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ABSTRACT

AIMS: To estimate age- and sex-specific incidence rates and time trends of post-stroke hip fracture (HF) in the Australian Capital Territory (ACT) and to present projections of future post-stroke HF incidence in Australia until 2051.


RESULTS: Over the study period among 1784 stroke survivors HF was recorded in 61 (3.42%) subjects (40 women and 21 men), indicating a HF incidence rate of 6.31 per 1000 stroke person-years. The standardized annual post-stroke HF incidence rate (per 100,000 person-years) in women was 1.7 times higher than in men (18.9 vs. 11.1 per, p = 0.008), and in the oldest group (>80 years) compared to aged 60–69 years was 10 times higher for women (47.54 vs. 4.73) and 4 times higher for men (26.65 vs. 6.50). Post-stroke HF occurred on average within the first 2.3 years, about 2 times more often in women aged ≥75 years (p = 0.033) and in survivors after an ischaemic stroke (p = 0.052), but age per se did not affect the time to HF. During the 11-year period the incidence rates of post-stroke HF decreased annually in total by 17.9%.

CONCLUSIONS: Post-stroke HF is relatively common, prevalent in women and occurs on average within 2.3 years after the stroke. The incidence of post-stroke HF in elderly people is decreasing. However, because of population ageing and increasing number of stroke survivors, the absolute number of post-stroke patients sustaining a HF and their proportion among the total HF population could be expected to increase.

KEYWORDS: hip fracture, stroke, epidemiology, trends, projections, elderly, Australia

Introduction

Osteoporotic hip fractures (HF) and stroke in the aged represent two major health problems globally with an increasing burden on the health care systems as the ageing population rises. Stroke is recognized as an important risk factor for HF, but the available data on post-stroke HF epidemiology remains limited and controversial. The reported increase in incidence of HF after stroke (compared to the general population) varied between 1.5 and >7 times.1–7 However, this was not observed in other studies.1–7 The data on time course of post-stroke HF also ranges significantly. HF occurred mainly within the first year of hospitalisation in one study,2 but 5.4 ± 6.4 years after stroke (median 2.9 years) in another.8 Some previous epidemiologic studies of post-stroke HF were based on self-reported history of stroke5,6 and the type of stroke often was not analyzed.1,2,4

The topic is further complicated by the large geographical variations in incidence rates and temporal trends of both HF9–15 and stroke.16–24 In the last decade in different Australian states and territories, the age-standardized osteoporotic HF incidence rates decreased, although the absolute number of HF cases has continued to rise.25–29 For stroke, there was an annual reduction of 4.0% in mortality rate,30
resulting in an increase of stroke survivors. In order to obtain comprehensive data on post-stroke HF trends and to estimate future burden, it is important to analyze and compare changes in both stroke survivors and HF standardized incidence rates, but no such studies have been performed.

Despite increasing evidence of shared risk factors and a pathophysiological link between bone metabolism and the vasculature, including an increased risk of stroke, and the documented twin epidemic (HF and stroke), studies on post-stroke HF, the most common fracture location (33%-45%) and the most serious and disabling post-stroke complication, are rare. Data regarding incidence rates, temporal trends, and time course of post-stroke HF in relation to age, gender and stroke type remain scarce and controversial. The analysis of temporal trends and projections of post-stroke HF incidence may provide better understanding of the contributing factors, indicate preventive strategies, predict the health care burden and help in health care planning and provision of resources in coming decades. However, to our knowledge, no studies have presented projections of future trends in post-stroke HF.

The aims of this study were to (1) estimate age- and sex-specific incidence rates and time trends of post-stroke HF in the population of 60 years and over in a 11-year period between 1999/2000 and 2009/2010 in the Australian Capital Territory (ACT) and provide standardized rates of post-stroke HF, (2) evaluate the role of gender, age and stroke type in temporal trends and (3) present projections of future post-stroke HF incidence in Australia until 2051.

Methods

Study sample. All patients with HF occurring in the ACT are hospitalized only in the Canberra public hospital, and all stroke patients are treated only in the Canberra and Calvary public hospitals. This provides a unique opportunity for population-based epidemiologic research. We utilized administrative databases to identify patients discharged with a diagnosis of stroke. We performed a retrospective screening of medical records of all suspected stroke cases. Separations with a principal diagnosis of International Classification of Diseases, 10th Revision (ICD-10-AM) codes 160 through 164 were included in the dataset. HF was defined by the following codes: S72.0–S72.05, S72.08, S72.10, S72.11 and S72.2. Criteria for exclusion were pathological (malignancy-associated, multiple myeloma or Paget’s disease) and multi-trauma related (e.g., motor vehicle accident) HF. In this study only cervical (neck, intracapsular) and trochanteric (extracapsular) fractures of the proximal femur were included while subtrochanteric and shaft fractures were excluded. To prevent double counting inter- and intra-hospital transfers for the same event and readmission were identified by matching date of birth, patient ID number and admission and separation dates and were excluded from this analysis. Thus, each stroke and each HF was counted only once and for stroke cases only if the patient was alive at the time of discharge. Although both patients with first-ever and recurrent strokes were included in the primary database, only the first event was included in the final analysis. Patients aged <60 years were excluded in the present study. A “stroke survivor” was defined as a person discharged after a non-fatal stroke.

