Sex differences in the management and outcomes of non-ST-elevation acute coronary syndromes

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Sex differences in the characteristics of acute coronary syndromes (ACS) have been described. Women present more frequently than men with non-ST-elevation myocardial infarction (NSTEMI),[1] have atypical symptoms,[2] more frequently have non-obstructive coronary artery disease (NOCAD),[2-4] and less frequently receive evidence-based therapies.[1,2]

In this study, we assessed differences in the evidence-based treatment received by men and women with non-ST-elevation ACS (NSTEACS) and in their outcomes (in-hospital and at 6-month follow-up). We also separately assessed these differences in patients with documented coronary artery disease (CAD).

We analysed Cooperative National Registry of Acute Coronary care, Guideline Adherence and Clinical Events (CONCORDANCE)[5] registry data for patients diagnosed with NSTEACS (NSTEMI or unstable angina) in 43 Australian hospitals during 23 February 2009 – 16 October 2018. Patients with type 2 myocardial infarction were excluded. The clinical outcomes assessed were receipt of guideline-based medications and invasive therapies, including cardiac catheterisation and revascularisation (percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG]). In-hospital outcomes were all-cause deaths and major adverse cardiac events (MACE: cardiac death, myocardial infarction, stroke), adjusted for age group and comorbid conditions. Procedures and outcomes at the 6-month follow-up were assessed by telephone interview. Our study was approved by the Sydney Local Health District Human Research Ethics Committee (CH62/6/2008-141).

A total of 7783 patients were eligible for our analysis, including 2422 women (31%). Mean age was higher for women than men (67.9 years; standard deviation [SD], 14 years *v* 65.3 years; SD, 13 years), as was the median GRACE risk score (105.6; interquartile range [IQR], 82–129 *v* 100.8; IQR, 81–123). The proportion of women who underwent cardiac catheterisation was smaller (1710, 71% *v* 4134, 77%), and the median time to catheterisation was longer (53 h; IQR, 28–91 h *v* 47 h; IQR, 25–77 h); NOCAD was detected in a larger proportion of women than men during catheterisation (602, 35% *v* 566, 14%). At discharge, fewer women were prescribed aspirin (85% *v* 91%), a second

Baseline characteristics and management of 7783 patients with non-ST-elevation acute coronary syndromes, Australia, 2009–2018, by sex

Variable	All patients	Women	Men	Difference (percentage points*) (95% CI)
Number of patients	7783	2422 [31%]	5361 [69%]	
Baseline characteristics				
Age (years), mean (SD)	66.1 (13)	67.9 (14)	65.3 (13)	2.7 (2.0–3.3) years
GRACE risk score (Fox), median (IQR)	102.3 (81–125)	105.6 (82–129)	100.8 (81–123)	4.8 (2.9–6.6) points
Prior myocardial infarction	2793 (36%)	738 (30%)	2055 (38%)	–7.9 (–10.1 to –5.6)
Prior heart failure	752 (10%)	225 (9%)	527 (10%)	–0.5 (–1.9 to 0.9)
Prior percutaneous coronary intervention	1957 (25%)	490 (20%)	1467 (27%)	–7.1 (–9.1 to –5.1)
Prior coronary artery bypass graft	1156 (15%)	239 (10%)	917 (17%)	–7.2 (–8.8 to –5.7)
Prior atrial fibrillation	959 (12%)	331 (14%)	628 (12%)	2.0 (0.3 to 3.6)
Chronic renal failure	817 (10%)	262 (11%)	555 (10%)	0.5 (–1 to 2)
Prior stroke/transient ischaemic attack	658 (8%)	202 (8%)	456 (9%)	–0.2 (–1.5 to 1.2)
Diabetes	2438 (31%)	796 (33%)	1642 (31%)	2.2 (0 to 4.5)
Hypertension	5242 (67%)	1688 (70%)	3554 (66%)	3.4 (1.2 to 5.6)
Dyslipidaemia	4783 (62%)	1430 (59%)	3353 (63%)	–3.5 (–5.9 to –1.2)
Smoking history (never smoked)	2931 (38%)	1264 (52%)	1667 (31%)	21.2 (18.9 to 23.5)
Peripheral arterial disease	549 (7%)	150 (6%)	399 (7%)	–1.3 (–2.4 to –0.1)
Lung disease	1048 (13%)	376 (16%)	672 (13%)	3 (1.3 to 4.7)

