

Unplanned 30-day readmission, comorbidity, and impact on mortality after incident atrial fibrillation hospitalization in Western Australia, 2001–2015



Courtney Weber, MPH,* Joseph Hung, FRACP,[†] Siobhan Hickling, PhD,* Ian Li, PhD,* Kevin Murray, PhD,* Tom Briffa, PhD*

From the *School of Population and Global Health, University of Western Australia, Crawley, Australia, and [†]Medical School, Faculty of Medicine and Health Sciences, University of Western Australia, Crawley, Australia.

BACKGROUND The healthcare burden of atrial fibrillation (AF) is dominated by hospitalizations, but data on 30-day unplanned readmissions after AF hospitalization and impact on mortality are limited.

OBJECTIVE To assess causes and trends of 30-day unplanned readmission in incident (first-ever) hospitalized AF patients, and the risk of readmission for subsequent all-cause mortality.

METHODS Patients aged 25–94 years, with an incident AF hospitalization (principal diagnosis) between 2001 and 2015, and surviving 30 days post discharge, were identified from linked Western Australian hospitalization and mortality data. Unplanned 30-day readmissions were categorized by principal diagnosis. Multivariable logistic and Cox regression analyses determined the independent predictors of readmission and the hazard ratio (HR) with 95% confidence intervals (CI) of readmission for subsequent 1-year mortality.

RESULTS Of 22,814 patients, 57.7% male, mean age 67.8 ± 13.8 (standard deviation) years, 9.5% experienced 1 or more 30-day unplanned readmissions, with standardized rates increasing 2.0% annually (95% CI, 1.0%–3.1%). Among all readmissions, 64.8%

were cardiovascular-related, with AF (31.7%), coronary events (12.2%), and heart failure (8.5%) being the most frequent. In 30-day survivors, 4.3% died within 1 year. Patients with any cardiovascular or noncardiovascular readmission (vs none) had a multivariable-adjusted mortality HR of 2.12 (95% CI, 1.82–2.45). Coexistent comorbidities were independently associated with 30-day unplanned readmission and 1-year mortality.

CONCLUSION Following incident AF hospitalization, 30-day unplanned readmissions were common, mostly cardiovascular-related, but any readmission, regardless of cause, was associated with a 2-fold higher adjusted mortality risk. Our findings also support the importance of comorbidity optimization within an integrated care pathway to reduce adverse outcomes in AF patients.

KEYWORDS Atrial fibrillation; Hospitalization; Outcomes; Comorbidity; Mortality

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Introduction

Atrial fibrillation (AF) is a major health problem with rising global prevalence and considerable associated morbidity and mortality burden.^{1–3} Further, AF is associated with large healthcare costs, with hospitalizations being the major cost driver.^{4,5} Concomitant with rising prevalence is the escalating hospitalization frequency, partly driven by advances in procedural AF management.^{6–8} In addition, patients with AF have increased risk of cardiovascular and noncardiovascular hospitalizations from a range of comorbidities.^{1,2,9,10} Measuring hospitalization rates in pa-

tients with AF is therefore a valuable surrogate marker of related morbidity, mortality, and healthcare expenditure. Unplanned 30-day readmissions are also widely regarded as a quality healthcare metric, but information on the causes and trends of 30-day readmissions after AF hospitalization in the recent era is limited.^{6,7} Further, the association between unplanned readmission and subsequent mortality is unknown.

We assessed the frequency, causes, and trends of 30-day unplanned readmission in patients with an incident (first-ever) hospitalization for AF in Western Australia (WA) between 2001 and 2015 and the relative risk of unplanned readmissions in 30-day survivors for all-cause mortality over the subsequent year. Secondly, we determined factors independently associated with readmission and subsequent mortality, which may inform risk stratification and interventions for secondary prevention.

Address reprint requests and correspondence: Ms Courtney Weber, School of Population and Global Health, University of Western Australia Clifton Street Building, Clifton St, Nedlands, WA 6009, Australia. E-mail address: courtney.weber@uwa.edu.au.

KEY FINDINGS

- In this population-based study, we found that 1 in 10 patients will experience 1 or more unplanned readmission within 30 days after first-ever hospitalization for atrial fibrillation.
- Standardized unplanned 30-day readmission rates increased 2.0% annually between 2001 and 2015.
- Around two-thirds of all unplanned readmissions were for cardiovascular causes, with atrial fibrillation, heart failure, and coronary events being the most frequent.
- Any unplanned 30-day readmission was associated with a 2-fold higher adjusted risk of death within the subsequent year.
- Coexistent cardiovascular and other comorbidities were independently associated with both readmission and mortality risk.

Methods

Data sources

Hospitalization and mortality records for all patients residing in WA with a cardiovascular-related hospitalization from January 1, 1991, to December 31, 2016, were obtained from the Hospital Morbidity Data Collection (HMDC) and the Death Registry.¹¹ These routinely collected data are audited for quality control and are regularly linked through probabilistic matching.^{3,8,11} The HMDC contains public

and private hospitalization records covering demographics, admission and discharge date, the principal and additional diagnoses, and procedural fields, using the International Classification of Diseases (ICD), versions 9 (ICD-9) and 10–Australian modification (ICD-10-AM). The Death Registry includes demographics, date of death, and underlying causes of death.

Patient selection

We identified all patients aged 25–94 years with an incident AF hospitalization (ICD-10-AM, I48) as a principal diagnosis between January 1, 2001, and December 31, 2015.^{3,8,12} A 10-year lookback was used to exclude prevalent cases. Exclusion criteria included all-cause death up to 30 days after discharge and prior chronic renal dialysis because of recurrent dialysis readmissions (Figure 1). Patients surviving 30 days post discharge were followed for a further 12 months or until death, whichever occurred first.

