Heartbeat: time for action to eliminate sex disparities in management and outcomes of patients with an acute coronary syndrome

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Sex differences in the clinical presentation of patients with chest pain and acute coronary syndromes (ACS) are well known. Even so, sex disparities persist in management and outcomes of women with chest pain. To better understand whether sex-differences in the initial assessment of patients with non-traumatic chest pain contribute to later adverse clinical outcomes, Mnatzaganian and colleagues¹ retrospectively analysed data on 54 138 adults presenting to three emergency departments (EDs) in Melbourne with non-traumatic chest pain. On multivariable analysis, women (49% of patients) were 18% less likely to be triaged as urgent, 16% less likely to be examined by a physician within 1 hour, 20% less likely to have a troponin measured and 36% less likely to be admitted to a specialised care unit. Yet, these women clearly were even sicker than the men with a 35% higher risk of death in the ED and a 36% higher risk of death during that hospitalisation. (figure 1)

As stated so clearly in the accompanying editorial by Mackay²: 'these discouraging findings should not come as a surprise to the cardiology community. Study after study, though perhaps drawn from slightly different populations and examining slightly different outcomes, has reached similar conclusions. But, time's up. Mnatzaganian and colleagues' work¹ should provide strong motivation to design and test interventions aimed at improving the care provided to women with symptoms of ACS in the first hours after presentation so that their overall outcomes can be improved.'

Sex differences in normal cardiac dimensions also have not been adequately addressed in many of the 'normal value' tables used in imaging laboratories around the world. Changes in cardiac dimensions with ageing, while possibly not 'normal' also are typical and sex-differences with ageing have not been well documented. In a series of 2505 patients over age 55

Figure 1 Admission to ICU or CCU by median age and emergency department diagnosis of acute myocardial infarction: OR (95% CI), comparing women with men. AMI, acute myocardial infarction; CCU, coronary care unit; ICU, intensive care unit; NSTEMI, non-ST elevation myocardial infarction; STEMI, ST elevation myocardial infarction.

Figure 2 Distribution of the ascending and descending aortic diameters for both men (blue) and women (red), marking mean values, the 90th and 95th percentiles.

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Table 1 Comparisons between superiority and non-inferiority trials

Characteristics	Superiority trials	Non-inferiority trials
Null hypothesis	New treatment not superior to standard treatment/placebo	New treatment inferior to standard treatment
Alternative hypothesis	New treatment is better than standard treatment/placebo	New treatment non-inferior to standard treatment
Non-inferior margin	Not applicable	Predetermined
Sequential testing	Not possible	Can be performed
Significance level	$P < 0.05$ (two-sided)	$P < 0.025$ (one-sided)
Comparator	Standard treatment or placebo	Standard treatment (seldom placebo)
Possible outcomes	1. New treatment superior (or inferior) to standard treatment/placebo 2. Inconclusive	See figure 1
Subgroup analyses	Possible	Possible

years (mean age 69 years) enrolled in the population-based Rotterdam Study, Bons and colleagues³ found that aortic diameters measured by non-contrast computed tomographic imaging were significant larger in men compared to women. In addition, mean and 95% CIs for aortic

diameters in this cohort of patients were considerably larger than normal values derived from younger populations. Mean diameter of the ascending aorta was 38 mm in men and 35 mm in women with 18.6% of men and 5.9% of women having an aortic diameter larger than 40 mm.(-

factors in clinical decision making, along with aortic size compared to age and sex stratified normal values.

Further support for the increased cardiovascular risk associated with feeling lonely is provided by a study in this issue of *Heart* of over 13 000 patients with heart disease.⁷ In patients who felt lonely the risk of all-cause mortality at 1 year was almost threefold higher in men and twofold higher in women compared to patients who did not feel lonely. However, living alone cannot be equated with loneliness because while living alone was associated with a higher risk of cardiac events in men, women living alone were not at higher risk.

In a concise and readable review article, Leung and colleagues⁸ explain the design and interpretation of non-inferiority trials. Both clinicians and trainees will want to read this article to better understand the pitfalls of this type of study design, as well as the rationale for choosing a non-inferiority over a superiority trial ([table 1](#)). They emphasise that we should focus on effect size and confidence intervals, not *p* values, in interpreting the significance of the data presented.

Patients with complex congenital heart disease resulting in a single functional ventricle often are treated early in life with a palliative Fontan procedure to connect the systemic venous return directly to the pulmonary artery, without an intervening ventricle. As these patients grow to adulthood, clinical cardiologists are increasingly expected to provide day-to-day clinical management, often in collaboration with subspecialists in adult congenital heart disease. A review article⁹ in this issue of *Heart* provides an overview on management of the adult Fontan patient, including possible complications and urgent issues ([figure 4](#)).

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Figure 3 Sex differences in vascular properties and clinical implications. AAA, abdominal aortic aneurysm; CEA, carotid endarterectomy.

Figure 4 Multiorgan dysfunction later after Fontan operation (reproduced with permission from Book *et al*¹⁰).

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Figure 5

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