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Variable	All patients	Women	Men	Difference (percentage points*) (95% CI)
Killip class				
1	6836 (88%)	2098 (87%)	4738 (88%)	−1.8 (−3.4 to −0.1)
2	759 (10%)	251 (10%)	508 (9%)	0.9 (−0.6 to 2.4)
3	159 (2%)	65 (3%)	94 (2%)	0.9 (0.2 to 1.7)
4	29 (< 1%)	8 (< 1%)	21 (< 1%)	−0.1 (−0.4 to 0.3)
Cardiac arrest on admission	127 (2%)	26 (1%)	101 (2%)	−0.8 (−1.4 to −0.3)
Diagnosis				
NSTEMI	5641 (72%)	1751 (72%)	3890 (73%)	−0.3 (−2.4 to 1.9)
Unstable angina	2142 (28%)	671 (28%)	1471 (27%)	0.3 (−1.9 to 2.4)
In-hospital management				
Aspirin	7373 (95%)	2275 (94%)	5098 (95%)	−1.2 (−2.3 to −0.1)
Second antiplatelet†	6650 (85%)	2027 (84%)	4623 (86%)	−2.5 (−4.3 to −0.8)
Heparin/low molecular weight heparin	6550 (84%)	2009 (83%)	4541 (85%)	−1.8 (−3.5 to 0.0)
Cardiac catheterisation	5844 (75%)	1710 (71%)	4134 (77%)	−6.5 (−8.6 to −4.4)
Admission to catheterisation time (h), median (IQR)	48.8 (26–82)	53.0 (28–91)	47.2 (25–77)	5.8 (2.3–9.2) hours
Vessels with ≥ 50% stenosis (catheterisation)				
None	1168 (20%)	602 (35%)	566 (14%)	21.5 (19 to 24)
One	1960 (34%)	564 (33%)	1396 (34%)	−0.8 (−3.5 to 1.9)
Two	1348 (23%)	293 (17%)	1055 (26%)	−8.4 (−10.7 to −6.1)
More than two	1368 (23%)	251 (15%)	1117 (27%)	−12.3 (−14.5 to −10.1)
Percutaneous coronary intervention (PCI)	2653 (34%)	637 (26%)	2016 (38%)	−11.3 (−13.5 to −9.1)
Coronary artery bypass grafting (CABG)	758 (10%)	133 (5%)	625 (12%)	−6.2 (−7.4 to −4.9)
Discharge medications and rehabilitation‡				
Aspirin	6748/7580 (89%)	2007/2355 (85%)	4741/5225 (91%)	−5.5 (−7.2 to −3.9)
Second antiplatelet†	4955/7580 (65%)	1399/2355 (59%)	3556/5225 (68%)	−8.7 (−11.0 to −6.3)
β-Blocker	5597/7580 (74%)	1664/2355 (71%)	3933/5225 (75%)	−4.6 (−6.8 to −2.4)
Angiotensin-converting enzyme inhibitor/ angiotensin II receptor blocker	5256/7580 (69%)	1600/2355 (68%)	3656/5225 (70%)	−2.0 (−4.3 to −0.2)
Statin/lipid-lowering therapy	6849/7580 (90%)	2024/2355 (86%)	4825/5225 (92%)	−6.4 (−8.0 to −4.8)
Referral to cardiac rehabilitation	4564/7580 (60%)	1263/2355 (54%)	3301/5225 (63%)	−9.6 (−12.0 to −7.2)
Patients who underwent PCI	2103/2638 (80%)	480/631 (76%)	1623/2007 (81%)	−4.8 (−8.5 to −1.1)
Patients who underwent CABG	606/739 (82%)	97/126 (77%)	509/613 (83%)	−6.1 (−14.0 to 1.9)

CI = confidence interval; GRACE = Global Registry of Acute Coronary Events; IQR = interquartile range; NSTEMI = non-ST-elevation myocardial infarction; SD, standard deviation. * Unless otherwise indicated. † Clopidogrel, ticagrelor, or prasugrel. ‡ The denominators are the numbers of patients discharged from hospital alive. ◆

antiplatelet medication (59% *v* 68%), β-blockers (71% *v* 75%), or statins (86% *v* 92%), or referred to cardiac rehabilitation (54% *v* 63%) (Box).

A total of 4676 patients had documented CAD, including 1108 women (24%). Smaller proportions of women with CAD than of men underwent CABG (110, 10% *v* 563, 16%) or were prescribed statins at discharge (94% *v* 96%) (Supporting Information, table 1). Fewer women than men were referred to cardiac rehabilitation (750, 69% *v* 2652, 75%), including among those who had been revascularised (CABG: 97, 77% *v* 509, 83%; PCI: 480, 76% *v* 1623, 81%).

In multivariable analyses adjusted for hospital clustering and differences in baseline characteristics, adjusted mortality rates in hospital (adjusted odds ratio [aOR], 1.02; 95% confidence interval [CI], 0.71–1.46) and at six months (aOR, 0.85; 95% CI, 0.60–1.21) were similar for men and women, as were MACE rates in hospital (aOR, 0.97; 95% CI, 0.78–1.20) and at six months (aOR, 0.92; 95% CI, 0.75–1.14) (Supporting Information, tables 2–6).

The women with NSTEACS in our study received less evidence-based treatment, consistent with previous reports.[1,3] The larger proportion of women with NOCAD may partly explain the difference. However, NOCAD is not a benign condition, and

patients can benefit from secondary prevention therapies.[6] In Australia, adherence to guideline-based therapy for people with NSTEACS could be improved, especially for women in hospital and for both sexes at discharge.

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Supporting Information

Additional Supporting Information is included with the online version of this article.