Covariates

Demographics were identified from the incident admission. Aboriginal and Torres Strait Islander (Indigenous) status was identified using a previously constructed method.¹³ Comorbidities were determined using any diagnosis field within hospitalization records in the 10 years preceding and including incident admission. Conditions included heart failure (HF), hypertension, ischemic heart disease (IHD), myocardial infarction (MI), cerebrovascular disease, stroke, transient ischemic attack (TIA), peripheral arterial disease, valvular heart disease, syncope, chronic obstructive

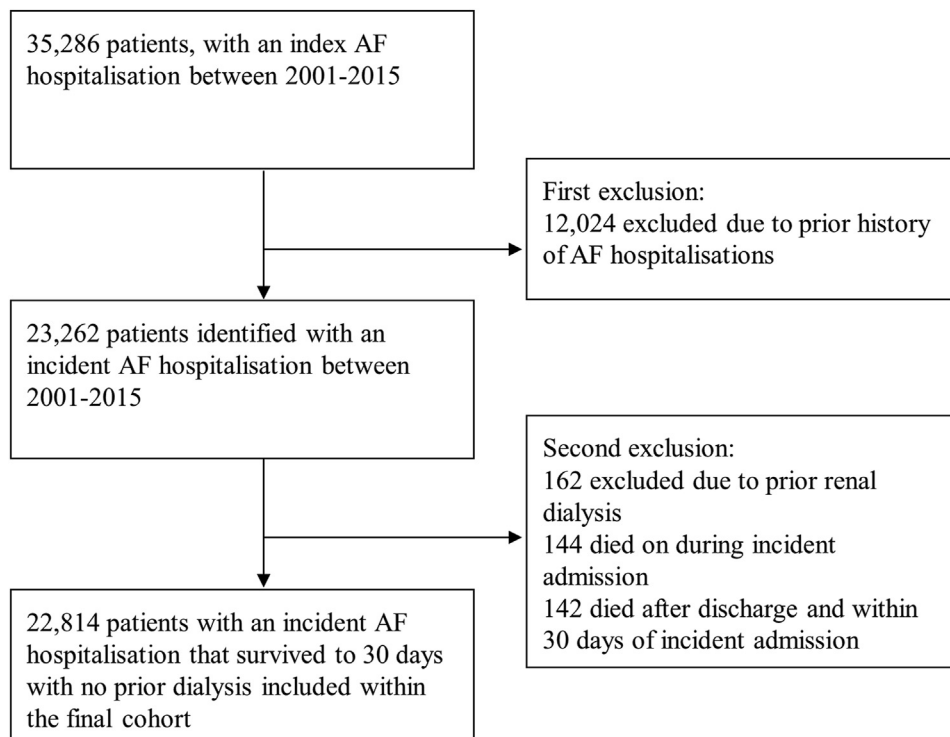


Figure 1 Flow diagram showing cohort selection. AF = atrial fibrillation.

Table 1 Clinical characteristics of 30-day survivors after incident atrial fibrillation hospitalization, stratified by occurrence of unplanned 30-day readmission

Characteristics	Total	Unplanned 30-day readmission	
		None	Any
Count, n (%)	22,814	20,648 (90.5)	2166 (9.5)
Male, n (%)	13,163 (57.7)	12,050 (58.6)	1113 (51.4)
Age (years), mean (SD)	67.8 (13.8)	67.4 (13.8)	71.2 (13.4)
25–64	8813 (38.6)	8177 (39.6)	636 (29.4)
65–74	6185 (27.1)	5628 (27.3)	557 (25.7)
75–94	7816 (34.3)	6843 (33.1)	973 (44.9)
Indigenous status, n (%)	347 (1.5)	290 (1.4)	57 (2.6)
LOS (days), median (IQR)	1 (0,3)	1 (0,3)	2 (1,5)
Comorbidities/procedures, n (%) [†]			
Heart failure	2941 (12.9)	2470 (12.0)	471 (21.8)
Ischemic heart disease	4496 (19.7)	3925 (19.0)	571 (26.4)
Myocardial infarction	1214 (5.3)	1046 (5.1)	168 (7.8)
Hypertension	7092 (31.1)	6192 (30.0)	900 (41.6)
Cerebrovascular disease	1192 (5.2)	1046 (5.1)	146 (6.7)
All stroke/TIA	1032 (4.5)	902 (4.4)	130 (6.0)
Peripheral arterial disease	945 (4.1)	780 (3.8)	165 (7.6)
Valvular heart disease	1822 (8.0)	1559 (7.6)	263 (12.1)
Syncope	1052 (4.6)	926 (4.5)	126 (5.8)
Diabetes	3023 (13.3)	2643 (12.8)	380 (17.5)
Obesity	1178 (5.2)	1026 (5.0)	152 (7.0)
COPD	1592 (7.0)	1327 (6.4)	265 (12.2)
Pneumonia	1225 (5.4)	1017 (4.9)	208 (9.6)
Chronic kidney disease	1192 (5.2)	1010 (4.9)	182 (8.4)
Cancer	5633 (24.7)	5024 (24.3)	609 (28.1)
Anemia	1202 (5.3)	1024 (5.0)	178 (8.2)
Thyroid abnormalities	479 (2.1)	412 (2.0)	67 (3.1)
Electrical cardioversion	6747 (29.6)	6350 (30.8)	397 (18.3)
Catheter ablation	642 (2.8)	582 (2.8)	60 (2.8)
CHA ₂ DS ₂ -VA score, [‡] mean (SD)	1.80 (1.62)	1.75 (1.60)	2.36 (1.73)
CHA ₂ DS ₂ -VA score category, n (%)			
0	6294 (27.6)	5932 (28.7)	362 (16.7)
1	4620 (20.3)	4236 (20.5)	384 (17.7)
2+	11,900 (52.0)	10,480 (50.8)	1420 (65.6)

COPD = chronic obstructive pulmonary disease; IQR = interquartile range; LOS = length of stay; SD = standard deviation; TIA = transient ischemic attack.

