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C_2HEST and CHA_2DS_2-Vasc for predicting recurrence after catheter ablation of paroxysmal atrial fibrillation

Aim	The C_2HEST score was developed mainly for predicting atrial fibrillation (AF) in cryptogenic stroke. This study investigated the performance of the C_2HEST score in predicting AF recurrence after radiofrequency catheter ablation (RFCA).
Material and methods	189 patients with paroxysmal AF were included in the study. AF recurrence and AF-free survival during follow-up was analyzed. The Cox proportional-hazards model was used to identify independent predictors of AF recurrence after RFCA. Receiver operating characteristic curve analysis and the Hanley and McNeil method were performed to evaluate the performances of the C_2HEST and CHA_2DS_2-VASc scores in predicting AF. AF-free periods of the with C_2HEST<2 and C_2HEST >2 were compared using Kaplan-Mayer analysis and a log-rank test.
Results	The AF recurrence rate within 3–12 months after RFCA was 17.5%. C_2HEST score >2, hypertension, left atrial (LA) diameter, and LA volume were independent predictors for AF recurrence ($p<0.05$). The C_2HEST score had better discriminatory performance in predicting AF recurrence than CHA_2DS_2-VASc (area under curve: 0.769 vs 0.644; $p=0.021$). The patients with a C_2HEST score >2 had a significantly shorter AF-free period compared those with a C_2HEST SCORE <2 ($p<0.001$).
Conclusion	In patients who underwent a RFCA procedure due paroxysmal AF, LA diameter and volume and the C_2HEST score were independent predictors of AF recurrence. C_2HEST is a simple clinical score, and it can be the readily performed to identify the risk of AF recurrence. The C_2HEST score has greater diagnostic power than the CHA_2DS_2-VASc score.

Keywords	C_2HEST score; atrial fibrillation recurrence; CHA_2DS_2-VASc score; radiofrequency catheter ablation; pulmonary vein isolation
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Introduction

One of the most common cardiac arrhythmias in the general population is atrial fibrillation (AF), with a prevalence of approximately 2% suffering from this condition [1]. It is one of the leading causes of thromboembolism, heart failure, cardiovascular disease, and death worldwide [2]. With the predisposing factors, including advanced age, hypertension, heart failure, coronary artery disease, and chronic obstructive pulmonary disease (COPD), the incidence of AF increases significantly [3]. Catheter ablation (CA) has recently become one of the most widely used treatments for rhythm control in symptomatic AF that has failed to respond to antiarrhythmic medications [4]. Nevertheless, even after catheter ablation, AF recurrence rates as high as 20% to 45% have been reported [5]. In previous studies, factors such as the left atrial (LA) volume, QT interval, advanced age, smoking, and non-paroxysmal AF were found to be associated with a higher risk of AF recurrence after CA [6, 7].

The C_2HEST score [C2, coronary artery disease/COPD (1 point each); H, hypertension (1 point); E, elderly (age ≥75, 2 points); S, systolic heart failure (HF) (2 points); T, thyroid disease (hyperthyroidism) (1 point)] is a clinical score validated for predicting AF in the general population [3]. The C_2HEST score has been shown to outperform the CHA_2DS_2-VASc and Framingham risk scores in determining the incidence of AF in post-ischemic stroke patients [8].

Although a previous study showed that the C_2HEST score predicted the recurrence of AF in cryoablation patients, no data are available for the more commonly used radiofrequency catheter ablation (RFCA) [9]. The aim of the study was to investigate whether the C_2HEST score can predict the recurrence of AF after RFCA.

Material and methods

Study Population

This retrospective cohort study was conducted at a single center. 347 patients underwent RFCA for AF between April 2018 and May 2020. All patients were symptomatic and had not responded to beta-blockers or antiarrhythmic drugs (AAD). Patients with persistent AF, moderate-to-severe

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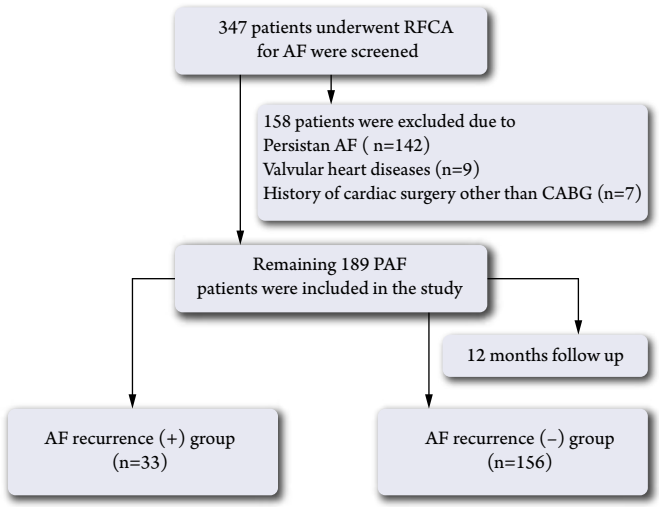
valvular heart disease or a history of cardiac surgery other than coronary artery bypass grafting were excluded from the study. Two or more episodes of intermittent AF lasting fewer than seven days during the last 12 mos and ending spontaneously were defined as paroxysmal AF. This study defined persistent AF as the occurrence of an episode of AF lasting over 7 days that required cardioversion to restore sinus rhythm. 189 patients were eligible for the study after the exclusion criteria were applied (Figure 1).