We used the World Health Organization (WHO) standard definition of stroke. All stroke cases were identified with the first-listed ICD code. Cases were further categorized into subarachnoid haemorrhage (SAH, ICD-10-AM 160), intracerebral haemorrhage (ICH, ICD-10-AM 161–162), cerebral infarction (ICD-10-AM 163), ill-defined (unspecified) stroke (ICD-10-AM 164). Patients with post-stroke HF were grouped according to their age: 60–69, 70–79, and ≥80 years.

Population data. Population estimates were obtained from the Australian Bureau of Statistics. The ACT in 2006 (the time of census) had a total population of 334,119 people (1.75% of 19.9 million Australians), of whom 96.3% were white, 1.2% indigenous and 2.6% Asian, with 13.8% aged 60 years and over. Our study covered the period from July 1, 1999 until June 30, 2010. Over this 11-year period there was a 13.5% increase in the total ACT population (females +13.8%, males +13.3%) with a shift toward higher age: a 50.4% increase in people aged ≥60 years (females +48.3%, males +53.0%) and a 86.8% increase in people aged ≥80 years (females +73.5%, males +113.1%). Population estimates from 2011 onwards were obtained from the ABS population projection Series B that is based on the 2011 census and trends in fertility rates, life expectancy at birth, and migration, and most closely reflects recent trends.

Statistical analysis. Annual sex- and age-specific incidence rates (per 100,000 person-years) were determined using the population data obtained from population census of the ABS. In non-census years, population estimates from ABS were used. The annual age- and sex-specific incidence rates of stroke survivors and HFs were based on the numbers in 5-age groups. Then we calculated incidence rates of post-stroke HF for three age groups: 60–69, 70–79 and ≥80 years. The rates were also determined for haemorrhagic and ischaemic stroke subtypes. Assuming a Poisson distribution of the number of post-stroke HFs, 95% confidence intervals (CI) for the rates were calculated and the difference between incidence rates was tested.

To look into the overall trend in post-stroke HF incidence rates, sex-specific age-standardized incidence rates were calculated by the direct method using the Australian 2006 population aged ≥60 years as the standard. We also estimated in each calendar year the post-stroke HF sex-specific standardized incidence rate as a percentage of the stroke survivors incidence rate and calculated the mean over the 11-year period (1999/2000–2009/2010). Group differences were analyzed using Student’s t-test for continuous variables and chi-squared tests for categorical variables. The analyses on the association of age, gender and stroke type with time to post-stroke HF were also performed using Kaplan-Meier analysis and log-rank statistics. In addition we performed
survival analyses using Cox proportional hazards with correction for age, gender and stroke type.

The secular changes in post-stroke HF incidence over the study period were examined with a Poisson regression model in which time was considered an independent variable, whereas age and sex were covariates. The Poisson regression model used to estimate the number of post-stroke HF (PSHF) was:

$$\text{PSHF} (x_1; x_2) = e^{x_1 + x_2}$$

where \(x_1\) is the age in years and \(x_2\) the year of post-stroke HF occurrence.

To project the number of post-stroke HF in 2021 and 2051 we applied age- and sex-specific post-stroke HF incidence rates to the Australian population projections (ABS Series B "medium" data) assuming that incidence rates would remain stable at the average level in the first decade of the 21st century. Separate predictions for males and females and for three age groups (60–69, 70–79, and ≥80) were made.

The data were analyzed using the Stata software version 10 (StataCorp, College Station, TX, USA). All statistical tests were 2-sided and the level of significance was \(P < 0.05\).

The study was approved by the ACT Health Human Research Ethics Committee.

Results

Epidemiology of post-stroke hip fracture. Over the studied period (from 1999/2000 to 2009/2010), in the ACT, there were 2228 first-ever stroke hospitalized patients (1111 men, 1117 women) aged 60 years and over; 150 recurrent stroke events which occurred in 131 patients (2–5 stroke events in each person) were not included. From the analysis we also excluded 444 (19.93%) subjects who died (205 men and 239 women). The final sample included 1784 discharged alive first-ever stroke patients aged ≥60 years (9662 patient-years). The cases were classified as cerebral infarction (74.9%) and intracerebral (21.5%) or subarachnoid (3.6%) hemorrhage. No difference in incidence of cerebral infarction and hemorrhagic stroke subtypes between genders was observed. The distribution of stroke subtypes did not change over time.

