The interplay between atrial fibrillation and heart failure on long-term mortality and length of stay: Insights from the, United Kingdom ACALM registry

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ABSTRACT

Background: There is concern that the development of heart failure and atrial fibrillation has a detrimental influence on clinical outcomes. The aim of this study was to assess all-cause mortality and length of hospital stay in patients with chronic and new-onset concomitant AF and HF.

Methods: Using the ACALM registry, we analysed adults hospitalised between 2000 and 2013 with AF and HF and assessed prevalence, mortality and length of hospital stay. Patients with HF and/or AF at baseline (study-entry) were compared with patients who developed new-onset disease during follow-up.

Results: Of 929,552 patients, 31,695 (3.4%) were in AF without HF, 20,768 (2.2%) had HF in sinus rhythm, and 10,992 (1.2%) had HF in AF. Patients with HF in AF had the greatest all-cause mortality (70.8%), followed by HF in sinus rhythm (64.1%) and AF alone (45.1%, $p < 0.0001$). Patients that developed new-onset AF, HF or both had significantly worse mortality (58.5%, 70.7% and 74.8% respectively) compared to those already with the condition at baseline (48.5%, 63.7% and 67.2% respectively, $p < 0.0001$). Patients with HF in AF had the longest length of hospital stay (9.41 days, 95% CI 8.90–9.92), followed by HF in sinus rhythm (7.67, 95% CI 7.34–8.00) and AF alone (6.05, 95% CI 5.78–6.31).

Conclusions: Patients with HF in AF are at a greater risk of mortality and longer hospital stay compared to patients without the combination. New-onset AF or HF is associated with significantly worse prognosis than long-standing disease.

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1. Introduction

Heart failure (HF) and atrial fibrillation (AF) are two common and important cardiovascular disease entities of the 21st century. Despite considerable advances in management for both conditions, there remains debate regarding widely used therapies, including rate versus rhythm control [1], beta-blockers [2] and cardiac glycosides [3] with recent meta-analyses demonstrating limited prognostic impact. In the United Kingdom (UK), HF affects 900,000 patients and has an estimated 10-year mortality of 42.8% [4], with an associated economic burden on the National Health Service (NHS), contributing to 2% of all NHS in-patient bed days and 5% of hospital admissions [5,6]. Aside from the financial impact, the length of stay (LoS) also has important implications on clinical outcomes and is associated with increased readmission and greater mortality [7]. Additionally, AF is the most common cardiac arrhythmia, with increasing prevalence [8,9]. If left untreated, AF is a significant risk factor for systemic thromboembolism and cardiomyopathy, placing patients at risk of death [10].

The presence of AF or HF increases the likelihood of the other, with HF being the strongest risk factor for the development of AF. Similarly, AF precipitates and exacerbates LV dysfunction, giving rise to AF-induced cardiomyopathy [11]. In the Framingham Heart Study (1980–2012), among 1737 individuals with new AF, 37% had HF, and among 1166 individuals with new HF, 57% had AF [12]. Prevalence rates of AF in patients with HF and vice versa is dependent upon the disease severity, for example, AF prevalence increased from 4 to 40% as New York Heart Association (NYHA) functional class increased from I to IV [13].

The mechanisms behind these associations is likely mediated by multiple factors: abrupt changes in heart rate and an irregular rhythm may compromise cardiac output; persistent tachycardia may precipitate tachycardia-mediated cardiomyopathy; loss of atrial systole impairs optimal ventricular filling; left atrial stretch; and activation of neurohumoral factors hastens maladaptive responses.

With regard to survival, most observational analyses that have assessed the impact of concomitant AF and HF were performed over a decade ago, which raised concern that the combination is an independent predictor of mortality [14–19]. Accordingly, the aim of this study was to provide an up to date analysis of prevalence, mortality and length of stay in patients with HF and/or AF in a large robust database of patients admitted to hospitals in England. Additionally, we investigate the clinical consequence of developing new onset AF or HF during long-term follow-up.

2. Methods

2.1. Study population

We examined the prevalence and impact of concomitant AF and HF on all-cause mortality and LoS using an entirely anonymous database of adult patients compiled using the ACALM Algorithm of Comorbidities, Associations, Length of stay and Mortality (ACALM) study protocol, which has been previously used and described by our group [20–23]. The ACALM study protocol used International Classification of Diseases and Related Health Problems, revision 10 (ICD-10) and Office of Population Censuses and Surveys Classification of Interventions and Procedures version 4 (OPCS-4) codes to identify patients from completely anonymous electronic hospital records. Mortality status at the end of the study period was determined by record linkage to the National Health Tracing Services (NHS strategic tracing service) which utilises data from the Office for National Statistics (ONS).

The study population consisted of all 929,552 adult patients admitted to seven hospitals in North of England, UK, between 1st January 2000 and 31st March 2013. Patients under the age of 18 were excluded. Follow-up of individual patients began at their first hospitalisation during this study period. This start date was selected because it is when ICD-10 coding started being used widely in the hospitals included in the study. HF and/or AF was diagnosed according to NICE guidelines [6,24], and given an ICD-10 code for HF or AF. Data on LoS, age, gender, ethnicity, mortality and co-morbidities were available from the local health authority computerised hospital activity analysis register for all patients. The ACALM study protocol was subsequently applied to transfer this raw data into a useful search database. Prevalence rates for comorbidities presented refer to coding at any point during the study timeframe (at baseline or follow-up). We do not have access to any laboratory results or drug information. The final diagnoses, comorbidities and procedural codes at discharge were entered for each patient in the hospital electronic diagnosis database that eliminates the possibility of duplicating patients.