[†]Comorbidities were detected based on hospitalization records in the 10 years preceding and including incident admission, but procedures were restricted to occurrence on incident admission.

[‡]CHA₂DS₂-VA score comprises the following risk factors: congestive heart failure, hypertension, age \geq 75 years, diabetes, prior stroke or transient ischemic attack, vascular disease, and age 65–74 years.

pulmonary disease (COPD), pneumonia, chronic kidney disease (CKD), cancer, obesity, diabetes, anemia, and thyroid disease. Electrical cardioversion and catheter ablation were identified on the incident admission (definitions in [Supplemental Table 1](#)). The CHA₂DS₂-VA risk score (1 point congestive HF, hypertension, diabetes, vascular disease, or age 65–74 years; 2 points prior stroke/TIA or age \geq 75 years) was also calculated for each patient.²

Outcomes

Primary outcomes were the frequency, reasons, and trend for 30-day unplanned readmissions; and all-cause mortality over the subsequent year in 30-day survivors. Readmissions within 30 days after AF hospitalization were identified and counted. Subsequent records within 1 day of each readmission record were considered transfers and not counted. Readmissions were stratified by unplanned (emergency) status, then categorized by principal diagnosis into disease groups,

and subgrouped as either cardiovascular or noncardiovascular (definitions in [Supplemental Table 2](#)). The secondary outcomes were the predictors of 30-day unplanned readmission and 1-year all-cause mortality in 30-day survivors.

Statistical analysis

Continuous variables were presented as mean (standard deviation) or median (interquartile range), and categorical variables as number and proportion. Unplanned 30-day readmission rates were age- and sex-standardized using the distribution of incident AF patients admitted in 2015. Poisson regression analysis (age group [25–54, 55–64, 65–74, 74–84, 85–94 years] and sex adjusted) determined the annual rate ratio with 95% confidence interval (CI) of 30-day unplanned readmission between 2001 and 2015.

Multivariable logistic regression modeling determined the covariates independently associated with 30-day unplanned readmission and have been presented as odds ratios with

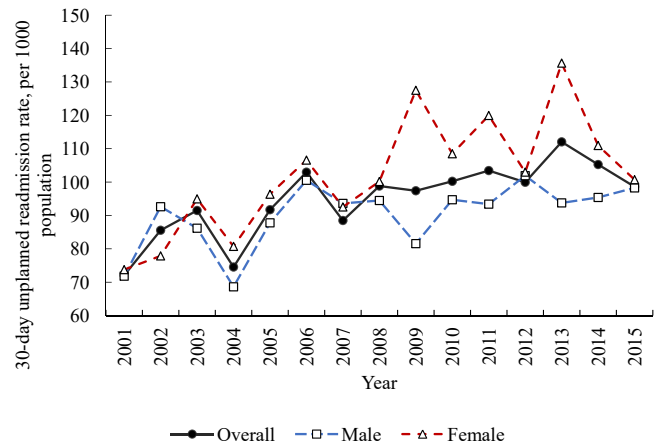
Table 2 Counts and principal reasons for 30-day unplanned readmissions in patients who survived 30 days after incident hospitalization for atrial fibrillation

Causes of readmission by category	Count	%
Cardiovascular	1553	64.8
Atrial fibrillation/flutter	759	31.7
Other arrhythmias	110	4.6
Heart failure	204	8.5
Myocardial infarction	34	1.4
Unstable angina / other ischemic heart disease	101	4.2
Chest pain	160	6.7
All stroke/transient ischemic attack	46	1.9
Valvular disease	26	1.1
Hypotension/shock	19	0.8
Pulmonary embolism	14	0.6
Other cardiovascular [†]	80	3.4
Noncardiovascular	843	35.2
Chronic obstructive pulmonary disease/other respiratory	102	4.3
Pneumonia	47	2.0
Digestive disease	96	4.0
Injury, poisoning, and other consequences of external causes (including bone fractures and procedural complications)	93	3.9
Cancer	52	2.2
Bleeding	50	2.1
Renal	49	2.0
Mental	43	1.8
Musculoskeletal disease	40	1.7
Infection	27	1.1
Disease of skin	23	1.0
Diseases of the nervous system	16	0.7
Fluid and electrolyte abnormality	15	0.6
Anemia	12	0.5
Diabetes	12	0.5
Other noncardiovascular [†]	166	6.9
Total	2396	100.0

[†]Other cardiovascular and noncardiovascular categories include conditions that could not be categorized into groups containing more than 0.5% of all readmissions.

95% CI. After adjustment for sex, age group, Indigenous status, length of stay (LOS), and calendar admission year, all measured comorbidities (Table 1) were included in the multivariable analysis if they were univariately associated with the outcome ($P < .05$) and lacked high levels of collinearity.

