JACC: ADVANCES VOL. 2, NO. 8, 2023

EDITORIAL COMMENT

Aortic Dissection in Women

Still Underappreciated?*

Richmond W. Jeremy, MBBS, PhD[a,b]

Acute aortic dissection (AAD) is an uncommon event with severe clinical consequences; however, it only represents the tip of the iceberg for the burden of thoracic aortic disease in the community. For each individual suffering dissection, there are many more with aneurysmal disease. Multiple studies during the last 30 years have examined the epidemiology of AAD, finding that the incidence of AAD increases with age and that AAD appears to be more frequent in men than in women. Current evidence describes the incidence of type A dissection as 3 to 6 per 100,000 person years with a male:female ratio of approximately 2:1.[1,2]

The findings of Marume et al,[3] published in this issue of the journal, challenge previous understanding of the epidemiology of AAD. This study describes a consecutive clinical and autopsy series of AAD over a 12-year period. In contrast to earlier studies, the incidence of AAD in patients dying before hospital admission is also examined. Key findings are that nearly 7% of patients with out-of-hospital cardiac arrest (OHCA) have underlying AAD; the incidence of AAD appears to be higher than previous reports; men and women actually have an equal incidence of AAD, but women are more likely to die before reaching hospital (prehospital mortality of 37% vs 21% for men).

These observations invite a reassessment of previous evidence on AAD in women. A study of 1,078 patients from the International Registry of Acute Aortic Dissection reported that 32% of patients with AAD were women and noted that women were older and presented to hospital later than men.[4] Similar findings have been reported by others, including a recent study of 394 patients admitted to hospitals with AAD, which reported that 32% were women, who were older and had a more aggressive clinical course.[5]

The data presented by Marume et al[3] describes a higher incidence of AAD than previous reports (men 16.7, women 15.7 per 100,000 person-years). Several factors may explain this difference, including counting of prehospital deaths from AAD and the older population in the present study. As incidence of AAD increases with age, the age distribution of a study population will influence the observed incidence of AAD. The mean age of the population in the present study is a decade older than that in past studies, including the IRAD (International Registry of Acute Aortic Dissection) study.[4] Population-specific factors, such as prevalence of hypertension, can also impact observed incidence of AAD, while genetic variation within and between populations is also likely to influence the risk of AAD.

While Marume et al[3] do not describe the hospital course and outcomes of patients admitted with AAD, multiple studies have observed poorer outcomes in women.[4,5] These include worse surgical outcomes and poorer neurological recovery, with higher in-hospital mortality. There is now a considerable body of evidence showing that women with cardiovascular disease have worse outcomes than do men.[6] There appear to be numerous factors contributing to the worse risk profile for women, including atypical symptoms, delay in presentation and diagnosis, and differences in management approaches.

An important question arising from the present findings is why women with AAD are more likely to

*Editorials published in *JACC: Advances* reflect the views of the authors and do not necessarily represent the views of *JACC: Advances* or the American College of Cardiology.

From the [a]Central Clinical School, Faculty of Medicine and Health, University of Sydney. Sydney, New South Wales, Australia; and the [b]Marfan and Aortic Disease Service, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia.

The author attests they are in compliance with human studies committees and animal welfare regulations of the author's institution and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

ISSN 2772-963X https://doi.org/10.1016/j.jacadv.2023.100624

die before hospitalization. As the authors note, more women had type A dissection, while more men had non-A and non-B dissection. Secondly, women with AAD present at a mean age of 7 years older than men, with likely age-related increase in mortality. Thirdly, other factors including atypical symptoms or delay in seeking assistance may increase mortality risk. There may well be other more subtle factors at play. Older women tend to have stiffer aortas with exaggerated systolic pulse amplification,[7] which may adversely impact hemodynamics, location of intimal tear, and propagation of aortic dissection. The tissue architecture and mechanical properties of the aorta may differ between men and women,[8] predisposing the latter to partial or complete rupture. Indeed, bloodstained pleural effusions were observed more often in women in the present study.