Figure 1. Study flowchart



RFCA: Radiofrequency catheter ablation, AF: atrial fibrillation, PAF: paroxysmal atrial fibrillation, CABG: coronary' artery bypass grafting

Data Collection, Calculation of CHA_2DS_2-VASc and C_2HEST Scores

The patients' clinical, demographic, and laboratory data were recorded. Patients with signs and symptoms of HF were considered to be HF positive. Patients with an ejection fraction of less than 40% by the Simpson method were considered to have systolic HF. Patients who had a brachial blood pressure >140/90 mmHg at least twice during hospitalization or who were treated with antihypertensive medications were considered hypertensive. Patients who received antidiabetic therapy or whose fasting blood glucose was >126 mg/dl during hospitalization were defined as diabetic. A history of peripheral arterial disease, previous myocardial infarction, or presence of aortic plaque were considered to have a vascular disease. Patients with a history of coronary revascularization or an invasive coronary angiogram showing >50% stenosis in at least two major epicardial arteries were considered to have coronary artery disease. Patients who were diagnosed with COPD and had started medical treatment by pulmonologists were considered COPD positive. Patients who were evaluated as hyperthyroid when calculating the C_2HEST score included those who previously had hyperthyroidism but had become euthyroid with pre-procedural treatment.

Echocardiography

A transthoracic echocardiogram was performed within one week before the ablation procedure by two clinicians using a Vivid-6 system (Vivid S6; GE Healthcare, Horten, Norway) with a 3.6-MHz probe. All the patients were in sinus rhythm during the procedures. The Bland-Altman analysis showed that the agreement between the measurements of the two clinicians (inter-observer agreement) performing echocardiography was very good (r: 0.995 CI: 0.0991–0.997, p<0.01). Echocardiographic measurements were performed according to the expert consensus document of the European Association of Cardiovascular Imaging [10].

RFCA Procedure

All RFCA procedures were performed by a single operator. Before the procedure, all patients were informed about the ablation procedure in detail, and all provided written informed consent. Transesophageal echocardiography was performed within 24 hr before the procedure to determine the structure of the interatrial septum and to rule out the presence of a potential LA thrombus. During the periprocedural period, neither NOACs nor oral vitamin K antagonists were discontinued, except for an INR value greater than three in patients treated with oral vitamin K antagonists. To achieve sedation during the ablation procedure, midazolam and fentanyl were administered.

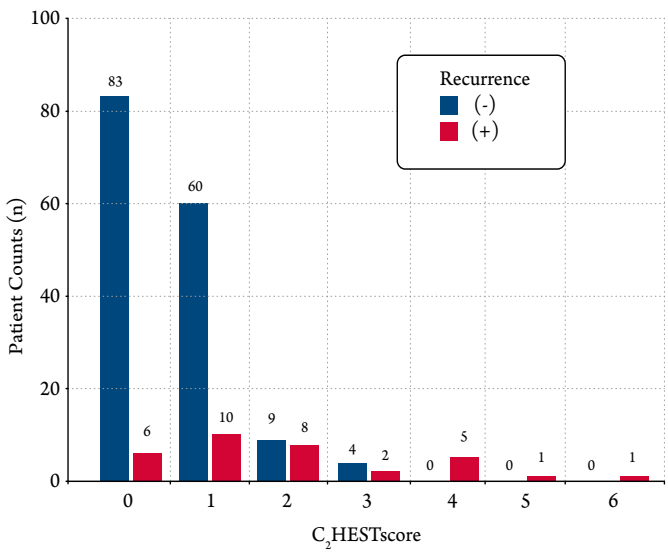
Regarding the ablation procedure: First, a decapolar catheter was placed into the coronary sinus via the left femoral venous access. The double transseptal puncture catheterization was performed under fluoroscopic guidance. A bolus of unfractionated heparin (UFH) was administered immediately after the transseptal puncture, and the infusion was titrated to maintain an activated clotting time (ACT) of 300–350 sec throughout the procedure. The ACT was measured every 45 min. The esophagus was not monitored during the ablation procedure. The duration of the procedure, from femoral vein puncture to sheath removal, and the fluoroscopy duration were recorded for each case. A LASSO® circumferential mapping catheter (CMC) (Biosense Webster, Irvine, CA 92618 USA) was inserted into the LA with an 8.5 Fr SL1 sheath. Subsequently, a Thermocol® SmartTouch® contact force (CF) sensing, ablation catheter (Biosense Webster) was advanced into the LA simultaneously with the CMC using a second 8.5 Fr SL1-long sheath. Reconstruction and mapping of pulmonary veins (PVs) and LA were performed through the CMC and the ablation catheter using the CARTO® Mapping System (Biosense Webster, Inc). The ablation strategy consisted of pulmonary vein (PV) isolation (PVI), defined by creating

large circumferential radiofrequency lesions (RF) around both ipsilateral PVs with verification of complete isolation. The circumferential lesions were generated at the level of the PV–LA junctions, i.e., the PV antrum, using the point-by-point technique. 35–40 W power (flow rate, 17–20 ml/min) was used until there is an initial impedance reduction>10 ohm. As necessary, a lower power of 25–30 W (flow rate, 17 ml/min) and time settings were used to avoid damage to the esophagus and the formation of vapor bubbles on the posterior LA wall and roof area. CF data were displayed to the operator during the procedure. RF energy was delivered with a target CF of 10–40 g until a bipolar signal reduction of at least 70% was achieved. Successful PVI was defined as the recording of both the entry and exit block (bidirectional block) for the four PVs after the ablation procedure. RF energy was delivered in the earliest potential recorded in the carina between the superior and inferior PVs when the bidirectional block was not achieved with antral isolation. At the end of the procedure, a waiting period of at least 20 min was observed to evaluate the LA-PV connections, and then the bidirectional block was reevaluated.

