Comprehensive approach to atrial fibrillation in primary care

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Abstract

Introduction: Integrated care has been proposed as a solution to the growing disease burden of atrial fibrillation

Objective: To assess whether integrated care of AF organized in primary care is not inferior to usual care.

Methods: A pragmatic, open-label, cluster-randomized, noninferiority study was conducted in 26 primary care practices.

Results: the reduction in the risk of noncardiovascular mortality was more pronounced than the reduction in the risk of cardiovascular mortality [adjusted HR for noncardiovascular mortality 0.47 (95% CI 0.27-0.82).

Conclusions: All-cause mortality was reduced by providing integrated care for the elderly with AF in primary care compared to usual care.

Keywords: atrial fibrillation, mortality, primary care, elderly

Source: DeCS

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Resumen

Introducción: La atención integrada se ha propuesto como una solución para la creciente carga de morbilidad de la fibrilación auricular

Objetivo: Evaluar si la atención integrada de la FA organizada en atención primaria no es inferior a la atención habitual.

Método: Se realizó un estudio de no inferioridad pragmático, abierto, aleatorizado por grupos realizado en 26 prácticas de atención primaria.

Resultados: la reducción del riesgo de mortalidad no cardiovascular fue más pronunciada que la reducción del riesgo de mortalidad cardiovascular [CR ajustado para mortalidad no cardiovascular 0,47 (IC 95% 0,27-0,82

Conclusiones: Se redujo la mortalidad por todas las causas al brindar atención integrada a los ancianos con FA en la atención primaria, en comparación con la atención habitual.

Palabras clave: fibrilación auricular, mortalidad, atención primaria, ancianos

Fuente: DeCS

Introduction

Embedded care has been proposed as a solution to the growing disease burden of atrial fibrillation (AF) and is recommended in the 2016 European Society of Cardiology (ESC) guidelines on the management of AF (Class IIa recommendation, level of evidence B)[1]. The rationale for the incorporated care is founded on the criticism that AF is not simply a secluded heart rhythm disorder with a greater danger of cerebrovascular mishap but rather, generally, a "hypercoagulable state" caused by (or associated with) the existence of various underlying and interacting comorbidities[2]. Consequently, especially for elderly patients with AF, management is evolving toward more integrated care that also includes the management of comorbidities.

A meta-analysis of studies investigating integrated care coordinated by tertiary care hospitals showed a reduction in all-cause mortality and cardiovascular hospitalization[3]. More recently, the RACE 4 trial confirmed that nurse-led integrated care reduced cardiac mortality and hospitalization, but only when provided in clinics with AF expertise[4]. Thus, it remains unknown whether such integrated care could be safely orchestrated in primary care, a setting characterized by nonspecialist physicians and nurses and AF patients who are often older, frailer, and with multimorbidity. Nevertheless, when proven safe, integrated AF care in primary care may be instrumental in controlling the increasing prevalence of AF and the associated burden and mortality, especially among the elderly[5,6].

Therefore, the study aimed to assess whether integrated AF care organized in primary care is not inferior to the usual care performed by cardiologists and anticoagulation clinics.

Method

A pragmatic, open-label, cluster-randomized, noninferiority study was conducted in primary care practices characterized by small teams with one or more general practitioners (GPs); 26 practices were randomized: 15 to the integrated care intervention and 11 to usual care in the city of Ambato. This study was approved by the Universidad Regional Autónoma de Los Andes (UNIANDES).

Given the uncertainty as to whether primary care could safely orchestrate such integrated care, it aimed to demonstrate that AF treatment in primary care was at least as safe and effective as current care provided (primarily) in secondary care. Therefore, this study was designed as a noninferiority study for the primary outcome of all-cause mortality[21].

After randomization, all patients within the participating practices with documented AF and older than 65 years were screened at the practices for eligibility using their electronic medical records. The following exclusion criteria were applied: (i) the presence of an internal automatic defibrillator or cardiac resynchronization therapy device; (ii) cardioversion, cardiac ablation, or cardiac surgery <3 Months prior to inclusion or planning; (iii) past heart valve surgery; (iv) rheumatic mitral valve stenosis; (v) pulmonary vein isolation in the past or planned; (vi) being legally unable to give informed consent; (vii) a life expectancy of fewer than three months; and finally (viii) participation in another randomized AF trial.