As noted by the authors, the limitations of the present report include those inherent to a retrospective single-site study. Similarly, the limitations of an image-based postmortem diagnosis are identified. Further reporting of clinical outcomes after hospital admission would be of interest, given the older age of the study population.

Notwithstanding these considerations, the present paper establishes that the true incidence of AAD for a given population can only be established when prehospital deaths due to AAD are identified in addition to hospital admissions. Further work will, however, be needed before the findings can be generalized. Thus, the incidence of AAD should be compared between men and women across all ages in different populations. While the present findings may be applicable to societies with older populations, the epidemiology may be different in younger populations. Secondly, comparison data is required for populations with a high vs low prevalence of hypertension and also for other comorbidities, such as cigarette smoking and diabetes.

The present study provides further impetus to address barriers to women's access to health care,[9] as well as to improve understanding of differences in fundamental cellular, biomechanical, and histopathological features of aortic disease in men and women.

There is also an important clinical caveat arising from the present findings. Multiple conditions can underlie OHCA, notably coronary artery disease with myocardial ischemia or scar, cardiomyopathy, and genetic channelopathies. When an individual complains of chest pain and then suffers OHCA, the event is usually ascribed to coronary artery disease, and the underlying AAD may be missed. This may be a critical omission, as some cases of AAD are consequent upon a genetic aortopathy, with vital implications for family screening and prophylactic treatment.[10] Given that approximately 7% of OHCAs are due to AAD, this diagnosis should be considered in all cases of OHCA.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The author has reported that he has no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Richmond W. Jeremy, Royal Prince Alfred Hospital, Suite 407, 100 Carillon Avenue, Newtown, New South Wales 2042, Australia. E-mail: richmond.jeremy@sydney.edu.au.

REFERENCES

1. Yu HY, Chen YS, Huang SC, Wang SS, Lin FY. Late outcome of patients with aortic dissection: study of a national database. *Eur J Cardio Thorac Surg*. 2004;25:683-690.

2. Howard DP, Banerjee A, Fairhead JF, Perkins J, Silver LE, Rothwell PM. Population-based study of incidence and outcome of acute aortic dissection and premorbid risk factor control: 10-year results from the Oxford vascular study. *Circulation*. 2013;127:2031-2037.

3. Marume K, Noguchi T, Kaichi R, et al. Women with acute aortic dissection have higher prehospital mortality than men. *JACC: Adv*. 2023;2:100623.

4. Nienaber CA, Fattori R, Mehta RH, et al. For the International Registry of Acute Aortic Dissection. Gender-related differences in acute aortic dissection. *Circulation*. 2004;109:3014-3021.

5. Gasser S, Stastny L, Kofler M, et al. Type A aortic dissection is more aggressive in women. *Eur J Cardiothorac Surg*. 2022;62(2):ezac040. https://doi.org/10.1093/ejcts/ezac040

6. Khraishah H, Daher R, Gareinabi M, Karere G, Welty FK. Sex, racial, and ethnic disparities in acute coronary syndrome: novel risk factors and recommendations for earlier diagnosis to improve outcomes. *Arterioscler Thromb Vasc Biol*. 2023;43:1369-1383.

7. Nethononda RM, Lewandowski AJ, Stewart R, et al. Gender specific patterns of age-related decline in aortic stiffness: a cardiovascular magnetic resonance study including normal ranges. *J Cardiovasc Magn Reson*. 2015;17:20. https://doi.org/10.1186/s12968-015-0126-0

8. Tong J, Abudupataer M, Xu X, et al. Gender differences in the dissection properties of ascending thoracic aortic aneurysms. *Interact Cardiovasc Thorac Surg*. 2022;35(2):ivac068. https://doi.org/10.1093/icvts/ivac068

9. Woodward M. Cardiovascular disease and the female disadvantage. *Int J Environ Res Public Health*. 2019;16(7):1165. https://doi.org/10.3390/ijerph16071165

10. Robertson EN, van der Linde D, Sherrah AG, et al. Familial non-syndromal thoracic aortic aneurysms and dissections - incidence and family screening outcomes. *Int J Cardiol*. 2016;220:43-51.

KEY WORDS aortic dissection risk, cardiac arrest, sex