The cumulative incidence of 1-year mortality was estimated using Kaplan-Meier analyses, stratified by readmission occurrence/type. Immortal time bias was avoided by using landmark analysis in patients who survived 30 days post discharge. Multivariable Cox proportional hazards modeling including all baseline characteristics (Table 1) determined the factors independently associated with 1-year mortality and the relative mortality risk of unplanned/cause-specific readmission as hazard ratios (HR) and 95% CI. Indigenous Australians with AF have a higher mortality compared with other Australians,¹³ and therefore Indigenous status was included as an adjustment within multivariate analyses, but their data are not shown owing to Indigenous data

**Figure 2** Annual age- and sex-standardized 30-day readmission rates in patients after incident atrial fibrillation hospitalization, and age-standardized rates stratified by sex.

sovereignty. Interactions between age group, sex, admission year, and unplanned readmission were tested but were nonsignificant, and therefore were not included in the final regression models. No major violations were found when testing the proportional hazards assumption. A $P < .05$ was considered as statistically significant. The statistical analysis was conducted in SAS V.9.4 for Windows (SAS Institute Inc, Cary, NC).

Ethics

Ethical approval was obtained from the WA Department of Health, Human Research Ethics committee (ethics number: 2014/55; date: September 5, 2016). The research reported in this paper adhered to the Helsinki Declaration on ethical conduct in Human Research and is consistent with Australia's National Statement on Human Research (2007, updated 2018). Informed consent by participants was not required for this study of administrative, unidentified linked data.

Results

A total of 35,286 patients had an AF hospitalization between 2001 and 2015. Of these, 12,024 were excluded owing to a prior AF hospitalization. A further 286 patients who died within 30 days of admission (0.8% case fatality), and 162 on chronic renal dialysis were excluded (Figure 1). The final cohort comprised 22,814 patients, mean age 67.8 ± 13.8 (standard deviation) years, 57.7% male, and 1.5% Indigenous (Table 1). Females were generally older than males, and had a higher prevalence of comorbidities and lower occurrence of electrical cardioversion and catheter ablation on incident admission (Supplemental Table 3). Further exploratory analysis indicated that the overall age and sex distribution of the cohort did not change between 2001 and 2015, but with a decline in prevalence of most cardiovascular and other comorbidities except for diabetes and cancer, which increased (Supplemental Table 4).

Of the study cohort, 2166 patients (9.5%) experienced any unplanned 30-day readmission. Readmitted compared to

Table 3 Logistic regression showing univariate and multivariable-adjusted predictors of 30-day unplanned readmission in patients who survived 30 days after incident atrial fibrillation hospitalization

Variable	Odds ratio (95% confidence interval) of unplanned readmission	
	Univariate	Multivariable
Female sex	1.33 (1.21–1.45)**	1.09 (0.99–1.20)
Age per 10-year increment above age group 25–54 years	1.26 (1.21–1.31)**	1.13 (1.08–1.18)**
Length of stay (days)	1.03 (1.02–1.03)**	1.01 (1.00–1.02)*
Calendar admission year	1.02 (1.01–1.03)**	1.03 (1.02–1.04)**
Heart failure	2.05 (1.83–2.28)**	1.40 (1.24–1.59)**
Ischemic heart disease [‡]	1.53 (1.38–1.69)**	1.09 (0.97–1.22)
Myocardial infarction [†]	1.58 (1.33–1.87)**	–
Hypertension	1.66 (1.52–1.82)**	1.18 (1.06–1.32)**
Cerebrovascular disease [‡]	1.38 (1.13–1.68)**	0.88 (0.73–1.07)
Any stroke/transient ischemic attack [†]	1.49 (1.19–1.86)**	–
Peripheral arterial disease	2.10 (1.77–2.50)**	1.48 (1.23–1.78)**
Valvular disease	1.69 (1.47–1.94)**	1.30 (1.12–1.50)**
Syncope	1.32 (1.09–1.59)**	0.97 (0.80–1.18)
Diabetes	1.45 (1.29–1.63)**	1.03 (0.91–1.18)
Obesity	1.44 (1.21–1.72)**	1.17 (0.97–1.42)
Chronic obstructive pulmonary disease	2.03 (1.77–2.34)**	1.40 (1.20–1.62)**
Pneumonia	2.05 (1.75–2.40)**	1.30 (1.10–1.54)*
Chronic kidney disease	1.78 (1.51–2.10)**	1.03 (0.86–1.23)
Cancer	1.22 (1.10–1.34)**	1.08 (0.98–1.20)
Anemia	1.72 (1.45–2.03)**	1.14 (0.95–1.36)
Thyroid disease	1.57 (1.21–2.04)**	1.18 (0.90–1.54)
Electrical cardioversion [§]	0.51 (0.45–0.57)**	0.59 (0.52–0.66)**
Catheter ablation [§]	0.98 (0.75–1.29)**	0.97 (0.73–1.28)
CHA ₂ DS ₂ -VA score ^{,†}	1.24 (1.21–1.27)**	–

Asterisks denote statistical significance: * significant at P value $< .01$ and. ** significant at P value $< .001$; no asterisk denotes result is nonsignificant at P value $> .05$.

[†]Not tested within the multivariable model owing to collinearity with other included covariates.

[‡]Broad disease categories were used for prediction of readmission.

[§]Procedure performed on incident admission.