The total mean duration of follow-up was 5.1 ± 3.1 (SD) years: in females 5.2 ± 3.1 years and in males 5.1 ± 3.1 years. There were 878 (49.2%) females and 906 (50.8%) males providing a female to male (F:M) ratio of 0.97. However, amongst 60–69 year old survivors 62.3% were men (F:M ratio 0.60), while in the ≥80 years old group 55.0% were woman (F:M ratio 1.22). The mean age at stroke in the study population was 77.2 ± 8.7 years. Females were significantly older (78.6 ± 8.7 vs. 75.9 ± 8.6 years, \(p < 0.001\)).

In total, over the study period among 1784 stroke survivors HF was recorded in 61 (3.42%) subjects, in 40 women and 21 men, indicating a HF incidence rate of 6.31 (95% CI 6.02–6.70) per 1000 stroke person-years. Table 1 displays the standardized incidence rates of post-stroke HF compared to the rates of stroke survivors and HF for the whole study period. Although the total incidence rates for stroke survivors and HF in the elderly were comparable, men exhibited a 1.74 times higher risk for stroke, while women had a 1.60 times higher rate for HF. The F:M ratio for incidence rates among the stroke survivors was 0.83, and among subjects with HF was 2.31. The average annual incidence rate of HF among stroke survivors was 1.43 times higher than in the general population (631.3 vs. 436.5 per 100,000 person-years). The standardized annual post-stroke HF incidence rate in women was 1.7 times higher than in men (18.9 vs. 11.1 per 100,000 person-years, \(p = 0.008\)). The average annual post-stroke HF incidence rate as a percentage of the total stroke survivors incidence rate was 3.9%, for males 2.6% and for females 5.1%. On the other hand, the average annual post-stroke HF incidence rate as a percentage of the total HF incidence rate was 3.5%, for males 4.3% and for females 3.2%. These indicate that in the elderly post-stroke population the incidence (and risk) of HF is about 2 times higher in females than in men, but among the older subjects with HF the relative incidence rate of stroke survivors is higher for men. The Kaplan-Meir survival analysis showed that the risk of post-stroke HF in females is significantly higher than in men (Fig. 1A) and the Cox proportional hazard analysis confirmed that it is 2 times higher (HR = 1.96, 95% CI 1.15–3.32, \(p = 0.013\)).

The incidence rates of stroke survivors (per 100,000 person-years) increased exponentially with advancing age

<table>
<thead>
<tr>
<th>PATIENTS GROUP</th>
<th>MALES</th>
<th>FEMALES</th>
<th>TOTAL</th>
<th>P VALUE (M-F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke survivors</td>
<td>447.5 ± 56.9</td>
<td>371.3 ± 62.8</td>
<td>402.1 ± 50.1</td>
<td>0.002</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>257.0 ± 43.2</td>
<td>594.5 ± 128.3</td>
<td>436.5 ± 86.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Post-stroke HF</td>
<td>11.1 ± 10.6</td>
<td>18.9 ± 16.5</td>
<td>15.3 ± 13.1</td>
<td>0.016</td>
</tr>
<tr>
<td>*Post-stroke HF, %</td>
<td>2.6 ± 2.5</td>
<td>5.1 ± 4.4</td>
<td>3.9 ± 3.3</td>
<td>0.008</td>
</tr>
</tbody>
</table>

*The average annual post-stroke HF incidence rate as a percentage of the stroke survivors incidence rate.

Data presented as mean ± SD.

Abbreviation: HF, hip fracture.

Table 1. Age- and sex-adjusted and standardized (to 2006 Australian population) incidence rates (per 100,000 person-years) of stroke survivors, hip fractures (HF) and post-stroke HF in the elderly population (≥60 years) of ACT (1999/2000–2009/2010).

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in both sexes from 154 in 60–69 year old to 406 in aged 70–79 years and to 1000 in the ≥80 years old. In all three age groups the incidence rates were significantly greater in men than in women (F:M ratio 0.58, 0.82 and 0.70, respectively). While among stroke survivors men dominated, there were more women among subjects with post-stroke HF aged 70–79 years (F:M ratio 1.71) and aged ≥80 years (F:M ratio 1.78), suggesting that at younger ages post-stroke women are protected from HF (F:M ratio 0.73). As shown in Table 2, the standardized incidence rates of post-stroke HF in both sexes were low before 70 years of age, rose exponentially with increasing age, and in the oldest group compared to the aged
60–69 years the incidence in females was about 10 times higher, while in males only 4 times higher. Cox proportional hazards analysis showed that age ≥75 years was associated with near 2 times higher HF occurrence (HR = 1.89, 95% CI 1.05–3.38, p = 0.033). More than one-half (52.5%) of post-stroke HF occurred in the aged ≥80 years, and three forth of these age group patients were women.

Post-stroke HF occurred within the first year in 32%, within two years in 59.0%, within three years in 72.1%, within 5 years in 85.3% and within 7 years in 96.7%. The mean time of HF occurring after the stroke was 2.34 ± 2.08 years and it did not differ significantly by age of stroke survivors neither in women, nor in men (Table 3). There was no significant difference in the mean time to post-stroke HF between patients with an ischaemic (2.30 ± 1.96 years) and haemorrhagic stroke (2.51 ± 2.79 years, p = 0.790), but the Kaplan-Meir survival analysis (Fig. 1C) indicated that risk of HF was possibly greater for survivors after an ischaemic stroke compared with haemorrhagic one (p = 0.052), and did not differ by age (Fig. 1B).