Follow-up after RFCA

After discharge, patients were followed up in the outpatient clinic every 2 wks for the first 3 mos if no symptoms, and care was taken to send a new ECG recording by telephone or by direct contact in the outpatient clinic after the procedure. After the blanking period, patients were asked to call to report any symptoms. When symptoms persisted, the ECG recordings were examined by telephone or, in some cases, directly in the clinic. During first three months following ablation, known as the blanking period, anti-arrhythmic drugs (AADs: propafenone, amiodarone, sotalol or flecainide) was used to prevent early recurrences. If symptomatic recurrence occurred after the blanking period, ablation was repeated. In some asymptomatic patients, AADs were resumed and assessed every three months or when symptoms reappeared. A 24-hour Holter ECG recording was performed at each three-month clinic visit. Holter monitoring was extended to 48 hr in evident symptomatic patients. A recurrence AF was defined as an AF episode of ≥30 sec duration during the Holter recording.

Figure 2. The distribution of patients according to the C_2HEST score



Statistical Analysis

Continuous variables with normal distribution according to the Kolmogorov-Smirnov test are expressed as mean+standard deviation (SD) values, and those that did not have a normal distribution are expressed as median and 25^{th}-75^{th} quartiles. Categorical variables were expressed as numbers (n) and percentages (%). The variables were compared between two groups (recurrence/no recurrence) using the Chi-square test, Mann-Whitney U-test, and the Independent Samples t-test. Multivariate Cox regression analysis was conducted to identify independent predictors of AF recurrence after ablation. The variables determined as statistically significant in the univariable analysis were used in a multivariable analysis.

The diagnostic significance of the C_2HEST and CHA_2DS_2VASc scores for predicting AF recurrence was assessed by receiver operating characteristic (ROC) curve analysis. The Cox proportional-hazards model was used to identify independent predictors of AF recurrence after RFCA. Which C_2HEST score to use as the threshold value in the Kaplan-Mayer and regression analysis was decided according to the ROC curve analysis. Accordingly, the threshold value with the optimal sensitivity and specificity values was selected. The ROC curves of the two scores were statistically compared using the Hanley and McNeil method [11]. Kaplan-Meier survival analysis and the log-rank test were used to compare the AF-free periods at different C_2HEST scores (<2 and≥2). The Bland-Altman test was conducted in 30 randomly selected patients to analyze correlations between clinicians' transthoracic echocardiographic measurements. The results were considered significant at $p<0.05$. The Hanley and McNeil method and the Bland-Altman test were conducted using MedCalc statistical software (MedCalc Software Ltd, Ostend, Belgium). The other analyses were conducted using IBM® SPSS® vr. 25.0 software (International Business Machines Corporation, Armonk, NY, USA).

Results

The study incorporated 189 patients, 45.5% males and 54.5% females, with a mean age of 59.81+10.25 yrs, and a follow-up period of 12 mos post-operatively. All patients

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ПОВЫШЕННОЕ СОДЕРЖАНИЕ ТРИГЛИЦЕРИДОВ В КРОВИ – НЕЗАВИСИМЫЙ ФАКТОР РИСКА СЕРДЕЧНО-СОСУДИСТОЙ И ОБЩЕЙ СМЕРТНОСТИ[1]

ДИАГНОСТИКА ДИСЛИПИДЕМИИ:

Всем лицам старше 40 лет рекомендуется скрининг, включающий анализ крови по оценке нарушений липидного обмена биохимический (липидный профиль) с целью стратификации сердечно-сосудистого риска по шкале SCORE-2

Определение ХС не-ЛВП рекомендовано всем пациентам для дополнительной оценки риска в системе SCORE-2

Пациентам любой категории риска рекомендован целевой уровень

ТГ 1,7 ммоль/л

Класс	Уровень
IIa	C

АЛГОРИТМ ТЕРАПИИ ГИПЕРТРИГЛИЦЕРИДЕМИИ

Категория пациентов	Высокого и очень высокого риска, достигшим на терапии статинами уровня ТГ 1,7–2,3 ммоль/л	С уровнем ТГ > 2,3 ммоль/л на терапии статинами	С уровнем ТГ > 5,0 ммоль/л
Рекомендация	+ Лекарственный препарат ПНЖК **ОМЕГА-3** доза: до 2 грамм 2 раза в день	**ФЕНОФИБРАТ** / **ФЕНОФИБРАТ + СТАТИН** предпочтительно в одной таблетке* **ИЛИ** + Лекарственный препарат ПНЖК **ОМЕГА-3** доза: до 2 г 2 раза в день	**ФЕНОФИБРАТ** **И** + Лекарственный препарат ПНЖК **ОМЕГА-3** доза: до 2 г 2 раза в день
Класс	IIa	IIa	IIa
Уровень	B	B	B

Достижение и удержание целевого уровня ХС ЛНП, ТГ является ключевым фактором, влияющим на прогноз и улучшающим сердечно-сосудистые исходы у пациентов как с ССЗ, так и СД

ВАЖНЫМИ ЦЕЛЯМИ ПРИ ЛЕЧЕНИИ ДИСЛИПИДЕМИИ ЯВЛЯЮТСЯ:

- максимальное снижение риска развития ССО и смертельных исходов;
- коррекция всех модифицируемых факторов риска (курение, избыточная масса тела, ожирение, гипергликемия, АГ).

