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Trends in long-term cardiovascular mortality and morbidity in men and women with heart failure of ischemic versus non-ischemic aetiology in Western Australia between 1990 and 2005

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ABSTRACT

Background: It is uncertain if improvements in long-term cardiovascular (CV) mortality have occurred in both men and women with ischemic and non-ischemic forms of heart failure (HF).
Methods: The Western Australia Hospital Morbidity Database was used to identify all index (first-ever) hospitalizations for HF between 1990 and 2005. Patients were followed until death attributed to cardiovascular causes or censored on December 31, 2006 to determine 5-year survival. Cox proportional hazards models were used to compare the adjusted mortality hazard ratio (HR) during the study follow-up (4-year periods).
Results: A total of 21,507 patients (mean age 73.9 years, 49.1% women) were identified. Women were significantly older than men, and less likely to have ischemic HF (38.8% versus 46.1%). Over the period, age-standardized incidence of first HF hospitalization declined but with the least decline in women with non-ischemic HF (−13.3%) compared to other subgroups. Risk-adjusted 5-year CV mortality declined over the study period, with HR 0.64 (95% CI 0.60–0.68) for patients admitted in 1998–2001 compared to 1990–1993, with significant improvement in both forms of HF, and in both sexes and across age groups. However, overall total HF hospitalizations increased (+26.7%) over the period, particularly for non-ischemic HF (+43.7%), of which elderly women formed the predominant group.
Conclusions: Risk-adjusted long-term survival improved similarly in men and women, including the elderly, with ischemic and non-ischemic forms of HF during 1990–2005 in Western Australia. However, there was a growing burden of HF hospitalizations particularly for HF of non-ischemic aetiology.

1. Introduction

Heart failure (HF) is a major public health problem [1]. Although population-based studies have suggested an improved prognosis for HF since the late 1980s [2–4] survival in HF remains poor, with a 5-year all-cause mortality of 60% or more after HF hospitalization [5–7]. The advent of proven HF treatments in the 1990s, including angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, and aldosterone antagonists, has been shown to improve survival in patients with HF related to left ventricular systolic dysfunction [8–10]. Similarly, advances in evidence-based treatments including revascularization procedures in ischemic heart disease (IHD) have the potential to prolong survival in patients with IHD at high risk of developing HF [11–13]. Conversely, there is a paucity of evidence-based treatments for HF with preserved systolic function (PSF) [14].

In contrast to the usual patients included in clinical trials, population-based studies have shown that HF is predominantly a condition of older age and as much as half of the patients hospitalized with HF have PSF, which comprises women as a predominant group [14–16]. Additionally, gender differences in the genesis and treatment of HF have been reported, with men being more affected by IHD and less by hypertension than women, and with less aggressive procedure-based treatments reported in women [15–17]. Population-based studies are important as they reflect the full spectrum of patients hospitalized with HF, and can assess the impact of changing HF management on long-term survival in the total population.

We have previously reported improved mortality at 30-days and 1-year in patients after index hospitalization for HF in Western

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Australia (WA) over the period 1990 to 2005, coincident with a growing uptake of evidence-based HF treatments [17,18]. The present study extends our investigation, first, to examine trends in long-term (5-year) cardiovascular (CV) cause-specific mortality of patients after index hospitalization for HF; second, to compare trends in long-term CV mortality and hospitalization of patients with ischemic and non-ischemic forms of HF and third, to examine differences in gender and age-specific trends in these patients.

2. Methodology

2.1. Study population

The WA Hospital Morbidity Database (HMD) records principal and secondary discharge diagnoses in 21 fields for all public and private hospitalized patients in WA since the 1970s, and is routinely linked to other health data such as the death register [19]. The WA HMD was used to identify patients with an index non-elective hospitalization for HF between 1990 and 2005, defined as no prior HF admissions in WA in the previous 10 years [18]. Patients were followed until death attributed to cardiovascular causes or censored on December 31, 2006. The analyses were restricted to WA residents aged ≥ 20 years at time of the index HF hospitalization.

2.2. Identification of heart failure

HF was identified using International Classification of Diseases, ICD9 and ICD10 diagnostic codes. For the first-listed (principal) diagnosis of HF, ICD9 codes were 428x, 402.01, 402.11, 402.91, 404.1, 404.3, 425x, 518.4, 514, 391.8 and 398.91; and ICD10 codes were I50x, I11.0, I13.0, I13.2, I42x, J81, I01.8 and I020. We also identified index cases of HF as a secondary diagnosis who had a principal diagnosis of a cardiovascular condition excluding acute myocardial infarction (AMI) (ICD9 codes 411x–427x and 429x and ICD10 codes I24x–I48x and I51x) [18]. Most index HF cases (72.7%) coded HF as a principal diagnosis. The majority of cases with HF as a secondary diagnosis had a principal diagnosis of IHD (55.5%) or atrial fibrillation (AF) (34.6%).

In a random sample of 1006 patients in the WA HMD, a principal diagnosis of HF had a positive predictive value of 92.4% when compared to the HF Boston 'definite' score criteria and 98.8% for a combined 'possible' and 'definite' HF Boston score [20].