In order to investigate whether age, gender and stroke type were independently associated with time to post-stroke HF, we performed Cox proportional hazards analysis. When all data were entered in a single model, female gender (HR = 1.93, 95% CI 1.13–3.30, p = 0.016) was associated with time to post-stroke HF and ischaemic stroke (HR = 1.98, 95% CI 0.97–4.02, p = 0.059) tended to be associated with this outcome, but age was not associated when analyzed either as a continuous (p = 0.728), or as a categorical variable (p = 0.078).

Taken together, post-stroke HF occurs on average within the first 2.3 years, in total about 2 times more often in women, in the aged 75 years and above, and in survivors after an ischaemic stroke, but age per se does not affect the time to HF.

**Temporal trends.** Since survival after stroke is an important factor in determining the trends in post-stroke HF, data on the standardized annual incidence rates of stroke survivors and HF in those aged ≥60 years during the 11-year observation period are given in Figure 2. During the 11-year period, despite annual variations, there was a trend for the incidence of HF to decline in both women and men (mean annual decrease: in total −4.0%, in women −4.7% and men −3.8%) and for the incidence of stroke survivors to increase (annually +1.9% in total, +1.3% for women and +2.4% for men). Because of an increase in stroke survivors it could be expected to result in an increase in post-stroke HF incidence. In contrast to such expectation, the absolute number of post-stroke HF, in general steadily decreased among both men and women. In the last three years studied (2007/2008–2009/2010) compared to the first three (1999/2000–2001/2002), the temporal sex-specific age-adjusted standardized incidence rates substantially declined: in total by 77.2% (from 29.65 to 6.77 per 100 000 person-years), in females by 77.7% (from 38.77 to 8.65 per 100 000 person-years), in males by 75.1% (from 18.80 to 4.67 per 100 000 person-years).

The influence of age and calendar stroke year on the number and incidence rates of post-stroke HF in the 11-year period was further examined by Poisson regression analyses (Tables 4 and 5). These models explore the combined effects of age (in 10-year intervals) and the calendar period of stroke onset. Generally, the absolute number of post-stroke HF increased with increasing age (β₁) and decreased with time of stroke (β₂) by 4.6% and 14.0%, respectively (Table 4). However, stratification for sex revealed that changes related to these factors were statistically significant only in women but not in men. In women, the absolute number of post-stroke HF increased by 7.3% with each 10 years of age (p = 0.001), and decreased by 15.7% (p = 0.003) with each calendar year of stroke (β₂). The lack of significance in men (who demonstrated a similar direction of changes with calendar period) may be due to fewer cases and insufficient statistical power (rather than indicating gender difference).

In other words, in women the decreased number of post-stroke HF during the study period was influenced by the calendar year of the stroke, despite the increases with increasing age, while in men both factors (especially the year) have negative effects, which, however, were not statistically significant.

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**Table 2.** Standardized incidence rates of post-stroke hip fracture (per 100,000 person years) in the elderly by age and sex.

<table>
<thead>
<tr>
<th>AGE GROUP (YEARS)</th>
<th>FEMALES MEAN ± 95% CI</th>
<th>MALES MEAN ± 95% CI</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>60–69</td>
<td>4.73 ± 2.17</td>
<td>6.50 ± 2.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>70–79</td>
<td>12.50 ± 2.08</td>
<td>7.32 ± 2.20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥80</td>
<td>47.54 ± 2.69</td>
<td>26.65 ± 2.08</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Table 3.** Mean time (years) to post-stroke hip fracture by age and gender.

<table>
<thead>
<tr>
<th>AGED GROUP (YEARS)</th>
<th>FEMALES (n = 40) MEAN ± SE</th>
<th>MALES (n = 21) MEAN ± SE</th>
<th>BOTH SEXES (n = 61) MEAN ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>60–69</td>
<td>2.19 ± 1.27</td>
<td>2.78 ± 3.00</td>
<td>2.55 ± 2.63</td>
</tr>
<tr>
<td>70–79</td>
<td>2.86 ± 1.96</td>
<td>2.20 ± 3.25</td>
<td>2.65 ± 2.34</td>
</tr>
<tr>
<td>≥80</td>
<td>2.26 ± 1.79</td>
<td>1.60 ± 1.40</td>
<td>2.09 ± 1.71</td>
</tr>
<tr>
<td>Total</td>
<td>2.41 ± 1.85</td>
<td>2.19 ± 2.50</td>
<td>2.34 ± 2.08</td>
</tr>
</tbody>
</table>
The incidence rates of post-stroke HF in both sexes increased with ageing but decreased to a larger degree with stroke year, in total by +11.4% and −17.9%, respectively, in females by +12.4% and −18.8%, in males by +9.0% and −15.8% (Table 5). According to the model for the sex-specific incidence rates, explained variances were moderate ($R^2$ 0.28 – 0.46).  