2.2. Data analyses

Using this dataset both cross-sectional and longitudinal analyses were performed for patients admitted with a diagnosis of HF and/or AF. In the cross-sectional analysis, disease groups (AF without HF [AF alone]; HF in SR; HF in AF) were compared to the control group composed of the remainder of the study population without a HF or AF diagnosis. Kaplan–Meier curves were used to illustrate the effect of the disease on survival and the time variable was the period from first admission to death with time zero defined as the date the patient was admitted to hospital for the first time within the study period. To determine the influence of developing new-onset AF ± HF on mortality we performed a longitudinal analysis. Patients were categorised into baseline (if the disease was present at study-entry) and developed groups (if new-onset disease was identified during follow-up) for all patients with AF, HF and the combination.

Unadjusted crude mortality rates were expressed as a percentage and unadjusted odds ratio (calculated according to Altman [25]). Adjusted mortality rates were utilised in the cross-sectional analysis and were performed by multivariate logistic regression accounting for variations in gender, ethnic group and other cardiovascular comorbidities (ischaemic heart disease, cerebrovascular disease, hypertension, chronic kidney disease, hyperlipidaemia, type 1 diabetes mellitus, type 2 diabetes mellitus, peripheral vascular disease, prior angioplasty, prior coronary artery bypass graft, prior myocardial infarction). The multivariate logistic regression was modelled and performed in SPSS version 21.0 (SPSS Inc. Chicago, IL). p values <0.05 were taken as statistically significant.

LoS was defined as the number of inpatient days during the index hospitalisation. For patients with several hospitalisations, only the LoS data for their first hospitalisation was included in the study. LoS was calculated from the admission and discharge dates and included both of these days. LoS was treated as a continuous variable and since it was normally distributed a Student's t-test was applied comparing the mean LoS in each of the three experimental groups (AF alone; HF in SR; HF in AF) in turn compared to the control group. A Levene's test for equality of variances was applied prior to the t-test. p values were calculated two-tailed and $p < 0.05$ was taken as significant.

2.3. Research governance

The data used in this study was completely anonymous, non-identifiable and non-traceable conforming to local research ethics policies. Appropriate ethics and research and development approvals were sought and obtained. Access to the ACALM database was limited to members of the ACALM study unit (PC, HU, SC, RP). Confidentiality of information was maintained in accordance with the UK Data Protection Act.

3. Results

Baseline demographics are shown in Table 1. In general, patients with HF in AF were older (76.9 vs 71.9 years) and had more comorbidities [hypertension, peripheral vascular disease (PVD), chronic kidney disease (CKD) and ischaemic heart disease (IHD)] compared to HF in SR and AF alone. Male gender accounted for around half of the study population and the majority were of Caucasian origin. Out of 929,552 patients admitted during the study period, at baseline or follow-up 31,760 patients had HF (3.42%) and 42,687 had AF (4.59%). Of the HF group, 20,768 were in sinus rhythm (SR, 65.4%) and 10,992 were in AF (34.6%). Of the AF group, 31,695 (74.2%) had AF without HF (AF alone).

3.1. All-cause mortality

Follow-up was 100% complete, and all 929,552 patients could be analysed. During a follow-up period of 13.25 years 137,054 (14.7%) of patients died in the whole database. 45.1% of AF patients and 66.5% of HF patients died. Compared to the control group, crude mortality was greater in patients with AF alone (OR 6.16, 95% CI 6.02–6.31); HF in SR (OR 13.4, 95% CI 13.0–13.8); and HF in AF (OR 18.2, 95% CI 17.5–19.0; Table 2; Fig. 1). HF patients in AF had a higher crude mortality compared to those in SR (70.8% vs 64.1%; $p < 0.0001$).

In the multivariate adjusted model, although attenuated, the same pattern persisted with adjusted OR for mortality being 3.73 for AF alone (95% CI 3.62–3.84); 6.51 for HF in SR (95% CI 6.27–6.76); and 8.76 for HF in AF (95% CI 8.31–9.23) in comparison to the control group. Other comorbidities that were also significantly associated with

Table 1
Baseline demographics of patients admitted during the study period.

Characteristic	Control	AF alone	HF in SR	HF in AF
n (%)	866,097 (93.17%)	31,695 (3.41%)	20,768 (2.23%)	10,992 (1.18%)
Mean age (years ± SD)	48.1 ± 19.9	73.3 ± 12.9*	71.9 ± 14.5*	76.9 ± 11.0*
Male gender %	43.3	52.1*	51.0*	48.9*
Caucasian %	76.5	89.1*	82.9*	89.3*
South Asian %	8.2	1.7*	5.4*	1.9*
Afro-Caribbean %	3.0	0.6*	1.7*	0.9*
Oriental %	0.7	0.3*	0.2*	0.2*
Mixed %	0.8	0.1*	0.2*	0.1*
Other %	10.8	8.3*	9.7*	7.6*
Hypertension %	16.1	47.6*	42.2*	45.9*
PVD %	0.9	4.5*	5.9*	6.2*
CKD %	1.3	6.8*	14.4*	17.3*
IHD %	7.6	28.9*	42.8*	43.2*
CABG %	0.5	3.5*	1.4*	1.3*
PCI %	1.3	1.4	2.8*	1.1
MI %	2.1	6.8*	16.0*	12.2*
Stroke %	1.9	12.0*	7.0*	10.9*
T1DM %	1.1	1.1	2.7*	1.5*
T2DM %	6.5	16.2*	22.6*	21.1*
Hyperlipidaemia %	5.2	13.5*	12.0*	10.5*

* Represents $p < 0.05$ with a univariate comparison between the control group and each of the AF alone, HF in SR or HF in AF groups at baseline and during follow-up. AF, atrial fibrillation; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; HF in AF, heart failure in atrial fibrillation; HF in SR, heart failure in sinus rhythm; IHD, ischaemic heart disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; SD, standard deviation; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.