroborated with that of other studies.[27,28] All 4 risk scores had low predictive abilities, which is not consistent with previous reports of models used for predicting POAF.

The C_2HEST score has shown promising results as a simple practical tool for predicting incident AF based on clinical risk factors. Since its development and validation in a Chinese/ Korean population,[17] this risk model has been validated in both Western[10] and Asian populations[11,18] with good results. Correspondently, the CHA_2DS_2-VASc score has been tested in many populations undergoing cardiac surgery and a recent meta-analysis found a pooled AUC of 0.76 (95% CI 0.72-79).[13]

Possible explanations for the dissimilar findings in the present study could be (1) misclassifications in databases, (2) various definitions of AF/POAF in the study populations, (3) differences in ethnicity and access to healthcare, and (4) selection bias in the study populations, which was underlined in the study by Lip et al.,[29] where an investigation of the C_2HEST score as a screening tool in a healthy Danish population was evaluated.

Early detection and treatment of POAF are vital in preventing thromboembolic events and early death; therefore, a shorter follow-up and/or remote monitoring may be needed in selected high-risk patients postoperatively. Larger retrospective studies have shown an association between POAF and later atrial fibrillation,[30,31] and early identification and treatment may improve long-term outcomes for this patient group. Yin et al.[15] found increasing predictive abilities for patients with a $CHADS_2$ score ≥2 and CHA_2DS_2-VASc score of ≥4 and recommended the initiation of prophylactic use of ß-blockers and antiarrhythmic agents before cardiac surgery. Likewise, the authors of the aforementioned meta-analyses[13] recommended that patients with a CHA_2DS_2-VASc score of >3 receive prophylactic treatment. In contrast, the present study was unable to demonstrate a significant difference in various risk groups of the risk models with logistic regression analyses. The authors conjecture that the distribution of predictors included in the C_2HEST score may be similar in POAF patients versus non-POAF patients. Therefore, identifying patients at high risk of development of POAF (C_2HEST score ≥4) based on these variables alone results in an apparent paradox (OR 0.09 [0.01-0.16]).

A direct comparison between AUCs in this study and others testing the C_2HEST score's abilities should be made with caution, as the value depends both on the individual component's weights in the risk scores as well as the distribution of risk factors in the sample population. This study population differs from previous studies investigating the C_2HEST score in several aspects. Patients undergoing cardiac surgery are a selected

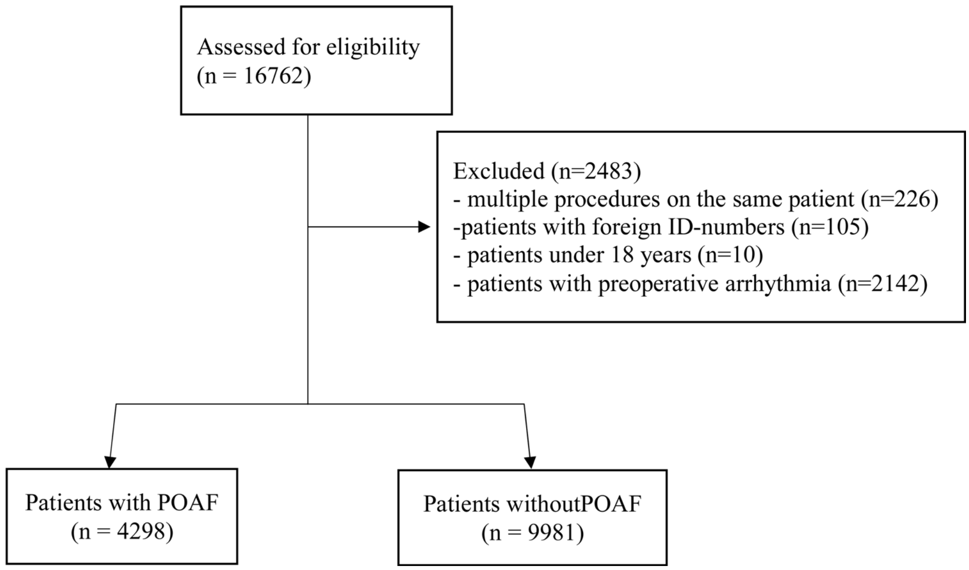

Fig. 1. Flowchart of patient selection.