Post-stroke hip fractures forecasts and economic impacts in Australia. These data were generated under the assumptions that the post-stroke HF incidence rates for those aged ≥60 years in the ACT region are reflective of the national Australian stroke survivors’ incidence rates and that age- and sex-specific post-stroke HF incidence rates would remain the
same over next 40 years (average for 1999/2000–2009/2010 period for each age group). The numbers of projected post-stroke HF s for the years 2021 and 2051 are based only on demographic changes (Table 6). These forecasts suggest that in Australia, compared to 2011, the total number of post-stroke HF patients aged ≥60 years may increase by 32.4% in 2021 (+30.2% in females and +36.7% in males) and by 162.5% in 2051 (+161.9% in females and +163.8% in males), of which 83.8% in 2021 and 86.6% in 2051 will be aged ≥70 while 55.2% and 67.4% will be ≥80 years, respectively. The gender distribution of post-stroke HF patients indicates that the F:M ratio among 60–69 (on average 3 women for every four men) and 70–79 year old (2 women for every man) post-stroke HF patients will not change, but among those aged 80 and above the F:M ratio will decrease from 2.76 in 2011 to 2.48 in 2021 and to 2.30 in 2051.

In 2021 post-stroke HF patients aged 70–79 years are predicted to have the largest increase (+55.6% in men and +50.6% in women), while in 2051 the greatest increase will occur in the ≥80 years old (+250.5% and +192.4%, respectively). This is likely due to the fact that the baby boom generation will reach age >70 at year 2021. Figure 3 shows the projected changes in absolute number of post-stroke HFs in 2021 and 2051 as a percentage to the numbers in 2011.

To evaluate the potential social and economic burden of the number of post-stroke HF we tried to quantify the costs. Currently no Australian data on the costs of post-stroke HF are available. However, it was reported that mean cost per hospital episode of HF ranges between AU $13,012–AU $15,984 and AU $26,023 on average AU $15,500–AU $19,500 for procedures such as partial joint replacement. No significant difference in costs between men and women was found.

It has also been estimated that direct hospital costs comprised only about 32% of the total cost. Assuming that hospital treatment of one post-stroke HF on average is also costing AU $13,012 (lowest estimated mean value), and this comprises 32% of total annual costs, each additional HF translates to an increase of AU $40,662 per year. Extrapolation of these data and applying the estimates to our projections suggest that the predicted annual post-stroke HF costs in Australia may reach AU $32,042,050 in 2021 and AU $65,710,600 in 2051. It should be, however, noted that these estimates are minimal as they do not account the history of stroke and that a significant percentage of these patients require long term residential care.

Although our data demonstrated a trend of marked annual decrease in post-stroke HF incidence rates for women and men, we did not use these results for the future forecasts because the number of cases each year was low, with substantial random variation; obviously, studies of larger populations are required before average annual percent change can be used for projections of future HF among the stroke survivors. If the incidence trends observed in Australia in the beginning of the 21st century continues, a levelling off or even decrease in the absolute number of post-stroke HF among the older adults may be expected, despite population ageing and increases in the number of stroke survivors; under such tendency scenario the health care costs should be revised.

**Discussion**

**Main findings.** This study has demonstrated that in the ACT, over the past decade in older (>60 years) stroke survivors HF was common, occurred on average 2.3 years after the stroke and tended to develop more often and earlier after an ischaemic stroke. The standardized incidence rate of post-stroke HF was near 2 times greater in women compared with men, and in the oldest group (>80 years) compared to aged 60–69 years was 10 times higher for women and 4 times higher for men. The overall incidence of post-stroke HF in the elderly has decreased. In coming decades, the total number of post-stroke HF patients and their proportion among all subjects sustaining a HF could be expected to increase due to ageing of the population (assuming that the average age- and sex-specific incidence rates of post-stroke HF observed during the study period remain unchanged).

**Post-stroke hip fracture incidence rates in the first decade of the 21st century.** Stroke increases the risk of falls,
Table 6. Forecast number of post-stroke hip fracture patients aged ≥60 years in Australia to 2021 and 2051 (incidence rates unchanged, similar to the average from 1999/2000 to 2009/2010).