^{||}CHA₂DS₂-VA score comprises the following risk factors: congestive heart failure, hypertension, age ≥ 75 years, diabetes, prior stroke or transient ischemic attack, vascular disease, and age 65–74 years.

nonreadmitted patients were more likely female and older (Table 1). All identified comorbidities were more frequent, the CHA₂DS₂-VA scores were higher, and electrical cardioversion or catheter ablation on incident admission were less likely among readmitted cases (Table 1). Patients who died within 30 days ($n = 286$) compared to those who survived

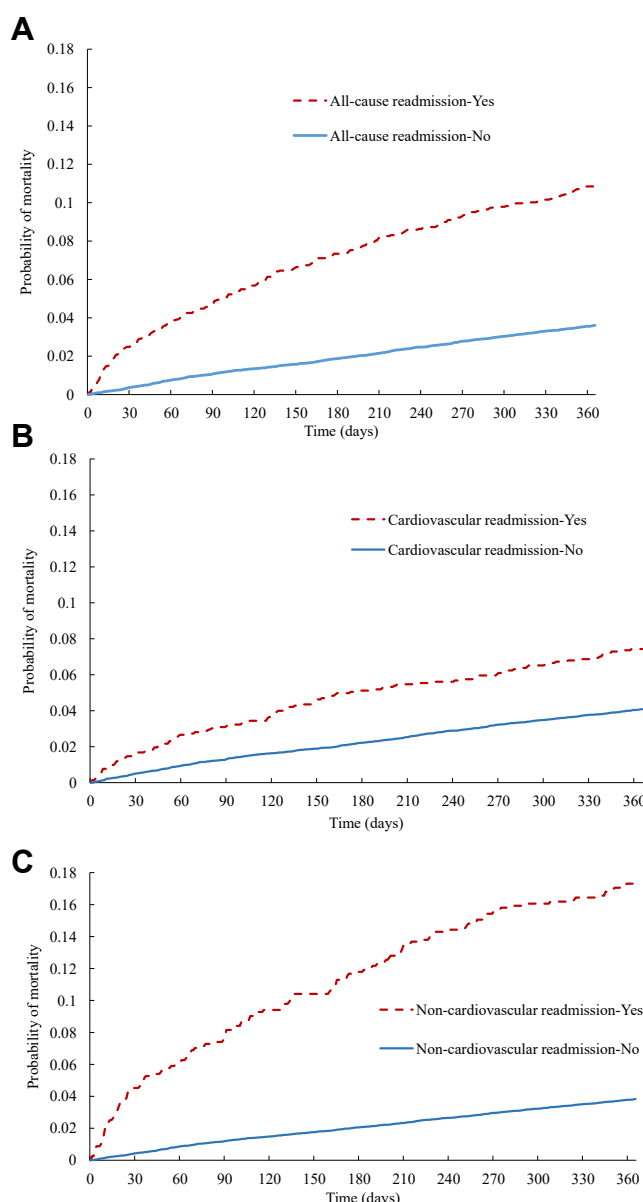


Figure 3 Cumulative probability of death over 1 year at 30 days after incident atrial fibrillation hospitalization, by presence or absence of 30-day unplanned readmission for **A**: any unplanned readmission; **B**: cardiovascular-related readmission; **C**: noncardiovascular-related readmission.

were on average 10 years older, had a longer initial LOS, and had a higher prevalence of comorbidities and higher proportion (25.2%) who experienced any nonfatal readmission before death (Supplemental Table 5).

A total of 2396 unplanned readmissions occurred among 2166 patients, with 82.7% experiencing a single 30-day readmission. Of all readmissions, 64.8% were cardiovascular-related: AF most frequently (31.7%), followed by IHD (12.2%), HF (8.5%), other arrhythmias (4.6%), and any stroke/TIA (1.9%) (Table 2). The most common noncardiovascular reasons were respiratory diseases including COPD/pneumonia (6.3%), digestive diseases (4.0%), and injury/poisoning/other consequences of external causes (3.9%) (Table 2).