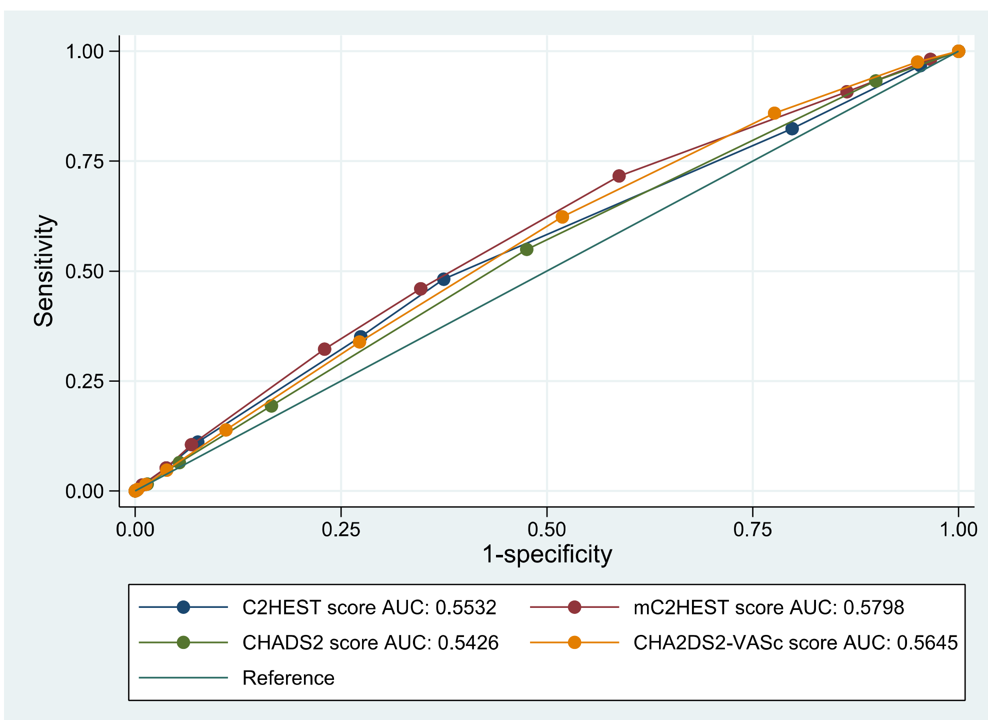

Fig. 2. Performance of the risk scores for predicting postoperative atrial fibrillation after cardiac surgery.

C_2HEST indicates coronary artery disease or chronic obstructive pulmonary disease (1point each), hypertension (1 point), elderly (age ≥75 years, 2 points), systolic heart failure (2 points), thyroid disease (1 point); mC_2HEST a modified version with one additional variable (m= age between 65-74 years, 1 point); $CHADS_2$, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke or transient ischemic attack; CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke or transient ischemic attack, vascular disease, age 65 to 74 years, sex category.

group of patients with severe cardiac diseases compared with a population under investigation for incident AF. For example, 88.3% of the patients in this study had a history of hypertension, and 17.7% had diabetes mellitus requiring either insulin and/or oral medication before the outcome POAF. For comparison Lip et al.[29] reported a prevalence of hypertension of 29.8% and CAD of 9.6% in septuagenarians. Another important risk factor is age, which is correlated with both POAF and incident AF. The C_2HEST score will most likely perform better when applied to a sample with a wide age range when compared with a sample with a narrow age range, which might be the case in the current study. Overall, the modest AUC values in this study are in line with other studies' predictive scores based on cohort data.

Although it is preferable to introduce an easy tool for screening (eg, pre surgery), the C_2HEST score might not reflect the true risk in a patient group undergoing cardiac surgery because it does not consider the type of surgery or the use and length of cardiopulmonary bypass, which has been shown to be associated with the development of POAF.[32,33]

Other risk scores primarily developed for incident AF prediction were considered in the evaluation of the performance of the C_2HEST score. The Atherosclerosis Risk in Communities score for Atrial Fibrillation (ARIC-AF)[34] includes several potential risk factors, but the variables concerning heart function (ie, Precordial murmur, LAE, LVH) are not available from WDHR. The same goes for the Framingham Heart Study score for Atrial Fibrillation.[35] Furthermore, this study population consisted mainly of patients of Caucasian ethnicity, and the race component would not come in use. The Maccabi Healthcare Services score[36] contains the variable "female with autoimmune/inflammatory disease," which is also out of the scope of the WDHR registry. The Atrial Fibrillation Risk Score System,[32] a prospectively developed and validated score, uses 5 clinical variables to predict POAF in patients undergoing coronary artery bypass grafting, valve surgery, or both, and reaches an AUC value of 0.7, but this clinical score includes added points for ethnicity and previously known AF, where the former is not applicable in every cardiac surgery center and the latter may mask the true risk of POAF if the population is pooled with patients with known AF. The pathophysiological distinction between nonsurgical AF and POAF is difficult, as the comorbidities, as well as the genetic and inflammatory responses, both overlap.