2.3. Definition of comorbidities

Comorbidities were identified from the ICD principal or secondary diagnosis codes recorded on any HMD record (with up to 21 non-specific diagnosis fields and 11 procedural fields) within 5 years prior or on index admission. The following conditions/procedures were identified: any IHD (including AMI and angina), AF, hypertension, diabetes, renal failure, chronic obstructive pulmonary disease (COPD), peripheral vascular disease (PVD), cerebrovascular disease, rheumatic heart disease, cardiomyopathy and coronary artery revascularization procedures (CARPs) including percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass graft surgery (CABG). A Charlson Comorbidity Index (CCI), as a weighted summary score, was also calculated for each person [21]. The ischemic subgroup of HF was identified as patients with a prior or coexistent history of any IHD including CARPs.

2.4. Definition of cardiovascular (CV) mortality

CV cause-specific mortality was considered as the underlying cause of death if the cause of death was assigned an International Classification of Diseases, ICD9 code (390 to 459) or ICD10 code (I00 to I99), as defined by the Australian Bureau of Statistics [22]. CV mortality rather than all-cause mortality was examined because of competing causes of death particularly among older individuals in a HF cohort.

2.5. Statistical analysis

Incident HF cases were divided into four equal calendar periods of 1990–1993 [base period], 1994–1997, 1998–2001, and 2002–2005, for comparison purposes. Survival times were calculated from the index HF admission to death (due to cardiovascular causes) within 5 years or until censored at December 31, 2006. We included all index HF cases between 1990 and 2001 for survival analysis to 5 years.

Categorical variables were presented as proportions and continuous variables as means ± standard deviation or median and interquartile range. Pearson's chi-square test was used to test for differences in categorical variables and *ANOVA*, *t*-test or non-parametric Mann–Whitney test for continuous variables. Trends (in proportions) were assessed using the Cochran–Armitage trend test. The age-standardized (index HF) rate per 100,000 population was calculated by direct standardization using the Australian 2001 population age distribution [23]. Poisson regression was used to assess trends in HF incidence rates.

Cox proportional hazards models were used to examine predictors of CV death within 5 years, with hazard ratios (HRs) and 95% confidence intervals (CIs) reported, and $p<0.05$ considered significant. For each univariate regression model, predictors with p values<0.15 were included in the multivariable models. Models included age, gender, calendar period, individual comorbidities, CCI and CARPs. CARPs performed prior to and concomitantly with the index HF admission were examined as separate covariates as they might affect subsequent mortality risk differently. The weighted summary score of CCI and individual comorbid conditions were included in the multivariable models as the inclusion of individual comorbidities as well as CCI provided better risk adjustment than the use of the CCI alone.

The statistical analyses were done with SAS 9.1 and STATA 10. Interactions were found between age and year of admission ($p<0.001$), sex and ischemic HF ($p=0.06$), and year of admission and ischemic HF ($p<0.001$). Hence, ischemic and non-ischemic analyses, stratified by age and sex, are presented. The median age (75 years) was used for age stratification.

2.6. Ethics approvals

Ethics approval was obtained from the Human Research Ethics Committees of the University of Western Australia and WA Department of Health.

3. Results

3.1. Population characteristics

Over the study period, 21,507 index HF cases (mean age 73.9 years, 49.1% women) were identified. Prior or coexistent IHD was present in 42.5% of cases (Table 1). Women were more likely to have non-ischemic HF and were on average 5 years older than men at first hospitalization irrespective of aetiology (Table 1). Both HF subgroups showed a significant increase in mean age over the study period, primarily in men with ischemic HF (from 71.5 years to 72.9 years, $p=0.001$) and in women with non-ischemic HF (from 75.3 years to 76.3 years, $p=0.018$).

In addition to IHD (including prior MI), common comorbid conditions recorded were: hypertension (47.4%), AF (34.4%), diabetes (23.7%), COPD (25.4%), renal failure (11.9%), PVD (14.2%), and cerebrovascular disease (16.3%) (Table 1). Hypertension was more prevalent in women than men (52.2% versus 42.9%), while IHD was more prevalent in men (55.2% versus 44.8%). As expected, comorbidities were more prevalent in older patients but notably diabetes was more prevalent in those aged <75 years with either form of HF (Table 1).

3.2. Trend in HF hospitalization

The age-standardized rate of index HF progressively declined over the study period for both ischemic and non-ischemic forms of HF and for both sexes. Comparing the last to first period, the greatest relative decline (−41.3%) was seen in women with ischemic HF (from 44.5 to 26.1 per 100,000 population). In contrast, women with non-ischemic HF had the smallest decline (from 62.2 to 53.9 per 100,000 population, a relative change of −13.3%). Similar trends and magnitude of relative change (−21.3% and −20.8%) were seen for men with ischemic and non-ischemic HF respectively.

Total non-elective hospitalizations for ischemic and non-ischemic HF combined increased overall by 26.7% over the study period. The increase was particularly for non-ischemic HF (+43.7%), of which elderly women formed the predominant group.

3.3. Crude mortality rates

Crude cumulative 30-day, 1-year and 5-year all-cause mortality rates for all HF patients admitted in 1990–1993 were 12.1%, 29.6%, and 62.6% respectively, and declined to 8.4%, 23.8%, and 54.1% respectively for patients admitted in 1998–2001. Similar improvements in 5-year crude CV mortality were seen in ischemic (−12.6%) and non-ischemic (−10.6%) HF subgroups (Table 2). The average declines in the 5-year crude CV mortality were not significantly different between genders for either form of HF (Table 2).

3.4. Determinants of 5-year mortality

Significant determinants of 5-year mortality identified by multivariable Cox regression models, stratified by ischemic and non-ischemic