Commentary: The X and Y of zero gender gap in outcomes of aortic dissection

Christoph A. Nienaber, MD, PhD, and Xun Yuan, MBBS, MMED

Acute aortic dissection is a disruptive event, changing life dramatically, with complex phenotypic presentation ranging from nonspecific chest or back pain to severe neurologic complications, syncope, or even sudden death. In this issue of the Journal, sex-based outcomes in acute type A aortic dissection derived from a meta-analysis and meta-regression of 9317 patients are reported. On the background of conflicting data on gender differences in perioperative outcomes of aortic surgery in acute dissection, meta-information was collected using the Newcastle-Ottawa Quality Assessment scale for bias in nonrandomized studies. Only 9 publications met criteria to analyze the primary end point of in-hospital or 30-day mortality, and the secondary cluster end-point of postoperative stroke, renal failure requiring dialysis, or reoperation for bleeding, and expressed in relation to the outcome of male counterparts. In addition, meta-regression analysis showed female sex was not associated with greater 30-day mortality (risk ratio [RR], 1.05; \( P = .67 \)), at low publication bias and medium data heterogeneity. Even the secondary cluster end point (RR, 1.07; \( P = .43 \)) need for dialysis (RR, 0.84; \( P = .32 \)) and reoperation for bleeding (0.84; \( P = .003 \)) was similar to men; only preoperative shock was associated with the first end point (RR, 1.1; \( P = .04 \)), but not female sex.

These results sound reassuring but somewhat surprising, as different from our traditional experience that women are diagnosed later with acute aortic dissection and treated less extensively than their male counterparts; along these lines, a closing gender gap was also recently reported in Germany, Japan, and Taiwan. Accordingly, decision-making for surgery should not depend on gender, but other risk factors, while the Japanese single-center study quoted similar early- and long-term mortality in female and male patients with a greater rate of reoperations in men. Finally, population-based cohort studies confirmed no significant gender differences with open repair (type A) and endovascular management (type B) in Asian patients, with a trend for better long-term outcome in male patients. So, is it time to say the gap is closed?

Well, I guess not! The problem with this meta-analysis and meta-regression is that the underlying reasons for equal outcomes in women could not be analyzed properly with only 30 days of follow-up. Moreover, type and extent of surgery has not been specified, and length of stay and managed complications are not reported; in addition, the percentage of women in those 9 studies was consistently lower than expected, which may be related to lower diagnostic yield of dissection in women, or later presentation to emergency care due to atypical symptoms and possibly greater mortality before hospital admission; thus, an element of selection bias is difficult to exclude. Underrepresentation of women could reflect biological selection, as admitted cases have declared themselves as likely survivors.

From the Cardiology and Aortic Centre, Royal Brompton and Harefield Hospitals, Guy’s and St Thomas’ NHS Foundation Trust; and Department of Cardiology, National Heart and Lung Institute, Faculty of Medicine, Imperial College London, London, United Kingdom.

Disclosures: The authors reported no conflicts of interest.

The Journal policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

Received for publication Feb 27, 2022; revisions received Feb 27, 2022; accepted for publication Feb 28, 2022; available ahead of print March 5, 2022.

Address for reprints: Christoph A. Nienaber, MD, PhD, Royal Brompton and Harefield Hospitals, Guy’s and St Thomas’ NHS Foundation Trust, Imperial College London, Sydney St, London SW3 6NP, UK (E-mail: c.nienaber@rbht.nhs.uk; J Thorac Cardiovasc Surg 2024;167:86-8 0022-5223/$36.00 Copyright © 2022 by The American Association for Thoracic Surgery https://doi.org/10.1016/j.jtcvs.2022.02.045

CENTRAL MESSAGE
Meta-analytic data are encouraging toward closing the gender gap after surgery for aortic dissection, but registries still mark worse outcomes for women and call for concerted action to close the gap.
When looking at established registries, the in-hospital mortality remains greater among women with acute type A aortic dissection, with some improvement over the last decade. The International Registry of Acute Aortic Dissection (IRAD) found differences in clinical presentation in women, including older age, distinct imaging features, and greater evidence of malperfusion, all suggesting a tailored surgical approach to reduce sex disparities and improve early outcomes. Despite more frequent complex operations in men, including Bentall, complete arch, and elephant trunk procedures, early mortality remained greater in women, with 16.7% versus 13.8% ($P = .039$); with adjustment differences between female and male mortality tapered off over the last decade. The National Patient Register and Cause of Death Register in Sweden recently published population-based figures with overall incidence of aortic dissection greater than in previous reports, but decreasing in men; surgical therapy was increasingly used in both sexes with more favorable outcomes, but less frequently offered to elderly patients with sustained difference in both incidence and outcomes among 8057 individuals, of whom 3035 (38%) were women. Remarkably, the proportion of women was greater among patients dying before admission than in hospitalized women (42% vs 36%; $P = .001$); those women were 5 years older than men at diagnosis with a 30-day mortality of 26% versus 21% in men ($P < .001$), and 17% versus 12% in men even after surgery.

It may be revealing that both analyses from IRAD showed consistently in 2004 and 2011 that women present later as a result of less typical, or less severe symptoms, causing delays to diagnosis and treatment, and subsequently, at least in the elderly subgroup, worse prognosis than men. It appears absolutely justified to question, where we stand today and what is true—are we indeed inching toward closing the gender gap of surgical outcomes in acute type A aortic dissection? From an aerial view, there is room for improvement to ensure equal treatment and better outcomes in both sexes. Delays to diagnosis and subsequent specialist treatment need to be minimized using standardized protocols and swift transportation to specialist centers. Better public awareness for typical symptoms and risk constellations, as well as ongoing education of our junior colleagues in emergency departments, are of utmost importance considering that aortic dissection is a relatively rare event. The threshold for computed tomography imaging in the emergency department should definitely be lower.

When it comes to surgery in proximal dissection, a strategic approach is probably the better option, with less aggressive surgery in women due to aortic size and fragility to improve survival rather than replacing the entire arch and even parts of the descending aorta at once. Staged strategies with a deferred endovascular component may minimize the surgical risk; other potential explanations for differences in surgical outcomes may be increased fragility of the aorta in women of older age, hormone deficiency, greater atherosclerotic burden, and long-lasting hypertension. While the overall message is encouraging, I take it with a pinch of salt, as meta-analytic approaches and meta-regression calculation provide powerful numbers but lose detail and granularity to explain observations. Conversely, IRAD and the Swedish registry provide detailed analysis of clinical comorbidity, temporal trends, and surgical technique applied over the years to male and female patients, showing us that gender gap is still reality, although with a trend to narrow. A multifaceted approach is needed to make sure that women are equally well diagnosed and treated in acute aortic dissection.

Campaigns by the Society of Thoracic Surgeons, the European Society of Cardiology, and the American College of Cardiology/American Heart Association are focusing on public awareness and teaching. Untreated hypertension needs to be understood as a serious risk factor for aortic dissection with recognition of a “new-normal” blood pressure. For the actual treatment of aortic dissection, no matter whether proximal or distal, an expert team of cardiologists, imaging specialists, and surgeons should be in place to optimize swift and relevant treatment according to standardized protocols. Finally, lifelong follow-up should be offered in specialized outpatient clinics, even reaching out to family members of patients detected and treated with dissection, to teach prevention, smoking cessation, as well as screening for hypertension. Patients with additional risk conditions such as connective tissue disorders should be informed of their elevated risk of dissection in later life and should be made aware of potential symptoms and signs of acute aortic syndrome. Only concerted efforts in our medical community may finally close the narrowing gender gap in aortic dissection.

References