1. Nordestgaard B. G. (2016). Triglyceride-Rich Lipoproteins and Atherosclerotic Cardiovascular Disease: New Insights From Epidemiology, Genetics, and Biology. Circulation research, 118(4), 547–563. https://doi.org/10.1161/CIRCRESAHA.115.306249. * Зарегистрирован розувастатин+фенофибрат; ЦУ – целевой уровень; ТГ – триглицериды; ХС ЛНП – холестерин липопротеинов низкой плотности; ХС не-ЛНП – холестерин липопротеинов невысокой плотности; ПНЖК – полиненасыщенные жирные кислоты; СД – сахарный диабет; ССО - сердечно-сосудистые осложнения; АГ - артериальная гипертензия.
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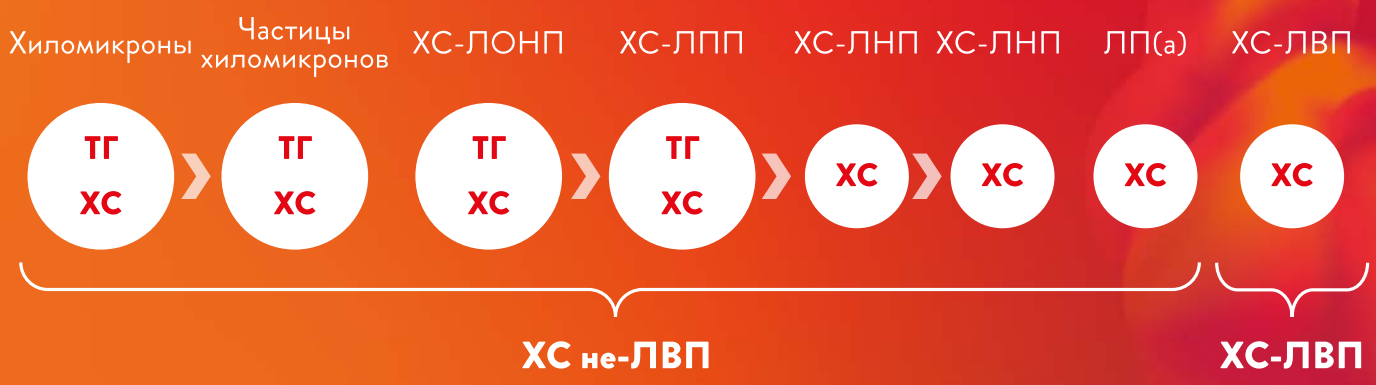
Информация предоставлена исключительно для медицинских и фармацевтических работников

RUS2274693 (v1.2)

ХОЛЕСТЕРИН НЕ-ЛВП — МИШЕНЬ ДЛЯ СНИЖЕНИЯ СЕРДЕЧНО-СОСУДИСТОГО РИСКА[1]

ХС не-ЛВП включает в себя все атерогенные классы липопротеинов[1]



ДЛЯ СНИЖЕНИЯ УРОВНЯ ХС НЕ-ЛВП ТРЕБУЕТСЯ КОНТРОЛЬ ВСЕХ АТЕРОГЕННЫХ ЧАСТИЦ

Целевые значения ХС не-ЛВП для пациентов с различным уровнем сердечно-сосудистого риска[2]

Основа SCORE-2

ХС не-ЛВП		
< 2,6 ммоль/л	< 2,2 ммоль/л	< 1,8 ммоль/л
желателен для лиц с высоким риском	у лиц с очень высоким риском	для лиц с экстремально высоким риском

Оценка ХС не-ЛВП не требует дополнительных затрат

Формула определения ХС не-ЛВП

Холестерин Не-ЛВП = ОХС - ХС-ЛВП

ХС не-ЛВП — достоверный индикатор сердечно-сосудистой смертности у пациентов:

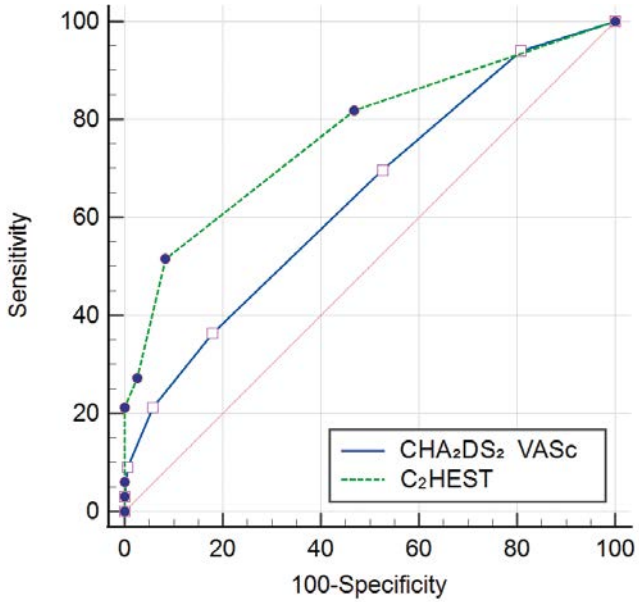
- с ожирением и метаболическим синдромом
- с ССЗ (ИБС, перенесенный инфаркт миокарда)
- с СД 2-го типа
- с гипертриглицеридемией
- с низким уровнем ХС-ЛНП

ХС — холестерин, ТГ — триглицериды; ХС-ЛОНП — холестерин липопротеинов очень низкой плотности; ХС-ЛПП (холестерин липопротеинов промежуточной плотности); ЛП (а) — липопротеин (а); ХС-ЛНП — (холестерин липопротеинов низкой плотности); ХС-ЛВП — холестерин липопротеинов высокой плотности; ССЗ — сердечно-сосудистые заболевания, ИБС — ишемическая болезнь сердца; СД — сахарный диабет.