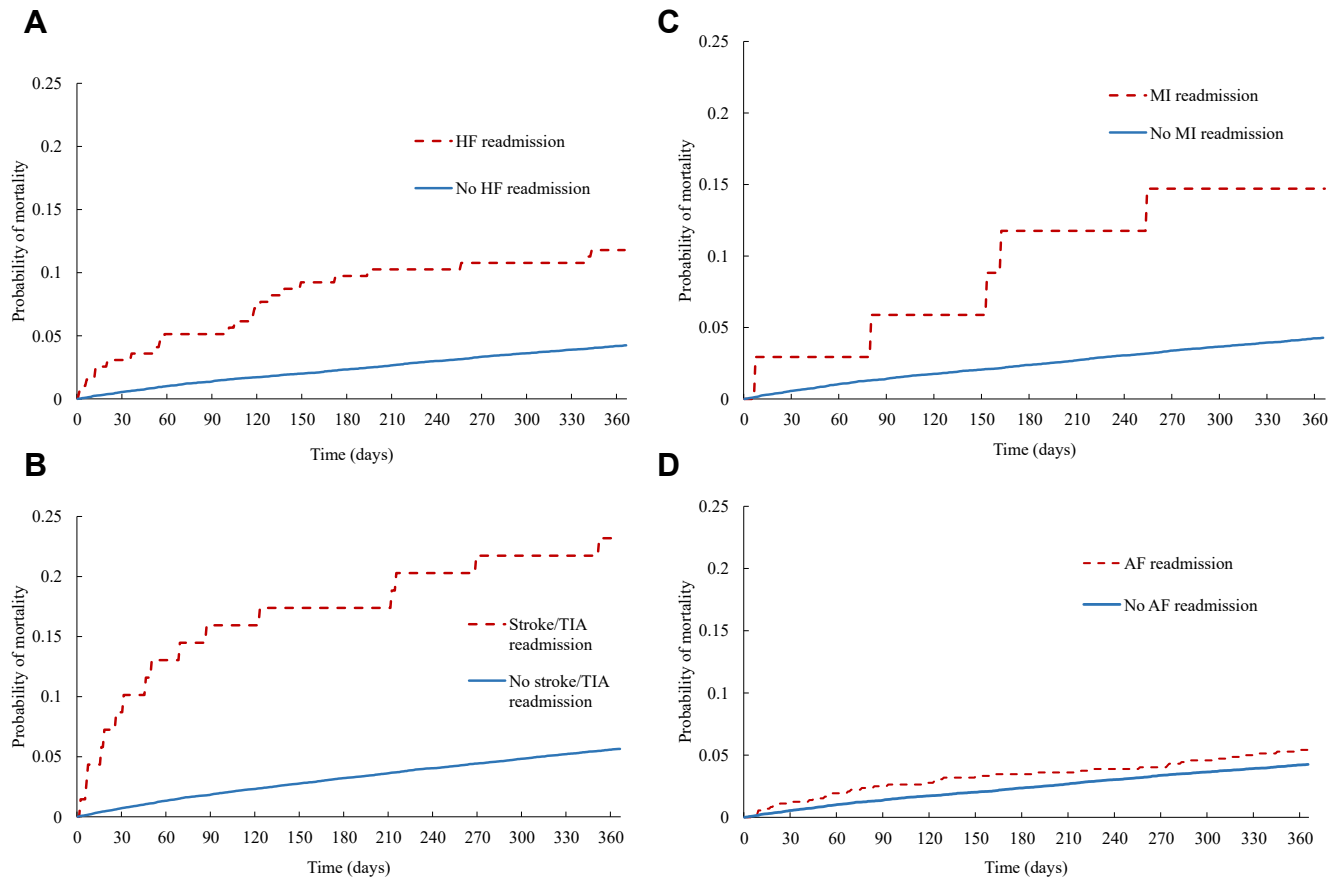


Figure 4 Cumulative probability of death over 1 year in 30-day survivors after incident atrial fibrillation hospitalization, by presence or absence of 30-day unplanned readmission for **A:** heart failure (HF); **B:** stroke or transient ischemic attack (TIA); **C:** myocardial infarction (MI); **D:** atrial fibrillation (AF).

The annual age- and sex-standardized rates of unplanned 30-day readmissions (per 1000 population) and age-standardized rates stratified by sex are shown in [Figure 2](#) ([Supplemental Table 6](#)). The overall age- and sex-standardized readmission rate increased from 72.1 (95% CI, 56.1–88.0) to 98.6 (95% CI, 84.4–112.9) between 2001 and 2015, representing a 2.0% annual increase (95% CI, 1.0%–3.1%). Annual age-standardized 30-day readmission rates, and the annual increment in readmission rate, were higher in females than in males (2.7% [95% CI, 1.2%–4.2%] vs 1.4% [95% CI, 0.0%–2.8%], respectively) ([Figure 2](#), [Supplemental Table 6](#)). Age- and sex-standardized readmission rate for AF-specific, cardiovascular, and noncardiovascular causes all rose annually over the study period, by 2.5% (95% CI, 0.7%–4.3%), 1.8% (95% CI, 0.6%–3.1%), and 2.7% (95% CI, 1.0%–4.5%), respectively.

[Table 3](#) shows the univariate and multivariable-adjusted predictors of 30-day unplanned readmission. Advancing age, female sex, LOS, year of incident AF admission, all cardiovascular and noncardiovascular comorbidities, and CHA₂DS₂-VA score were univariately associated with higher odds of readmission, and electrical cardioversion on incident admission with reduced odds (all $P < .001$). After multivariable adjustment, these same variables (excluding female sex, IHD, cerebrovascular disease, syncope, CKD, cancer, diabetes, obesity,

anemia, and thyroid disease) remained independent predictors of readmission.

Among the 30-day survivors, 981 (4.3%) died within the subsequent year. The cumulative proportion of patients who died was 10.9% vs 3.6% (log-rank $P < .001$) in the readmitted vs nonreadmitted group, respectively ([Figure 3A](#)); 7.4% vs 4.1% ($P < .001$) in patients with a cardiovascular vs noncardiovascular readmission ([Figure 3B](#)), and 17.3% vs 3.8% ($P < .001$) in patients with a noncardiovascular vs without a noncardiovascular readmission ([Figure 3C](#)). Patients with a readmission for HF, any stroke/TIA, or MI had higher cumulative probabilities of death compared to patients without these events (all $P < .01$), but unplanned AF readmission had no impact on death ($P = .13$) ([Figure 4A–4D](#)).

[Table 4](#) shows the Cox regression analyses for subsequent death in 30-day survivors. After multivariable adjustment, advancing age, male sex, and LOS were independently associated with increased mortality. Other positive independent predictors were HF, MI, peripheral arterial disease, COPD, pneumonia, CKD, cancer, and anemia, while electrical cardioversion and catheter ablation on incident admission were negative predictors of mortality ([Table 4](#)). The CHA₂DS₂-VA score was a univariate predictor of mortality, but calendar year of admission was not.