<table>
<thead>
<tr>
<th>AGE GROUP</th>
<th>FEMALES</th>
<th>MALES</th>
<th>TOTAL</th>
<th>F:M RATIO</th>
</tr>
</thead>
<tbody>
<tr>
<td>60–69</td>
<td>52</td>
<td>67</td>
<td>89</td>
<td>71</td>
</tr>
<tr>
<td>70–79</td>
<td>85</td>
<td>128</td>
<td>193</td>
<td>45</td>
</tr>
<tr>
<td>≥80</td>
<td>251</td>
<td>310</td>
<td>734</td>
<td>91</td>
</tr>
<tr>
<td>Total</td>
<td>388</td>
<td>505</td>
<td>1016</td>
<td>207</td>
</tr>
</tbody>
</table>

Accelerates muscle weakness, bone loss and subsequently leads to fractures. Not surprisingly, during the 11-year study period the incidence rate of HF in our cohort of stroke survivors was 1.4 times the rate in the general population. This is comparable with a 1.7 times increase in post-stroke HF incidence observed in Scotland,1 1.7–2.3 in Taiwan,15 1.9 in the North Carolina,5 2.0 in The Netherlands3 and 2–4 in Sweden,4 but much lower than a >7-fold increase reported in another Swedish study. On the other hand, no statistically significant difference in fracture rates between post-stroke patients and controls or between persons with and without self-reported history of stroke were observed in Minnesota, US7 and in Iowa, US.5

The post-stroke HF incidence of 6.31 per 1000 person years in our study is comparable to 7.0 per 1000 person-years reported by Dennis et al,1 but lower than 17,4 19.82 and 3256 per 1000 person-years reported by others.
In published studies, the cumulative incidence of HF at 3 years post-stroke was about 3%, 39,48,54 at 5 years 9.5%–10%, 39,57 and by 10 years 10.6%. These differences in reported fracture rates might be explained by case selection, patients’ age, rehabilitation and prevention schemes, medication used and environmental factors. Looked at another way, in Australian older adults, age- and sex-adjusted and standardized incidence rates of post-stroke HF (per 100,000 person-years) is 15.3 ± 13.1 (SD) which corresponds to 3.9% of stroke survivors incidence rate and 3.5% of HF incidence rate. It has to be mentioned that in addition to the differences in study design and case ascertainment methods, the high SD and wide confidence interval may explain, at least partly, the reported “differences” in incidence rates in the literature. Therefore, these figures, although confirming the markedly higher risk of HF after stroke, should be interpreted cautiously in respect to its magnitude. More importantly, the incidence rates should be considered in regard to age and gender: breakdown by age and sex demonstrates the marked increase with age and the predominance of women.

In our study, the mean time of HF occurring after the stroke was 2.34 ± 2.08 years and it did not differ significantly by age of stroke survivors neither in women, nor in men. About ¾ of post-stroke HFs occurred within the first three years: 32% in the first year, 59.0% at two years and 72.1% at three years. This is in accordance with other data showing higher HF incidence throughout the first 2–3 years after the stroke, 1,39,54,56,58 although some studies reported the highest incidence within the first year with a rapid decrease thereafter.2,4

Post-stroke HF, as shown in ours and other studies, 1,3,15,39,54 is 2-times more common among females, although in general stroke is more common in males (at least among <80–84 years of age), 39–62 and in our sample as in some others, 63,64 the incidence rates of stroke survivors in males were higher than in female across all age groups. Interestingly, the gender distribution of HF following a stroke mirrors HF distribution in the general population: in both cohorts roughly 70% of HF occurs in women. Moreover, in this study the influence of age on post-stroke HF incidence was greater in women than in men. Post-stroke patients aged >80 years, compared to the 60–69-year-old, showed an increased incidence rate of HF of 10 times in women and 4 times in men. In previous studies older age was also associated with increased risk of post-stroke HF. 39,56 However, in some reports, HF rate after stroke compared with that in the general population was highest in patients <69 years of age, 1 patients younger than 70 had a 23-fold increased risk for HF 3 and women aged 50 to 54 years at time of stroke had a 12-fold risk of HF in the first post-stroke year. 2

Our observations of female preponderance in post-stroke HF among those aged >70 years and a greater age effect in females than in males are in line with higher F:M ratio in the general population as age increases, higher falls rates, 65 lower bone mineral density (BMD) and higher prevalence of osteoporosis in women compared with men, 37,66 as well as with increased bone loss following stroke in women compared to men, especially with prolongation of the post-menopause period. 43,67,68 The data indicates that the development of low-energy post-stroke HF in women and men is influenced by different mechanisms and provides evidence that the phenomenon of lower BMD/osteoporosis in females at stroke onset and more severe bone loss thereafter results from the effects of altered sex hormone exposure and factors intrinsic to the sex chromosomes, suggesting that this group of stroke survivors requires specific interventions. Although postmenopausal hormone therapy for osteoporosis is controversial and the use of estrogens is supported only by some groups, 69 recent publications provide new evidence of the protective effects against HF of hormone therapy and these are augmented by calcium and vitamin D supplementation. 70 The critical role of α-oestrogen receptors in bone homeostasis and the preventive effect of selective agonists of these receptors have been shown in ovariectomized rats. 71,72 Both low serum free oestradiol levels 73–75 and α-oestrogen receptor-mediated activity are associated with osteoporotic HF. 75 On the other hand, while debate on risks and benefits of menopausal hormone therapy for stroke prevention continued over the last decade, 76,77 emerging data emphasized the neuroprotective effect of oestrogens 78 and increased risk of cerebral ischaemia in animal models with long-term oestrogen deprivation and loss of α-oestrogen receptor. 79–81 This complex issue deserves further intensive research to determine timing of initiation, safety and efficacy of formulation, dose (e.g. low-dose transdermal hormone therapy, selective oestrogen receptors modifiers) and duration. In this context in the meantime, exogenous oestrogens such as soy phytoestrogens, 82 although less effective than hormone therapy, 83 may be considered, among other interventions, in treatment of post-menopausal women. Notably, at the end of the study period, in 2010, the age group of ≥80 years comprised 4.04% of the total ACT population (3.20% among men and 4.85% among women), accounted for 44.5% of stroke survivors (39.4% among men and 49.8% among women) and 52.5% of post-stroke HFs (three quarters of whom were women).