1. Langlois, Michel R., et al. «Quantifying atherogenic lipoproteins: current and future challenges in the era of personalized medicine and very low concentrations of LDL cholesterol. A consensus statement from EAS and EFLM.» Clinical chemistry 64.7 (2018): 1006-1033. 2. Клинические рекомендации МЗ РФ Нарушения липидного обмена 2023 г. Рубрикатор КР (minzdrav.gov.ru) Дата доступа: 31.05.2023.

RUS2280609 (v1.1)

Figure 3. TROC curve analysis for C_2HEST and CHA_2DS_2-VASc



underwent a technically successful procedure. 33 patients (17.5%) had AF recurrence after the blanking period. The recurrence rates according to the C_2HEST score were as follows: 6.7% with score 0, 14.3% with score 1, 47.1% with score 2, 33.3% with score 3, 100% with score 4, 5, or 6. The distribution of patients based on score is illustrated in Figure 2.

Anti-arrhythmic medications used during the blanking period included propafenone (63%), amiodarone (23.3%), sotalol (10.6%), and flecainide (3.2%). No significant difference was found between the AF recurrence (+) and the AF recurrence (-) groups regarding the use of antiarrhythmic drugs (p=0.504). The rates of diabetes and hypertension were significantly higher in AF recurrence (+) patients (p<0.05). The C_2HEST and other clinical risk scores (CHA_2DS_2-VASc, HAS-BLED) were higher in AF recurrence (+) patients (p<0.05). Table 1 summarizes the clinical and demographic characteristics of the patients.

Patients with AF recurrence (+) had significantly shorter mean procedure times (p=0.027). Bland-Altman analysis revealed a strong correlation between the measurements made by the two clinicians performing the echocardiography (r=0.995 CI:0.0991–0.997, p<0.01). LA diameter, LA volume index, and E/e' ratio were significantly higher in the AF recurrence (+) group (p<0.001). The echocardiographic and laboratory findings of the subjects are shown in Table 2.

The ROC curve analysis indicated that the C_2HEST score has good diagnostic power for predicting AF recurrence, with an area under the curve (AUC) of 0.76 (95% CI:0.670–0.868; p<0.001). The C_2HEST score had a significantly better predictive value than the CHA_2DS_2-VASc score (0.769 vs 0.644; p=0.021) (Figure

Table 1. Demographic and clinical characteristics of the patients according to AF recurrence

Variable	AF recurrence (-)	AF recurrence (+)	p value
Age	59.43+10.11	61.64+10.87	0.262
Male	71 (45.5)	18 (54.5)	0.345
BMI	28.67+4.37	29.75+5.23	0.220
Hypertension	44 (28.2)	17 (51.5)	0.009
Diabetes	35 (22.4)	13 (39.4)	0.042
CAD	31 (19.9)	11 (33.3)	0.091
Smoking	46 (29.5)	8 (24.2)	0.545
COPD	6 (3.8)	4 (12.1)	0.054
Hyperthyroidism	8 (5.1)	3 (9.1)	0.377
Stroke	5 (3.2)	3 (9.1)	0.127
Beta blocker	120 (76.9)	26 (78.8)	0.816
CCB	37 (23.7)	9 (27.3)	0.666
ACE inh/ARB	65 (41.7)	16 (48.5)	0.509
Antiarrhythmic drug	124 (79.5)	26 (78.8)	0.928
SHF	9 (5.8)	4 (12.1)	0.190
CHA_2DS_2-VASc	2 (1-2)	2 (1-3)	0.007
HAS-BLED	1 (0-1)	1 (1-2)	<0.001
C_2HEST	0 (0-1)	2 (1-3)	0.004

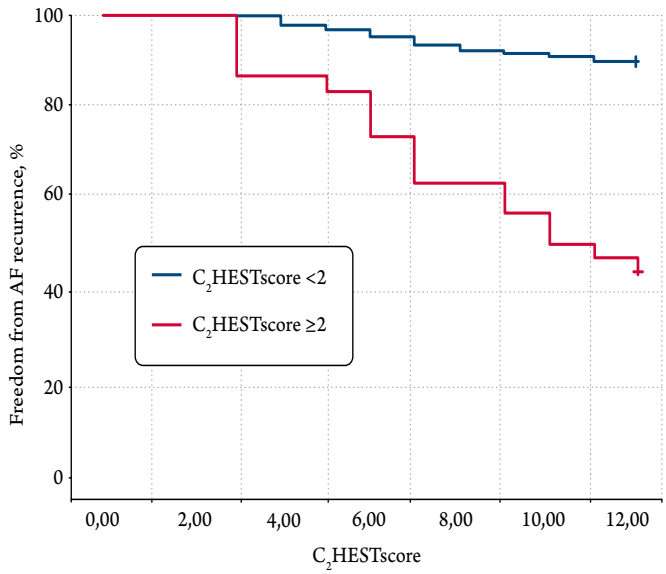
Data are mean+SD, number (percent), or median (25^{th}–75^{th} quartiles). ACE inh, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CAD, coronary artery disease; CCB, calcium channel blocker; COPD, chronic obstructive pulmonary disease; SHF. systolic heart failure.