Limitations

Although data for the present study were retrospectively retrieved, the majority of the variables included were registered prospectively (in WDHR), making the data relatively robust and with a lower risk of selection bias. However, there are limitations in relation to the study that should be mentioned. The validity of the hypertension and thromboembolism diagnoses in the DPR is somewhat low and misclassification bias may have occurred.[37] However, the authors have tried to minimize this by combining data from 3 different sources. Some risk factors and medications also may have changed over time, which the authors were not able to take into account.

Conclusion

Although higher C_2HEST scores are associated with an increased risk of POAF, the C_2HEST score seems to be of limited value as an initial screening tool for identifying patients at high risk of POAF, suggesting that clinical predictors alone may be insufficient for predicting POAF. The predictive abilities of the C_2HEST score were similar when compared with the $CHADS_2$ and CHA_2DS_2-VASc scores in the present study population. Additional studies are warranted to assess if routinely collected risk factors should be combined with perioperative data to further enhance the predictive capability of the C_2HEST score. The results from these studies may help to optimize a future impact analysis of the risk score.

CRediT author statement

Louise F. Rasmussen: investigation, software, data curation, formal analysis, writing – original draft preparation, **Jan Jesper Andreasen**: supervision, writing – review & editing, **Sam Riahi**: supervision, writing – review & editing **Gregory Y.H. Lip**: conceptualization, supervision, writing – review & editing, **Søren Lundbye-Christensen**: methodology, formal analysis, **Søren Paaske Johnsen:** writing – review & editing

Declaration of Competing Interest

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1053/j.jvca.2022.03.037.

References

1 LaPar DJ, Speir AM, Crosby IK, et al. Postoperative atrial fibrillation significantly increases mortality, hospital readmission, and hospital costs. Ann Thorac Surg 2014;98:527–33.

2 Villareal RP, Hariharan R, Liu BC, et al. Postoperative atrial fibrillation and mortality after coronary artery bypass surgery. J Am Coll Cardiol 2004;43:742–8.

3 Kosmidou I, Chen S, Kappetein AP, et al. New-onset atrial fibrillation after PCI or CABG for left main disease. J Am Coll Cardiol 2018;71:739–48.

4 Dobrev D, Aguilar M, Heijman J, et al. Postoperative atrial fibrillation: Mechanisms, manifestations, and management. Nat Rev Cardiol 2019;16:417–36.

5 Arsenault KA, Yusuf AM, Crystal E, et al. Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery. Cochrane Database Syst Rev 2013;2013:CD003611.

6 Gaudino M, Sanna T, Ballman KV, et al. Posterior left pericardiotomy for the prevention of atrial fibrillation after cardiac surgery: An adaptive, single-centre, single-blind, randomised, controlled trial. Lancet 2021;398:2075–83.

7 Romanov A, Pokushalov E, Ponomarev D, et al. Long-term suppression of atrial fibrillation by botulinum toxin injection into epicardial fat pads in patients undergoing cardiac surgery: Three-year follow-up of a randomized study. Heart Rhythm 2019;16:172–7.

8 Mathew JP, Fontes ML, Tudor IC, et al. A multicenter risk index for atrial fibrillation after cardiac surgery. JAMA 2004;291:1720–9.

9 Rader F, Costantini O, Jarrett C, et al. Quantitative electrocardiography for predicting postoperative atrial fibrillation after cardiac surgery. J Electrocardiol 2011;44:761–7.

10 Li Y-G, Bisson A, Bodin A, et al. C_2HEST score and prediction of incident atrial fibrillation in poststroke patients: A French nationwide study. J Am Heart Assoc 2019;8:e012546.

11 Hu W-S, Lin C-L. Prediction of new-onset atrial fibrillation for general population in Asia: A comparison of C_2HEST and HATCH scores. Int J Cardiol 2020;313;60-33.