The multivariable-adjusted mortality HR for any (vs no) readmission was 2.12 (95% CI, 1.82–2.45; $P < .001$)

Table 4 Cox regression models of univariate and multivariable-adjusted predictors of all-cause mortality over 1 year in 30-day survivors after incident atrial fibrillation hospitalization

Variable	Mortality hazard ratio (95% confidence interval)	
	Univariate	Multivariable-adjusted
Female sex	1.16 (1.02–1.31)**	0.69 (0.60–0.79)**
Age per 10-year increment above age group 25–54 years	2.33 (2.18–2.48)**	1.94 (1.81–2.08)**
Length of stay (days)	1.03 (1.02–1.03)**	1.02 (1.02–1.03)**
Calendar admission year	0.98 (0.97–1.00)	0.98 (0.97–1.00)*
Heart failure	3.73 (3.27–4.26)**	1.68 (1.45–1.94)**
Ischemic heart disease†	2.06 (1.80–2.35)**	–
Myocardial infarction	2.88 (2.40–3.46)**	1.40 (1.15–1.70)**
Hypertension	2.29 (2.02–2.60)**	0.97 (0.84–1.12)
Cerebrovascular disease†	2.65 (2.14–3.27)**	–
Any stroke/transient ischemic attack	2.50 (2.04–3.07)**	1.11 (0.90–1.37)
Peripheral arterial disease	3.65 (3.03–4.40)**	1.54 (1.27–1.88)**
Valvular disease	1.86 (1.55–2.23)**	1.10 (0.91–1.33)
Syncope	1.81 (1.44–2.29)**	0.99 (0.79–1.26)
Diabetes	1.76 (1.51–2.05)**	1.06 (0.90–1.26)
Obesity	1.13 (0.87–1.48)	0.93 (0.70–1.24)
Chronic obstructive pulmonary disease	3.50 (3.00–4.09)**	1.64 (1.39–1.94)**
Pneumonia	3.44 (2.90–4.08)**	1.37 (1.14–1.65)**
Chronic kidney disease	3.86 (3.26–4.56)**	1.40 (1.17–1.69)**
Cancer	2.57 (1.99–2.56)**	1.71 (1.50–1.94)**
Anemia	3.29 (2.76–3.92)**	1.42 (1.18–1.71)**
Thyroid disease	1.87 (1.25–2.60)**	1.07 (0.76–1.49)
Electrical cardioversion‡	0.31 (0.26–0.38)**	0.49 (0.40–0.60)**
Catheter ablation‡	0.28 (0.14–0.56)**	0.45 (0.22–0.90)*
CHA ₂ DS ₂ -VA score ^{§,†}	1.58 (1.53–1.64)**	–
Any unplanned readmission	3.15 (2.72–3.65)**	2.12 (1.82–2.45)**

Asterisks denote statistical significance: * significant at P value $<.05$ and ** significant at P value $<.001$; no asterisk denotes result is nonsignificant at P value $>.05$.

†Not tested within the multivariable model owing to collinearity with other covariates.

‡Procedure performed on incident admission.

§CHA₂DS₂-VA score comprises the following risk factors: congestive heart failure, hypertension, age ≥ 75 years, diabetes, prior stroke or transient ischemic attack, vascular disease, and age 65–74 years.

(Table 4). In separate Cox regression models (data not shown), cardiovascular (vs no cardiovascular) readmission was associated with an adjusted mortality HR of 1.20 (95% CI, 1.00–1.44; $P = .05$), and for any cardiovascular readmission excluding AF, the adjusted mortality HR was 1.30 (95% CI, 1.04–1.62; $P = .023$). Patients with a noncardiovascular

(vs without any noncardiovascular) readmission had an adjusted mortality HR of 2.71 (95% CI, 2.32–3.15; $P < .001$).

Discussion

In this contemporary Australian population-based study, we found that 9.5% of patients with incident AF hospitalization experienced 1 or more unplanned readmission within 30 days, with 65% being cardiovascular-related. To our knowledge, we are the first to show that any unplanned 30-day readmission, regardless of cause, is independently associated with a 2-fold excess risk of death over the subsequent year. Importantly, most patients with AF have comorbidities that are independently associated with readmission and mortality risk, which has important implications for risk stratification and secondary preventive care.

Principal causes for readmission

Similar to the US Nationwide Readmission Database study,⁶ we found that 30-day readmissions after AF hospitalization were most commonly cardiovascular-related, with AF, HF, and IHD being the most frequent. It is recognized that the economic burden of AF is driven mostly by hospital care for AF and related complications like stroke and HF.^{6–8,12}

The recent widespread use of direct oral anticoagulants for stroke prevention has been associated with a decline in stroke and mortality risk in AF population samples.^{1,14} Although management guidelines have emphasized optimizing anticoagulant treatment decisions, it should be noted that HF events are actually much more common than stroke after AF diagnosis and have a high mortality risk.^{6,12,15} Consistent with prior studies,^{6,9} a significant proportion of readmissions were driven by noncardiovascular conditions, adding to the case complexity of AF.

Trends in 30-day readmission

Only 2 studies^{6,7} have reported trends of 30-day readmission rates after AF hospitalization since 2010. Both US-based studies reported a progressive decline in 30-day (all-cause) readmission rates to 14%–15% between 2010 and 2014 in patients with a primary discharge diagnosis of AF.^{6,7} Our study focused on unplanned but potentially avoidable readmissions only, and we observed almost 1 in 10 patients had 1 or more readmissions within 30 days. Crucially, we found that patients who experienced unplanned 30-day readmissions were older, were more likely female, and had more comorbidities, which are factors known to adversely impact on clinical management and outcomes in patients with AF. Contrary to the US studies, our trends showed a progressive increase in age-standardized 30-day unplanned readmission rates between 2001 and 2015, which was more pronounced in females than in males. The reasons underlying the rising readmission trends are unclear and may not be driven by changes in case-mix complexity within the AF cohort. However, the fact that the readmission rates have increased for both cardiovascular (including AF) and noncardiovascular causes highlights the importance of optimal management of

AF along with comorbidities as part of an integrated holistic pathway of care.^{2,3} We also found that readmission rates were rising faster in females compared with males, which may partly reflect the fact that females were generally older, more comorbid, and less likely to receive proactive rhythm control including electrical cardioversion during initial AF hospitalization. Higher rates of interventional AF treatment during the recent era have impacted mainly on elective and not unplanned readmissions.^{5,8}