Table 2. Laboratory and echocardiographic findings of the patients according to AF recurrence

Variable	AF recurrence (-)	AF recurrence (+)	p value
Procedure time (min)	115.02+37.23	99.03+38.59	0.027
White blood cells ($\times 10^9$/l)	7.74+1.81	7.56+1.72	0.611
Lymphocytes ($\times 10^9$/l)	2.32+0.74	2.27+0.59	0.728
Neutrophils ($\times 10^9$/l)	4.64+1.35	4.53+1.24	0.673
Hemoglobin (gr/dl)	14.69+1.12	13.61+1.33	0.583
LDL (mg/dl)	110.65+35.05	106.98+33.31	0.587
Triglyceride (mg/dl)	149.59+66.67	166.88+73.91	0.191
HDL (mg/dl)	45.06+9.857	46.47+10.908	0.469
Creatinine (mg/dl)	0.96+0.30	0.92+0.22	0.551
TSH (mIU/l)	1.76+1.27	1.38+1.01	0.120
LVEF (%)	52.34+6.41	51.13+6.36	0.327
LA diameter (mm)	40.63+2.48	44.58+4.25	<0.001
LAVI (ml/m^2)	24.99+3.58	28.79+4.28	<0.001
E/e´ ratio	9.71+2.56	12.31+3.50	<0.001
LVEDV (ml)	103.70+17.37	105.21+17.30	0.651
LVESV (ml)	50.14+14.54	52.30+15.28	0.444

Data are mean+SD, HDL: high-density lipoprotein, LAVI: Left atrium volume index, LDL: Low-density lipoprotein, LVEDV: Left ventricular end-diastolic volume, LVEF: Left ventricular ejection fraction, LVESV: Left ventricular end-systolic volume, TSH: Thyroid-stimulating hormone.

Figure 4. Kaplan-Meier curve for the rates of freedom from AF recurrence C_2HEST by score equal to 2 and higher



3). With a score of ≥2 for C_2HEST, the sensitivity of the test decreased to 51.5% and specificity increased to 91.6%. CHA_2DS_2-VASc ≥2 score had a sensitivity of 69.7% and specificity of 47.4% in the ROC curve analysis. The Kaplan-Mayer analysis revealed that patients with a C_2HEST score >2 had a significantly shorter AF free period than those with a C_2HEST score of 0 or 1 (mean months: 9.10 vs 11.49; log-rank p <0.001) (Figure 4).

Univariate Cox regression analysis revealed that hypertension, C_2HEST score >2, LA diameter, LA volume index, and shorter procedure time was significantly correlated with AF recurrence. In the multivariate analysis, C_2HEST score>2, hypertension, LA diameter, and LA volume index remained independent predictors of AF recurrence (Table 3).

Table 3. Cox regression analysis to determine predictors of AF recurrence

Univariate Analysis			
Variable	**HR**	**95 % CI**	**p value**
Diabetes	1.479	0.726-3.013	0.282
Hypertension	2.453	1.157-5.200	0.019
COPD	0.570	0.194-1.669	0.305
CAD	1.514	0.726-3.160	0.269
C2HEST score >2	7.358	3.706-14.608	<0.001
CHA_2DS_2-VASc >2	1.967	0.936-4.132	0.074
Left atrial diameter	1.346	1.233-1.470	<0.001
LAVI	1.269	1.154-1.394	<0.001
Procedure time	0.987	0.975-0.999	0.034
E/e'	0.983	0.886-1.090	0.740
Multivariate Analysis			
Variables	**HR**	**95%CI**	**p value**
Hypertension	2.783	1.362-5.685	0.005
Procedure time	1.003	0.991-1.016	0.579
C_2HEST score >2	3.792	1.784-8.062	0.001
Left atrial diameter	1.324	1.193-1.468	<0.001
LAVI	1.164	1.055-1.284	0.002

CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, LAVI: Left atrium volume index.

Discussion

Based on current results, patients who underwent RFCA for paroxysmal AF experienced a 17.5% recurrence rate after a blanking period of 3–12 mos. According to ROC curve analysis, the C_2HEST score was significantly more effective in predicting AF recurrence after RFCA than the CHA_2DS_2-VASc score.

In a study of 1188 patients, Gaztanaga et al. reported an AF recurrence rate of 30.5% within 3–12 mos after CA [12]. In the CABANA study, AF recurrence rate within 3–12 mos after CA was 36.4% [13]. It is important to highlight the main factors contributing to the lower recurrence rate of AF observed in our study. First, in previous studies, patients with long-standing AF as well as those with paroxysmal AF were included, while in the present study, only the cases of paroxysmal AF were included into the analysis. A higher rate of AF recurrence after PVI has been reported in persistent and long-standing AF than in paroxysmal AF [14]. Second, in both the studies of Gaztanaga et al and the CABANA group, transtelephonic electrocardiographic monitoring (TTM) was preferred to detect recurrent AF in the follow-up after CA, which may facilitate detecting AF at an earlier stages. CABANA used 24-hr Holter recording with TTM, Gaztanaga et al used TTM.

Several scores have been previously studied for predicting recurrences after ablation. The CHADS2 and CHA_2DS_2-VASc scores have been reported to have moderate predictive power for arrhythmias after RFCA [15]. Two scores were developed to predict the recurrence of AF after CA, the ALARMEc and APPLE scores have been shown to be superior to the $CHADS_2$ and CHA_2DS_2-VASc scores for predicting arrhythmias after CA [16, 17]. The BASE-AF2 successfully predicted rhythm outcomes after cryoablation (AUC:0.94) [18]. Another validated score, the ATLAS score, identified the risk of the developing of AF recurrence at a high accuracy rate among patients who underwent PVI [19]. In the present study, the C_2HEST score with an AUC value of 0.769, was found to be a stronger index than the CHA_2DS_2-VASc for predicting AF recurrence. As only patients with paroxysmal AF were included in the study, the C_2HEST was not applied to patients with persistent AF, unlike in other studies.