12 Li Y-G, Bai J, Zhou G, et al. Refining age stratum of the C2HEST score for predicting incident atrial fibrillation in a hospital-based Chinese population. Eur J Intern Med 2021;90:37–42.
13 Chen Y, Zeng M, Liu Y, et al. CHA2DS2-VASc score for identifying patients at high risk of postoperative atrial fibrillation after cardiac surgery: A meta-analysis. Ann Thorac Surg 2020;109:1210–6.
14 Chua S-K, Shyu K-G, Lu M-J, et al. Clinical utility of CHADS2 and CHA2DS2-VASc scoring systems for predicting postoperative atrial fibrillation after cardiac surgery. J Thorac Cardiovasc Surg 2013;146:919–26;e1.
15 Yin L, Ling X, Zhang Y, et al. CHADS2 and CHA2DS2-VASc scoring systems for predicting atrial fibrillation following cardiac valve surgery. PLoS One 2015;10:e0123858.
16 Lip GYH, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: The euro heart survey on atrial fibrillation. Chest 2010;137:263–72.
17 Li YG, Pastori D, Farcomeni A, et al. A simple clinical risk score (C 2 HEST) for predicting incident atrial fibrillation in Asian subjects: Derivation in 471,446 Chinese subjects, with internal validation and external application in 451,199 Korean subjects. Chest 2019;155:510–8.
18 Guo Y, Wang H, Zhang H, et al. Population-based screening or targeted screening based on initial clinical risk assessment for atrial fibrillation: A report from the Huawei Heart Study. J Clin Med 2020;9:1493.
19 Collins GS, Reitsma JB, Altman DG, et al. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement. BMJ 2015;350:g7594.
20 Schmidt M, Maeng M, Madsen M, et al. The Western Denmark Heart Registry: Its influence on cardiovascular patient care. J Am Coll Cardiol 2018;71:1259–72.
21 Rasmussen LA, Bøtker HE, Jensen LO, et al. Quality assurance of the Western Denmark Heart Registry, a population-based healthcare register. Dan Med J 2017;64:A5414.
22 Munkholm SB, Jakobsen C-J, Mortensen PE, et al. Validation of postoperative atrial fibrillation in the Western Denmark Heart Registry. Dan Med J 2015;62:A5162.
23 Wallach Kildemoes H, Toft Sørensen H, Hallas J. The Danish National Prescription Registry. Scand J 2011;39:38–41.
24 DeLong E, DeLong D, Clarke-Pearson D. Comparing the areas under two or more correlated receiver operating characteristic curves: A nonparametric approach. Biometrics 1988;44:837–45.
25 Almassi GH, Pecsi SA, Collins JF, et al. Predictors and impact of postoperative atrial fibrillation on patients' outcomes: A report from the Randomized On Versus Off Bypass trial. J Thorac Cardiovasc Surg 2012;143:93–102.
26 Yamashita K, Hu N, Ranjan R, et al. Clinical risk factors for postoperative atrial fibrillation among patients after cardiac surgery. Thorac Cardiovasc Surg 2019;67:107–16.
27 Burgos LM, Seoane L, Parodi JB, et al. Postoperative atrial fibrillation is associated with higher scores on predictive indices. J Thorac Cardiovasc Surg 2019;157;2279-8.
28 Cameron MJ, Tran DTT, Abboud J, et al. Prospective external validation of three preoperative risk scores for prediction of new onset atrial fibrillation after cardiac surgery. Anesth Analg 2018;126:33–8.
29 Lip GYHH, Skjøth F, Nielsen PBB, et al. Evaluation of the C_2HEST risk score as a possible opportunistic screening tool for incident atrial fibrillation in a healthy population (from a nationwide Danish Cohort study). Am J Cardiol 2020;125:48–54.
30 Ahlsson A, Fengsrud E, Bodin L, et al. Postoperative atrial fibrillation in patients undergoing aortocoronary bypass surgery carries an eightfold risk of future atrial fibrillation and a doubled cardiovascular mortality. Eur J Cardiothorac Surg 2010;37:1353–9.
31 Caldonazo T, Kirov H, Rahouma M, et al. Atrial fibrillation after cardiac surgery: A systematic review and meta-analysis [e-pub ahead of print]. J Thorac Cardiovasc Surg 2021. https://doi.org/10.1016/j.jtcvs.2021.03.077. Accessed 6/5/2021.
32 Zhang W, Liu W, Chew STH, et al. A clinical prediction model for postcardiac surgery atrial fibrillation in an Asian population. Anesth Analg 2016;123(2):283–9.
33 Woldendorp K, Farag J, Khadra S, et al. Postoperative atrial fibrillation after cardiac surgery: A meta-analysis. Ann Thorac Surg 2021;112:2084–93.
34 Chamberlain AM, Agarwal SK, Folsom AR, et al. A clinical risk score for atrial fibrillation in a biracial prospective cohort (from the Atherosclerosis Risk in Communities [ARIC] study). Am J Cardiol 2011;107:85–91.
35 Schnabel RB, Sullivan LM, Levy D, et al. Development of a risk score for atrial fibrillation (Framingham Heart Study): A community-based cohort study. Lancet 2009;373:739–45.
36 Aronson D, Shalev V, Katz R, et al. Risk score for prediction of 10-Year atrial fibrillation: A community-based study. Thromb Haemost 2018; 118:1556–63.
37 Sundbøll J, Adelborg K, Munch T, et al. Positive predictive value of cardiovascular diagnoses in the Danish National Patient Registry: A validation study. BMJ Open 2016;6:e012832.