All eligible patients from practices randomized to the intervention were informed about the purpose of the study and asked for written informed consent before the intervention: intervention rate and usual care.

The intervention consisted of three key elements: (i) quarterly AF checks by the practice nurse on symptoms and comorbidities, in particular assessment of early signs and symptoms of heart failure and also patient education, (ii) case management of anticoagulation therapy, including international normalized ratio (INR) measurements performed by the interventional practice in those treated with a vitamin K antagonist (VKA), special attention to drug compliance and renal function monitoring in patients using a non-vitamin K antagonist oral anticoagulant (VKA), and (iii) easily accessible consultation of anticoagulation clinics and cardiologists, which truly allows for "shared care and responsibility" between primary care, anticoagulation clinics and cardiology care.

All patients were followed for at least two years. The primary outcome was all-cause mortality. Secondary outcomes were cardiovascular and noncardiovascular mortality, cardiovascular and noncardiovascular hospitalization, major adverse cardiac events (MACE), stroke, major bleeding, clinically relevant nonmajor bleeding (CRNMH), health-related quality of life (HRQoL), and cost-effectiveness. For clinically relevant major and nonmajor bleeding, the International Society on Thrombosis and Hemostasis (ISTH) definitions were used[7]. HRQoL was assessed using the 12-item Short Form Health Survey (SF-12), measured at baseline and after 1-year and 2-year follow-ups[8]. The SF-12 consists of a physical health component score (PCS) and a mental health component score (CSM), ranging from 0 to 100, with higher scores indicating better HRQoL.

For mortality, SCAD, ischemic stroke, and major bleeding outcomes, we used random-effects Cox proportional hazards regression models with clusters (practices) entered as a frailty term to account for clustering and adjustment for age, sex, and FI.

The database and statistical processing of the data were performed and analyzed in the statistical program SPSS 26 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used for the results collection, presentation and interpretation.

Results

A total of 119 practices were informed about the trial, of which 26 chose to participate. Between October 2018 and January 2020, these 26 practices were randomized. Within these 26 practices, 1657 (66.6%) of 2487 AF patients were eligible for inclusion. Fifteen practices were randomized to the intervention arm, with 32 primary care physicians and 28 practice nurses. In these intervention practices, 527 (56.0%) eligible patients gave informed consent to participate in the intervention and were included in our main analyses.

The median age was 77 years. Some differences in baseline characteristics were observed between the two groups, although not consistently in favor of one of the treatment arms.

During a median follow-up time of 2.3 years in the intervention arm and 2.2 years in the control arm, 39 patients died in the intervention arm and 96 patients in the control arm (7.4% and 13.5%, respectively). The hazard ratio (HR) for all-cause mortality, after adjusting for age, sex, and FI, was 0.55 (0.37-0.82).

Table 1. Cox regression analysis of primary and secondary outcomes and analysis of recurrent hospitalization and nonmajor clinically relevant bleeding events

	Intervention **Frequency (events)**	**Control** **Frequency (events)**	**Relative Risk (95 % CI)**
Primary Result			
All-cause mortality	3.45 (39)	6.72 (96)	0.55 (0.37-0.82)
Secondary Results			
Cardiovascular Mortality	1.86 (21)	3.22 (46)	0.63 (0.37-1.06)
Noncardiovascular mortality	1.59 (18)	3.50 (50)	0.47 (0.27-0.82)
ECAM	4.76 (50)	4.59 (62)	0.90 (0.62-1.32)
Ischemic stroke	1.35 (15)	1.28 (18)	1.19 (0.60-2.39)
Major bleeding	2.54 (28)	2.01 (28)	1.36 (0.70-2.62)
All-cause hospitalization	28.72 (323)	32.91(466)	0.84 (0.69-1.03)
Cardiovascular hospitalization	9.25 (104)	10.95(155)	0.86 (0.60-1.22
Noncardiovascular hospitalization	19.48 (219)	21.97 (311)	0.83 (0.66-1.05)
Bleeding not greater than	16.90 (190)	17.37(246)	0.99 (0.80-1.23)

Source: statistical analysis, $p \leq 0.05$. Rates are incidence rates per 100 person-years. Relative risks are adjusted hazard ratios, except for hospitalizations for recurrent events and clinically relevant nonmajor bleeding, which are adjusted incidence rate ratios (adjusted for age, sex, frailty index, and clustering accounted for).