Impact of readmission on mortality

We conducted a landmark analysis in 30-day survivors to determine the impact of prior 30-day readmission events on subsequent medium-term survival. Predictably, patients who died early after incident admission compared to survivors were much older, sicker, and prone to hospital readmissions before eventual death, and their exclusion reduces overestimating the mortality risk attributed to readmissions after AF. We demonstrated that any unplanned 30-day readmission was independently associated with a 2-fold increased mortality risk within the subsequent year. Further, noncardiovascular- compared with cardiovascular-related readmissions were associated with a higher relative mortality risk, in part because AF readmission did not impact on mortality despite being the most common readmission category. It would also appear that the observed temporal increase in readmission rates in our AF cohort did not adversely impact on mortality risk over the same time period. Overall our findings indicate that cardiovascular-related hospitalization is a marker for patients at increased risk of death,¹⁶ but also show that any unplanned rehospitalization may be used as a main outcome measure in clinical trials of AF management.

Risk factors

Finding common determinants of readmission and mortality is important for informing risk assessment and also interventions that may improve clinical outcomes. Advancing age was associated with higher readmission and mortality risk, likely owing to its positive association with comorbidity and frailty. Females were at higher odds of readmission than males, although the difference was not significant after age and comorbidity adjustment. However, females were less likely to receive electrical cardioversion on incident admission, which was associated with a ~50% lower adjusted odds of readmission and risk of subsequent mortality (Supplemental Table 3). Evidence of sex disparity in AF management has been reported previously.^{17,18} Nevertheless, females had a lower adjusted all-cause mortality risk compared with males, consistent with findings of the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) registry, which also found that females, compared to males, with AF had lower all-cause and cardiovascular mortality despite having more symptoms and a worse quality of life.¹⁸ However, the sex disparity in AF treatment remains a serious concern, needing to be addressed.

We confirmed that most coexistent cardiovascular and other comorbidities were independently predictive of rehospitalization,^{6,10} and many of the same comorbidities predicted medium-term survival after AF hospitalization. Since the CHA₂DS₂-VA score represents clustering of these same cardiovascular risk factors, it is not surprising that the aggregate score was also a good surrogate marker for predicting adverse outcomes beyond stroke. Comorbid conditions associated with AF, like HF and IHD, increased mortality risk, but noncardiovascular diseases, notably COPD, pneumonia, CKD, neoplasm, and anemia, were also strong independent associates of all-cause mortality. The impact of multimorbidity on survival has been demonstrated in other observational AF cohort studies.^{19,20} Our findings strongly support integrated care pathways, like the ABC pathway approach, where the “C” component includes identification and optimal management of concomitant cardiovascular and other chronic diseases, and unhealthy lifestyle factors, as part of the comprehensive care in patients with AF.¹ Importantly, clinical management adherent to the ABC pathway for integrated care is associated with significantly lower risk for cardiovascular events, cardiovascular death, and all-cause death in patients with AF.^{1,21}

Some trials and observational studies suggest that early and more aggressive rhythm control strategy after AF onset, including electrical cardioversion and catheter ablation, is associated with a lower risk of rehospitalization, improved survival, and better quality of life.^{6,7,22} We also noted that receipt of electrical cardioversion was independently predictive of lower unplanned readmission and mortality risk, while catheter ablation was also independently associated with reduced mortality risk. However, only a small proportion (~3%) of our AF cohort had catheter ablation on incident admission, and despite confounder adjustment there remains the possibility of survival bias by indication. More investigation is required to ascertain if catheter ablation, although relatively costly, may prove to be cost-effective in the long term by reducing risk of cardiovascular hospitalizations.

Strengths and limitations

Although we demonstrated an association between unplanned all-cause readmission and subsequent mortality, we cannot establish cause and effect. We are also unable to adjust for socioeconomic, health system, and nonprocedural treatment factors, including specialist care and medication use, especially direct oral anticoagulants, which may impact on readmission and mortality risk. Although we have previously shown that administrative data have a high predictive accuracy for AF,³ we are unable to assess AF pattern or burden and clinical data like symptom score and left ventricular ejection fraction, or risk factors like smoking, alcohol, and sleep-disordered breathing. However, inclusion of these data would unlikely change our main findings. Major strengths of this study include the whole-of-WA population-based design, the complete individual record linkage allowing ascertainment of incident AF cases and assessment

of comorbidities and procedures over 10-year lookback, and ability to detect all subsequent hospitalizations and deaths within our jurisdiction.

Conclusion

We found that 30-day unplanned readmission after incident hospitalization for AF was frequent, and the standardized readmission rate has been steadily increasing. Cardiovascular conditions were the most common readmission cause, but any unplanned readmission was independently associated with a 2-fold excess medium-term mortality. Notably, coexistent cardiovascular and noncardiovascular comorbidities were independently predictive of readmission and mortality risk. Our study findings provide strong support for an integrated AF care pathway encompassing optimal management of cardiovascular and other comorbidities, in addition to AF-targeted treatment, to reduce the hospitalization and mortality burden of AF.

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Ethics Statement: Ethical approval was obtained from the WA Department of Health, Human Research Ethics committee (ethics number: 2014/55; date: September 5, 2016). The research reported in this paper adhered to the Helsinki Declaration on ethical conduct in Human Research and is consistent with Australia's National Statement on Human Research (2007, updated 2018).

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at <https://doi.org/10.1016/j.hroo.2022.06.002>.

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