

Editorial

## Gender Differences in Patients with Acute Aortic Dissection—Insights from Clinical Features to Related Biological Mechanism

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### Editorial

Acute aortic dissection (AAD) is an age-related cardiovascular disease complicated with potentially high case fatality despite recent advances in diagnosis, surgical techniques, anesthesia, and medical/perioperative care. Epidemiology of gender-specific differences in AAD was recognized in several large series. In a large contemporary Swedish population study, 14,229 patients were found to have thoracic aortic disease from 1987 to 2002. In which, 62% were men and 38% were women<sup>[1]</sup>. The incidence of thoracic aortic disease was 16.3 per 100,000 per year in men and 9.1 per 100,000 per year in women. In this study, 40% of patients had dissection, 40% had nonruptured aneurysms, and 20% had aortic rupture. A population-based study in northern Italy showed the annual incidence of AAD was 6.7 per 100,000 in men versus 2.9 per 100,000 in women, with significant difference<sup>[2]</sup>. In spite of the predominance of male over female patients with thoracic aortic aneurysms, a higher incidence of ruptured rate has been demonstrated by epidemiologic studies<sup>[3,4]</sup>. Furthermore, a prospective population-based study<sup>[5]</sup> indicated that higher portion of out-of-hospital cardiac arrest patients with type A AAD were women. In other words, the distinctive nature of lower incidence but possible worse outcome was found in female patients.

Despite increasing interest in AAD, only few studies focus on gender-related differences in demographic, clinical presentation, treatment, and outcomes in clinical investigations. In our enrolled data, the female occupied 30.3% (43/142) of the patients with acute type A aortic dissection who received surgically treated<sup>[6]</sup>. A study from German Registry for Acute Aortic Dissection Type A (GERAADA)<sup>[7]</sup> showed that women constituted 38% of all patients and the age for female dominant was over 75 years old. Study from the International Registry of Acute Aortic Dissection (IRAD)<sup>[8]</sup> included 1078 patients (346 patients, 32.1%, were women) to examine the role of gender in AAD and its outcomes. In this study, more female patients had age over 70 years (49.7%) than that of the male patients (28.5%). The classic presentations of abrupt onset of pain in AAD were less likely found in women. Coma/altered mental status and congestive heart failure on presentation were more frequent in women, whereas pulse deficit(s) was less commonly found in women. Moreover, comparing men and women, a trend of an average delay of 4.7 hours from symptom onset to hospitalization was discovered in women and this phenomenon was further investigated by another seminal paper<sup>[9]</sup>. Considering the differences of clinical presentations of AAD between genders, the authors stated

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that in-hospital complications of cardiac tamponade and hypotension occurred more commonly among women and a trend toward higher frequency of coma/altered mental status was also found in female patients. Higher mortality was among women than men (30.1% versus 21.0%,  $P < 0.001$ ) in their report. Nevertheless, due to the relatively scarce literature, further investigation related to the topic of AAD in women should be continued in order to examine the effect of gender on presentations, management and outcomes in AAD clinically.

Even with emerging evidence of the role of gender in influencing the outcome of various cardiovascular diseases, the real biological mechanism behind diseases of the thoracic aorta and acute aortic dissection remain to be elucidated

in this setting. As we know, the large majority of the literature focused on the mechanism of aortic degeneration in aortic aneurysm. A rodent experimental model<sup>[10]</sup> implied that estrogen-mediated inhibition of matrix metalloproteinase (MMP) expression may cause less elastin fragmentation and prevent destructing the aortic walls. Moreover, Sokolis and Iliopoulos<sup>[11]</sup> analyzed and compared, via quantitative histology, tissue specimens from male and female which showed a trend of increased elastin and collagen contents in male than female tissue for most aortic wall layers in patients with ascending thoracic aortic aneurysm. MMP-2, MMP-9 staining intensity and immune-reactivity were significantly enhanced in females than males. Biomechanical examination also showed increased stiffness of female ascending thoracic aortic aneurysm and lower failure stress in female tissues in the several regions. While previous studies implied the possible role of gonadal hormone regulations and extracellular matrix degradation in the formation of aortic aneurysm between genders, such effects in AAD need further studies to be elucidated because of the different nature of clinical progression between aortic dissections and aortic aneurysms.

In summary, in spite of lower incidence in AAD, female patients have worse outcomes and higher mortality. Less typical pain characteristic and more serious clinical presentations were found during hospitalization. Some studies hypothesized hormonal or molecular explanation for such sex differences in aortic diseases. However, no specific focused studies have been reported the underlying pathophysiological changes of AAD in gender issue to date. Future efforts are needed to more clarify gender differences in the diagnosis, management, and outcome of AAD and to understand the possible causes of sex difference. Thus, it will help us begin to develop gender-specific strategies or therapies in order to improve clinical outcomes for women with acute aortic dissections.

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