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Also the present study showed that LA diameter and LAVI can independently predict AF recurrence. In line with these findings, a metanalysis conducted by Njoku et al. demonstrated that large LA volume and LAVI increases the likelihood of AF recurrence after RFCA [7]. Likewise, another metanalysis showed that LA diameter was significantly associated with AF recurrence in patients after catheter ablation [20]. Although it is still not clear whether AF is the cause or consequence of LA dilatation, there is much evidence to support that a large LA contributes to the structural and electrical changes leading to AF [21].

Moreover, there is insufficient evidence showing a relationship between advanced age and the recurrence of AF, since the vast majority of studies of AF ablation excluded patients with advanced ages. It has been shown that COPD, another variable in the C_2HEST score, is also related to an increased incidence of recurrence of AF following catheter ablation [22]. The increased rate of AF recurrence in COPD is associated with mechanisms such as sympathetic system activation due to hypoxia, increased pulmonary artery pressure on the LA and PV, chronic inflammation, use of beta-2 agonists and steroids, and prolonged atrial depolarization [22]. Hypertension, another variable included in the score, is associated with an increased rate of recurrence of AF after CA [23]. The increased recurrence of AF in hypertensive patients was attributed to atrial remodeling as a consequence of hypertension. In cohorts of AF and HF, validated predictive risk scores for recurrent AF after catheter ablation have limited predictive capabilities [24]. In patients with concomitant HF, additional tools are needed to facilitate risk stratification and patient selection for AF ablation. Wongcharoen et al. showed a relationship between increased AF after an ablation procedure and hyperthyroidism, which is one of the variables in the C_2HEST score [25]. It has been suggested that mechanisms such as increased automaticity in PVs, shortened action potential duration, formation of non-pulmonary venous foci, and simultaneous activation of the sympathetic and parasympathetic nervous systems may be responsible for increased AF recurrence in such hyperthyroid subjects [13, 25]. In the present study, the evidence that COPD, hypertension, advanced age, low LVEF, and hyperthyroidism were associated with increased AF recurrence after RFCA might explain why the C_2HEST score was found to be an independent predictor of AF recurrence at follow-up after ablation.

Limitations

Patients with persistent AF were excluded from this study, so the role of the score in these patients is unknown. The only way to differentiate between paroxysmal and persistent AF was by clinical diagnosis. During the follow-up, no devices other than 24-hour Holter monitoring, such as TTM and internal loop recerders, were used to record the rhythm, since those facilities were unavailable. Therefore, perhaps, AF recurrence could have been detected at lower rates. Only PVI with circumferential antral RF ablation was performed; no additional ablation lines were used except for recurrences. It was not tested whether the ablation procedures reduced AF recurrence. Finally, rather than predicting recurrence rates exclusively, the study tested the validity of the C_2HEST score.

Conclusıon

In patients who underwent RFCA procedure because of paroxysmal AF, together with LA diameter and volume, the C_2HEST, a simple clinical score, identified the risk of AF recurrence. It has greater diagnostic power than the CHA_2DS_2-VASc score.

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REFERENCES

1. Wilke T, Groth A, Mueller S, Pfannkuche M, Verheyen F, Linder R et al. Incidence and prevalence of atrial fibrillation: an analysis based on 8.3 million patients. Europace. 2013;15(4):486–93. DOI: 10.1093/europace/eus333
2. Ruddox V, Sandven I, Munkhaugen J, Skattebu J, Edvardsen T, Otterstad JE. Atrial fibrillation and the risk for myocardial infarction, all-cause mortality and heart failure: A systematic review and meta-analysis. European Journal of Preventive Cardiology. 2017;24(14):1555–66. DOI: 10.1177/2047487317715769
3. Li Y-G, Pastori D, Farcomeni A, Yang P-S, Jang E, Joung B et al. A Simple Clinical Risk Score (C_2HEST) for Predicting Incident Atrial Fibrillation in Asian Subjects. Chest. 2019;155(3):510–8. DOI: 10.1016/j.chest.2018.09.011
4. Calkins H, Hindricks G, Cappato R, Kim Y-H, Saad EB, Aguinaga L et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: Executive summary. EP Europace. 2018;20(1):157–208. DOI: 10.1093/europace/eux275
5. Darby AE. Recurrent Atrial Fibrillation After Catheter Ablation: Considerations For Repeat Ablation And Strategies To Optimize Success. Journal of Atrial Fibrillation. 2016;9(1):1427. DOI: 10.4022/jafib.1427
6. Diederichsen SZ, Darkner S, Chen X, Johannessen A, Pehrson S, Hansen J et al. QT as a predictor of recurrence after atrial fibrillation ablation and the impact of amiodarone: results from the placebo-controlled AMIO-CAT trial. EP Europace. 2019;21(7):1055–62. DOI: 10.1093/europace/euz028