For cause-specific mortality, the reduction in the risk of noncardiovascular mortality in the intervention practices was more pronounced than the reduction in the risk of cardiovascular mortality [adjusted HR for noncardiovascular mortality 0.47 (95% CI 0.27-0.82), compared with adjusted HR 0.63 (95% CI 0.37-1.06) for cardiovascular mortality

All-cause hospital admissions were 16% lower in the intervention arm, although the 95 % CI overlapped with 1.0 (adjusted IRR 0.84, 95 % CI 0.69-1.03). This effect was similar for cardiovascular and noncardiovascular hospitalizations.

No statistically significant differences were observed for ECAM, ischemic stroke, and major bleeding outcomes. However, the number of ischemic strokes and major bleeding events was particularly low. Changes between baseline and follow-up in HRQoL were minimal in both arms. The intervention arm experienced a 0.95-point decrease in the physical health component score (range 0 to 100) during two years of follow-up versus a 1.51-point decrease in the control arm (P = 0.130). For the mental health component score, this was a decrease of 2.04 vs. 0.75 points (P = 0.517).

Although the authors did not have complete data on the number of consultations and medication changes, they observed that the mean number of GP consultations per patient during 2.2 years of follow-up was 24.2 in the intervention arm and 15.2 in the usual care arm (data available from 19 of 26 practices). In addition, 10.2% of patients switched from VKA to ACON in the intervention arm, compared with 5.9% in the usual care arm (data available from 11 of 26 practices).

Discussion

In this large cluster-randomized trial, the effect of integrated care for AF patients in primary care was studied. Compared with usual care, this integrated care approach provided by primary care physicians and practice nurses significantly reduced all-cause mortality by 45% (95% CI 0.37-0.82).

The results are generalizable to the vast majority of patients with atrial fibrillation who, on average, are elderly and preferably managed close to home. The intervention can also be implemented in more rural areas, as it is predominantly provided by nurses and offers a more accessible alternative to the often greater travel distance to the nearest hospital [22].

Selection bias could have occurred, inherent in using a randomized cluster design with interventions administered at the individual patient level[9,10]. As such, it anticipated the potential for such bias and performed prespecified adjusted analyses for age, sex, and frailty, which did not substantially change the estimate of effect [crude vs. adjusted HR 0.51 (95% CI 0.33-0.76) and 0.55 (95% CI 0.37-0.82), respectively]. Furthermore, a cluster-randomized design is the best choice for evaluating the effects of integrated care interventions because randomization at the patient level would have resulted in considerable contamination.

Previous research, particularly the RACE 4 study and the study by Hendriks et al., studied the effect of integrated care in secondary or tertiary care[11]. In hospital care, patients often differ from those seen in primary care, as reflected in baseline characteristics. For example, our primary care study population was, on average ten years older than the population studied in a systematic review on integrated AF care in tertiary care (mean age 77.4 vs. 66.9 years) and more often suffered from comorbidities.

As proof of concept, the RACE 3 trial demonstrated that addressing classical cardiovascular risk factors has beneficial effects on ‘AF progression, defined as the proportion of time in sinus rhythm[12].

Moreover, the beneficial effect in our study was more pronounced for noncardiovascular mortality, probably because cardiovascular and noncardiovascular causes of death are often interrelated. For example, a patient dying of pneumonia might have survived if his or her underlying heart failure or AF had been better controlled [13,14].

The easy accessibility of primary care practice for patients and integrated anticoagulation monitoring with direct feedback of the INR value contribute to patient education and adherence, which could have been beneficial[15].

Currently, no mortality benefit has yet been demonstrated in AF trials investigating single-facet interventions such as antiarrhythmic drugs or ablation techniques (except in patients with AF and severe heart failure)[16,17]. Although these interventions have an important impact on HRQoL, our findings provide additional arguments for the view that AF is not simply a heart rhythm disorder but part of a systemic condition[18]. Although the exact underlying substrate and pathophysiology are currently being deciphered, it seems beneficial to focus on integrated care to treat underlying comorbidities such as obesity and hypertension, especially in elderly patients[19,20].

Conclusions

Compared to usual care, a 45% reduction in all-cause mortality was observed when providing integrated care to elderly AF patients, primarily in primary care.

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