Sex difference in specific-cause mortality after stroke: the Australian Stroke Clinical Registry (AuSCR)

Hoang T Phan,^{1,2} Seana L Gall,¹ Christopher L Blizzard,¹ Natasha A. Lannin,³ Amanda G Thrift,⁴ Craig S Anderson,⁵ Joosup Kim,⁴ Rohan Grimley,⁶ Helen C Castley,⁷ **Dominique A Cadilhac^{4,8}** on behalf of the AuSCR Consortium

¹ Menzies Institute for Medical Research Tasmania, University of Tasmania, Australia, ²Department of Health Management and Health Economics, Pham Ngoc Thach University of Medicine, Vietnam, ³College of Science, Health and Engineering, School of Allied Health, La Trobe University, Bundoora, Victoria, Australia, ⁴Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Victoria, Australia, ⁵The George Institute for Global Health, University of Sydney, Australia, ⁶University of Queensland, Brisbane, Australia, ⁷Neurology Department, Royal Hobart Hospital, Hobart, Tasmania, Australia, ⁸Florey Institute Neuroscience and Mental Health, Heidelberg, University of Melbourne, Australia.

- Women have a greater all-cause mortality after stroke than men.
- It is unclear whether there are sex differences in causes of death after stroke and the potential contributing factors.

Methods

- Participants were first-ever strokes admitted to 35 hospitals participating in the Australian Stroke Clinical Registry (AuSCR) from 2010-2013.
- Data on causes of death at 1 year were obtained from linkage to national death registrations
- Causes of death were categorised as:
 - Stroke
 - Ischemic heart disease (IHD)
 - Other cardiovascular disease (CVD; i.e. hypertension, atrial fibrillation, heart failure, peripheral vascular diseases, and others)
 - Cancer
 - Other conditions (e.g. digestive system, respiratory system)
- Study factors included sociodemographics, severity of stroke indicated ability to walk on admission, and acute care therapies provided in hospital
- Random-effects competing risk models, accounting for hospital, were used to estimate female:male specific hazard ratios of death with adjustment for factors that differed between men and women
- Analyses were performed by Stata 12.1. P-values ≥ 0.05 were considered as statistically significant.

Results

- Among **9,441** first-ever events 46% were women and the women were older than men (Table 1a).
- Women had fewer known causes of stroke (*defined according to the TOAST criteria Adams et al, Stroke. 1993;24:35-41*) and experienced more stroke events while in hospital for another condition (in-hospital stroke)

Table 1a. Patient characteristics

	Men (n=5059)	Women (n=4328)	p-value
	n (%)	n (%)	
Sociodemographics			
Age, median (IQR)	72.0 (61.8–81.0)	78.8 (67.8–85.9)	<0.001
Socioeconomic status			0.635
IRSAD1 (most disadvantage)	988 (19.5%)	783 (17.9%)	
IRSAD2	871 (17.2%)	752 (17.2%)	
IRSAD3	840 (16.6%)	705 (16.1%)	
IRSAD4	936 (18.5%)	840 (19.2%)	
IRSAD5 (least disadvantage)	1424 (28.2%)	1302 (29.7%)	
Born in Australia	3224 (63.7 %)	2939 (67.1%)	0.066
Cause of stroke known	2415 (47.7%)	1993 (45.5%)	0.001
In-hospital stroke	264 (5.2%)	278 (6.3%)	0.020

IRSAD: The Index of Relative Socio-economic Advantage and Disadvantage

- As shown in Table 1b, compared to men, women:
- Were less able to walk on admission (*which is used in AuSCR as a measure of initial stroke severity*)
 - Were less often discharged home

Table 1b. Patient characteristics and hospital stay

	Men (n=5059)	Women (n=4328)	p-value
Time (minutes) from onset to arrival, median (IQR)	181 (78–679)	170 (78–596)	0.983
Walking at admission	1949 (38.5%)	2812 (55.6%)	<0.001
Type of stroke			
Haemorrhagic	826 (16.3%)	744 (17.0%)	0.724
Ischaemic stroke	4071 (80.5%)	3490 (79.6%)	
Undetermined	159 (3.1%)	148 (4.4%)	
Length of stay, median (IQR) days*	6 (3–10)	6 (3–12)	1.000
Discharge destination			
Aged care	461 (9.1%)	552 (12.6%)	<0.001
Home	174 (3.4%)	337 (7.7%)	
Rehabilitation	2150 (42.5%)	1486 (33.9%)	
Hospitals/other	1510 (29.9%)	1339 (30.6%)	

* among those discharged

As shown in Figure 1, women and men received similar acute therapies. Figure 2 provides information on the proportion of deaths from different causes.

Figure 1. Evidence-based therapies

Figure 2. Causes of death up to 1 year after stroke

Among those deceased after stroke due to other CVD, compared to men, women were more likely to die from:

- Atrial fibrillation (49.2% vs 45.0%)
- Heart failure (5.5% vs 3.1%)

Figure 3: Cumulative incidence of cause-specific death up to 1 year after stroke

As shown in Table 2, compared to men, women:

- Had greater risk of death due to stroke or from other CVD
- Less often died from IHD or from cancer

However, these differences were substantially attenuated after adjusting for age and stroke.

Table 2: Specific hazard ratio (SHR) of death up to 1 year after stroke

Cause of death	Unadjusted		Adjusted for					
			age		severity		age & severity	
	SHR	95% CI	SHR	95% CI	SHR	95% CI	SHR	95% CI
Stroke	1.65	(1.42-1.91)	1.28	(1.10-1.49)	1.46	(1.25-1.71)	1.19	(1.02-1.40)
IHD	0.88	(0.65-1.18)	0.60	(0.45-0.79)	0.82	(0.60-1.12)	0.58	(0.43-0.77)
Other CVD	1.65	(1.29-2.12)	1.19	(0.91-1.56)	1.49	(1.16-1.93)	1.12	(0.85-1.48)
Cancer	0.69	(0.50-0.95)	0.67	(0.50-0.91)	0.69	(0.50-0.94)	0.67	(0.49-0.91)
Other conditions	1.17	(0.87-0.58)	0.99	(0.70-1.36)	1.08	(0.79-1.47)	0.94	(0.68-1.30)
Unknown	1.12	(0.84-1.49)	0.89	(0.64-1.21)	1.05	(0.78-1.40)	0.86	(0.63-1.17)
All-cause	1.39	(1.23-1.57)	1.08	(0.95-1.22)	1.26	(1.11-1.44)	1.01	(0.89-1.16)

There was no statistical interaction with the time to death.

Conclusions

- Cause of death after first stroke differed between genders with more deaths in women attributed to stroke or other CVD.
- Greater death in women after stroke was associated with age and stroke severity, but not access to acute care therapies.
- Our findings reinforce the need to better manage CVD risk factors in women to prevent stroke.