7. Njoku A, Kannabhiran M, Arora R, Reddy P, Gopinathannair R, Lakkireddy D et al. Left atrial volume predicts atrial fibrillation recurrence after radiofrequency ablation: a meta-analysis. EP Europace. 2018;20(1):33–42. DOI: 10.1093/europace/eux013
8. Li Y, Bisson A, Bodin A, Herbert J, Grammatico-Guillon L, Joung B et al. C 2 HEST Score and Prediction of Incident Atrial Fibrillation in Poststroke Patients: A French Nationwide Study. Journal of the American Heart Association. 2019;8(13):e012546. DOI: 10.1161/JAHA.119.012546
9. Levent F, Kanat S, Tutuncu A. Predictive Value of C_2HEST Score for Atrial Fibrillation Recurrence Following Successful Cryoballoon Pulmonary Vein Isolation in Paroxysmal Atrial Fibrillation. Angiology. 2023;74(3):273–81. DOI: 10.1177/00033197221102230
10. Galderisi M, Cosyns B, Edvardsen T, Cardim N, Delgado V, Di Salvo G et al. Standardization of adult transthoracic echocardiography reporting in agreement with recent chamber quantification, diastolic function, and heart valve disease recommendations: an expert consensus document of the European Association of Cardiovascular Imaging. European Heart Journal - Cardiovascular Imaging. 2017;18(12):1301–10. DOI: 10.1093/ehjci/jex244
11. Hanley JA, McNeil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology. 1983;148(3):839–43. DOI: 10.1148/radiology.148.3.6878708
12. Gaztañaga L, Frankel DS, Kohari M, Kondapalli L, Zado ES, Marchlinski FE. Time to recurrence of atrial fibrillation influences outcome following catheter ablation. Heart Rhythm. 2013;10(1):2–9. DOI: 10.1016/j.hrthm.2012.09.005
13. Poole JE, Bahnson TD, Monahan KH, Johnson G, Rostami H, Silverstein AP et al. Recurrence of Atrial Fibrillation After Catheter Ablation or Antiarrhythmic Drug Therapy in the CABANA Trial. Journal of the American College of Cardiology. 2020;75(25):3105–18. DOI: 10.1016/j.jacc.2020.04.065
14. Wang X, Li Z, Mao J, He B. A novel individualized substrate modification approach for the treatment of long-standing persistent atrial fibrillation: Preliminary results. International Journal of Cardiology. 2014;175(1):162–8. DOI: 10.1016/j.ijcard.2014.05.022
15. Letsas KP, Efremidis M, Giannopoulos G, Deftereos S, Lioni L, Korantzopoulos P et al. CHADS2 and CHA_2DS_2-VASc scores as predictors of left atrial ablation outcomes for paroxysmal atrial fibrillation. Europace. 2014;16(2):202–7. DOI: 10.1093/europace/eut210
16. Kornej J, Hindricks G, Shoemaker MB, Husser D, Arya A, Sommer P et al. The APPLE score: a novel and simple score for the prediction of rhythm outcomes after catheter ablation of atrial fibrillation. Clinical Research in Cardiology. 2015;104(10):871–6. DOI: 10.1007/s00392-015-0856-x
17. Wójcik M, Berkowitsch A, Greiss H, Zaltsberg S, Pajitnev D, Deubner N et al. Repeated catheter ablation of atrial fibrillation: how to predict outcome? Circulation Journal. 2013;77(9):2271–9. DOI: 10.1253/circj.cj-13-0308
18. Canpolat U, Aytemir K, Yorgun H, Şahiner L, Kaya EB, Oto A. A proposal for a new scoring system in the prediction of catheter ablation outcomes: Promising results from the Turkish Cryoablation Registry. International Journal of Cardiology. 2013;169(3):201–6. DOI: 10.1016/j.ijcard.2013.08.097
19. Mesquita J, Ferreira AM, Cavaco D, Moscoso Costa F, Carmo P, Marques H et al. Development and validation of a risk score for predicting atrial fibrillation recurrence after a first catheter ablation procedure – ATLAS score. EP Europace. 2018;20(FI_3):f428–35. DOI: 10.1093/europace/eux265
20. Jin X, Pan J, Wu H, Xu D. Are left ventricular ejection fraction and left atrial diameter related to atrial fibrillation recurrence after catheter ablation?: A meta-analysis. Medicine. 2018;97(20):e10822. DOI: 10.1097/MD.0000000000010822
21. Krummen DE, Swarup V, Narayan SM. The role of rotors in atrial fibrillation. Journal of Thoracic Disease. 2015;7(2):142–51. DOI: 10.3978/j.issn.2072-1439.2014.11.15
22. Gu J, Liu X, Tan H, Zhou L, Jiang W, Wang Y et al. Impact of Chronic Obstructive Pulmonary Disease on Procedural Outcomes and Quality of Life in Patients with Atrial Fibrillation Undergoing Catheter Ablation. Journal of Cardiovascular Electrophysiology. 2013;24(2):148–54. DOI: 10.1111/j.1540-8167.2012.02448.x
23. Han J, Li G, Zhang D, Wang X, Guo X. Predicting Late Recurrence of Atrial Fibrillation After Radiofrequency Ablation in Patients With Atrial Fibrillation: Comparison of C_2HEST and HATCH Scores. Frontiers in Cardiovascular Medicine. 2022;9:907817. DOI: 10.3389/fcvm.2022.907817
24. Black-Maier E, Parish A, Steinberg BA, Green CL, Loring Z, Barnett AS et al. Predicting atrial fibrillation recurrence after ablation in patients with heart failure: Validity of the APPLE and CAAP-AF risk scoring systems. Pacing and Clinical Electrophysiology. 2019;42(11):1440–7. DOI: 10.1111/pace.13805
25. Wongcharoen W, Lin Y-J, Chang S-L, Lo L-W, Hu Y-F, Chung F-P et al. History of hyperthyroidism and long-term outcome of catheter ablation of drug-refractory atrial fibrillation. Heart Rhythm. 2015;12(9):1956–62. DOI: 10.1016/j.hrthm.2015.06.004

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