Analyzing time of HF after the stroke in regards to the age, gender and stroke type (multivariate Cox regression), we found that gender (females) and possibly stroke type (ischaemic) but not the age of stroke survivors predict earlier occurrence of HF. In one recent study, post-stroke risk of HF did not differ by stroke type, but risk of any fracture was significantly greater for haemorrhagic compared with ischaemic strokes; 79 this association was not reported by others. 1,54

Temporal trends. Time trends of post-stroke HF should be considered in relation to the trends in incidence rates of both HF and stroke survivors. Changes in survival rates may, obviously, contribute to HF incidence rate,
especially in the elderly susceptible to osteoporosis before the stroke. Large geographic variations in incidence rates and divergent temporal trends of both HF and stroke further emphasize the importance of an integrative analysis in order to obtain comprehensive data. However, the few previous epidemiologic studies evaluated post-stroke HF separately, and comparable time trends of age- and sex-specific standardized post-stroke HF incidence rates are currently not available.

Our results show that in the ACT during the 11-year period there was a significant trend for the incidence rates of HF (in the general population) to decline (annually in total by 4.0%) and for the incidence of stroke survivors to increase (annually by 1.9% in total), but the first trend was more pronounced in females (4.7% vs. 3.8%), while the second in males (2.4% vs. 1.3%). The incidence rates of post-stroke HF decreased in total by 17.9% (in females by 18.8%, in males by 15.8%). Our data on declining HF incidence rates and a greater decrease in age-standardized HF incidence among females compared with males are comparable to those reported in other Australian states, and New Zealand, as well as in many developed countries, although a levelling off or even an increase was observed in other countries especially in the oldest. A sex-specific difference in HF incidence trends (decrease in women but not in men) was observed in some studies.

Similarly, data on secular trends of stroke incidence rates are also conflicting with declining, stable or increasing incidence reported. Some found sex-specific changes in stroke incidence rates (decreased in men but unchanged in women), other demonstrated trends for older age and toward milder strokes. In Australia, over recent decades the number of hospitalisations for stroke remained stable, and there was an annual reduction of 4.0% in mortality rate. The decline in stroke mortality, which was also observed in Western Europe and North America, together with population ageing may explain the rise of the number and incidence rates of stroke survivors observed in this study. Therefore, an increase in the proportion of stroke survivors among the HF population can be expected.

Our study has encouragingly shown that in the new millennium the standardized incidence rates for stroke survivors tended to increase and rates for HF (total) significantly declined. In this circumstance, one would expect an increase of post-stroke HF. However, we found that the incidence rates of post-stroke HF were declining. This may seem especially puzzling given that stroke is frequently associated with limb weakness, spasticity and cognitive decline, accelerates bone and muscle loss, increases the risk of falls, and subsequently leads to fractures. While increased survival reflects success of stroke treatment, the decreasing incidence of post-stroke HF may indicate improvement in post-stroke management of HF risks (secondary prevention). However, the divergent time trends in the incidence rates of stroke survivors and HF makes a definitive explanation for the rates of post-stroke HF difficult indicating the complexity of the interactions between biological, behavioural, environmental and socioeconomic factors in development of HF after a stroke. Of interest, in The Netherlands, a remarkable decline in ischaemic stroke mortality after 2000 (in all age-sex groups, except for young men) was not matched by a decline in the number of stroke survivors which slightly increased.

Potential explanations for the decrease in HF incidence include increase in antisteporotic pharma-therapy, changes in lifestyle risk factors (reduced prevalence of smoking), and a cohort effect (improved nutrition, the protective effect of raised body mass index [BMI], reduction in falls risk). Of note, the osteoporotic treatment does not fully explain the temporal reduction in HF incidence, especially in men, indicating the significant contribution of other factors, which are still unknown, and should be identified in further research.

Of modifiable risk factors (diagnosis and treatment of hypertension and diabetes, reduction in cigarette smoking, and general improvements in lifestyle) attributed to decline in stroke incidence and mortality rates in high-income countries, improvements in blood pressure control at the population level has been recognized as a consistent and powerful in some but not all studies. Although stroke and HF share several risk factors (older age, cigarette smoking, BMI), it should be acknowledged that the prevalence and importance of these factors may be different for the two diseases as the magnitude and direction of current changes are different for men and women (for instance, smoking rates decrease more in males, while systolic blood pressure trends are associated with stroke trends in women, but not in men, and the benefits of controlling some of the risk factors (hypertension, smoking) might be negated by increasing incidence of other (increased BMI).

Projections. The worldwide burden of stroke from 2002 to 2030 is predicted to increase due to population ageing and increased life expectancy. In Australia in coming decades a significant increase in older stroke survivors is predicted. Assuming that the average age- and sex-specific incidence rates of post-stroke HF observed during the study period remain unchanged and adopting population projections, in Australia in 2021 and in 2051, compared to 2011, there will be a 32.4% and 162.5%, respectively, increase in the number of patients with post-stroke HF. Based on our previous estimates and forecasts for osteoporotic HF in older Australians, the proportion of post-stroke HF among all HF between 2011 and 2021 may increase from 5.0% to 7.8% (7.7% for females and 8.1% for males). It is predicted that post-stroke patients will represent a substantial and growing component among the elderly with HF. Importantly, while in Australia as in other developed countries, HF rates over the
last two decades have decreased for both men and women, the number of fractures continues to rise as the population ages. Our data indicates that post-stroke patients will represent a substantial and growing segment among the total population of elderly with HF.

**Economic impacts.** Worldwide, despite the variability in estimates, HF was identified as the most expensive fracture type, especially high for the elderly, with medical costs higher than for all other osteoporosis-related fractures combined. A recent review found that in the year following a fracture, medical and hospitalization costs were 1.6–6.2 higher than pre-fracture costs and 2.2–3.5 times higher than those for matched controls. The burden of HF is comparable to that of strokes, but no data on post-stroke HF costs is currently available. However, it was shown that HF patients with muscle atrophy/weakness had significantly higher total health care costs and each increase in American Society of Anaesthesiologists (ASA) classification doubles the daily hospital costs for elderly patients with HF. Our data show that due to demographic transition post-stroke HF in 2021 and 2051, compared to 2011, may increase by 32.4% and 162.5%, respectively, with corresponding increases of the financial burden to the society. Based on the mean HF costs in Australia during the first year after the event (at least AU $40,662.5) we estimated that annual costs for post-stroke HF in Australia may reach AU $32,042,050 in 2021 and AU $65,710,600 in 2051. These cost estimates are minimal as they do not account the patients’ pre-fracture stroke-related disability, comorbidities and the often need of long term residential care (as disability may persist permanently), factors that significantly increase the total health care costs. Of note, Australian cost estimates per HF patient appear to be consistent with international reports, which considered hospitalization costs between $US 8,358 and $US 32,195 and average cost in the first year following a HF Canadian $46,664.

The reported results and projections highlight the need of strategies to prevent post-stroke HF and may have a potential of contributing to healthcare planning and resourcing for the elderly, in whom both HF and stroke remain major public health problems.

**Strength/Limitations**

This study is novel in that it analyzed data on incidence and secular trends for post-stroke HF, stroke survivors and HF (in total) in the population aged >60 years in ACT, Australia, a well-defined area, over the last 11 years. The population-based design, complete inclusion of all hospitalized stroke survivors and post-stroke HF patients and exclusion of transfers and readmissions provided the opportunity to minimize the selection bias. The case ascertainment should be near complete, because in Australia all cases of HF are hospitalized and the stroke admittance rate is also high. There are, however, several limitations that should be considered. First, our findings are limited to one Australian territory with predominantly Caucasian population and may not be representative in other ethnic populations. Second, we were unable to investigate the possible contribution to post-stroke HF trends of stroke severity, cognitive status, co-morbidities, pre-fracture function, BMI, anti-osteoporosis medication or hip protectors use, as well as the socio-economic status. Third, although we used the entire ACT population, the number of post-stroke HF each year was low, with substantial random variation. We were able to demonstrate a significant annual decrease in post-stroke HF throughout the 11-year period, but did not use these data for forecasts, because the statistical power of this study is limited by its small sample size indicating that larger populations are required.

**Conclusions**

Post-stroke HF is relatively common, prevalent in women and occurs on average within 2.3 years after the stroke. The incidence of post-stroke HF in elderly people is decreasing. However, because of population ageing and increasing number of stroke survivors, the absolute number of post-stroke patients sustaining a HF and their proportion among the total HF population could be expected to increase.

**Author Contributions**

Conceived and designed the experiments: AF. Analysed the data: AF, JM, WS. Wrote the first draft of the manuscript: AF. Contributed to the writing of the manuscript: WS, PS. Agree with manuscript results and conclusions: AF, JM, WS, PS. Jointly developed the structure and arguments for the paper: AF, JM, WS, PS. Made critical revisions and approved final version: AF, JM, WS, PS. All authors reviewed and approved of the final manuscript.

**DISCLOSURES AND ETHICS**

As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICMJE authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers reported no competing interests.

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