

## Abdominal aortic aneurysm: Sex differences

Christina Villard<sup>a,\*</sup>, Rebecka Hultgren<sup>a,b</sup>

<sup>a</sup> Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden

<sup>b</sup> Department of Vascular Surgery, Karolinska University Hospital, Stockholm, Sweden



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### ABSTRACT

**Objective:** Abdominal aortic aneurysm (AAA) predominantly affects an elderly male population. Even so, AAA appears more detrimental in women, who experience a higher risk of aneurysm rupture and a worse outcome after surgery than men. Why women are privileged from yet are worse off once affected has been attributed to an effect of sex hormones. This review summarizes the knowledge of sex differences in AAA and addresses the changes in the aneurysm wall from a gender perspective.

**Method:** Standard reporting guidelines set by the PRISMA Group were followed to identify studies examining AAA from a gender perspective. Relevant reports were identified using two electronic databases: PubMed and Web of Science. The systematic search was performed in two stages: firstly, using the terms AAA and gender/sex/women; and secondly, adding the terms “elastin”, “collagen” and “vascular smooth muscle cells”, in order to filter the search for studies relevant to our focus on the aneurysm wall.

**Conclusion:** Current studies support the theory that sex has an effect on aneurysm formation, yet are inconclusive about whether or not aneurysm formation is dependent on female/male sex hormones or a lack thereof. The studies in women are scarce and out of those most reports primarily address other end-points, which limit their ability to illuminate an effect of sex on aneurysm formation. The complexity of the human menstrual cycle and menopausal transition are difficult to mimic in animal models, which limit their applicability to AAA formation in humans.

### 1. Introduction

Abdominal aortic aneurysm (AAA) is a condition characterised by dilatation of the abdominal aorta, Fig. 1[1]. It is the result of a continuous degradation of the structural components of the arterial wall, for reasons that remain unknown [2].

Similar to other cardiovascular disorders (CVD), increasing age, male gender and smoking are important risk factors for the development of AAA [3,4]. In AAA, the male to female prevalence ratio is especially prominent: AAA is 4–6 times more common in men. Moreover, it develops later in women [5,6]. Even so, once established AAA appears more detrimental in women, who experience a higher risk of aneurysm rupture and a worse outcome after surgery than men [7,8]. Why women in general are privileged from AAA yet are worse off once affected has been associated with changes in sex hormones [9].

This review addresses the pathology in the aneurysm wall from a sex perspective and summarizes the knowledge of sex differences in AAA.

### 2. Literature search

Standard reporting guidelines set by the PRISMA Group were followed to identify studies that have examined AAA from a sex perspective [10]. Published articles were identified using two electronic databases: PubMed and Web of Science. The systematic search was performed in two stages: firstly, using the terms abdominal aortic aneurysm and gender/sex/women (controlled vocabulary medical subject heading (MeSH) and free text); and secondly, in order to filter the search for studies relevant to our focus on the aneurysm wall, the terms “elastin”, “collagen” and “vascular smooth muscle cells” were added. The search was restricted to articles in English. The final search date was 28 January 2017. 309 articles were found and 295 articles were determined to be relevant for this review after careful reading of the abstract, text and reference list by the two authors, Fig. 2.

#### 2.1. Presentation

AAA predominantly affects an elderly male population [4]. The prevalence in men aged 65 years and older is approximately 1.7%,

\* Corresponding author at: Center for Digestive Diseases K53, Karolinska University Hospital Huddinge, 141 86 Stockholm, Sweden.  
E-mail address: [christina.villard@ki.se](mailto:christina.villard@ki.se) (C. Villard).



Fig. 1. Infrarenal abdominal aortic aneurysm (AAA). Reconstructed CT scan.

whereas the prevalence in women 70 years and older is approximately 0.5% [11,12]. The occurrence is higher in smoking men and women: approximately 5–7.5% and 1–2%, respectively [4,6,13].

Present guidelines recommend screening for AAA in men at the age of 65 years and, as suggested by a recent national report, the efficiency of a screening programme can be sustained with even lower prevalence rates [14,15]. For women the recommendations are more controversial. Due to the low prevalence rate and later development of AAA in women some guidelines advise against screening in women, whereas others propose targeted screening in the presence of risk factors, i.e. smoking, CVD and family history of AAA [16–18]. A recent meta-analysis reported a prevalence of AAA above 1% in smoking women aged 70 years and above [6].

The abdominal aorta is defined aneurysmal if it measures 1.5 times to that of the adjacent or expected normal aortic diameter [1]. In women, the definition suggests an AAA to be present at a diameter of 2.7 cm [19]. It is somewhat lower than the generally accepted threshold of 3.0 cm [20]. Due to women's proportionally smaller aortas, the relative aneurysm enlargement in women's AAA exceeds that of men's at any given diameter [21]. Aortic size index (ASI) is a measurement which takes the relative enlargement into account. ASI is higher in

women at the time of elective repair and it is potentially an important determinant for rupture risk in women, Fig. 3. [22,23] Concurrent aneurysms in the popliteal and femoral arteries are more common in men, whereas a higher proportion of women have concurrent thoracic aortic aneurysms (TAAs) [24,25].

## 2.2. Risk factors

The principal risk factors for the development of AAA are male gender, increasing age, smoking and family history of AAA [4]. Further, AAA is associated with pre-existing hypertension, hyperlipidaemia and CVD [4].

Smoking is potentially the most important risk factor for AAA, since it can be modified, unlike age and sex. Smoking influences the levels of circulating sex hormones, yet the mechanism of its effect on the aortic wall and its role in AAA formation in both sexes remain to be elucidated [26,27]. Smoking trends differ in men and women; a decline in male smoking has been observed in the last decades, whereas in women the prevalence is increasing in several countries [28]. The decline in male smoking is believed to have contributed to the drop in the overall prevalence of AAA [29]. Women who smoke have a higher risk of developing AAA than men, which suggests that smoking is more detrimental for women [30]. Smoking cessation is of importance for preventing further aneurysm enlargement and risk of rupture but women have been shown to be less likely to achieve this than men [7,31].

The influence of heredity on the risk of AAA is strong for both sexes [32,33]. The prevalence in siblings of 65 years and younger is as high as 10%, with a higher prevalence in male siblings compared with female ones [32,33]. However, comparisons of the risk of AAA for women and men in the presence of a hereditary trait should be evaluated in relation to peers of the same sex in the population. [32]

Several studies have focused on identifying a strong genetic line but have not been able to explain the pattern found in clinical practice, which illustrates the complexity of AAA development [34].

## 2.3. Progression

The aneurysm growth rate varies widely in different reports (1mm–8 mm/year) [35,36]. A recent meta-analysis reported a mean aneurysm growth rate of 2.2 mm/year, independent of sex [7].

The risk of aneurysm rupture has been associated with increasing aneurysm diameter, smoking, arterial pressure and female sex [7]. A higher percentage of women than men with AAA present with rupture: 21% of women to compare with 16% of men [37]. Women with AAA have a fourfold risk of rupture compared with men and it occurs much

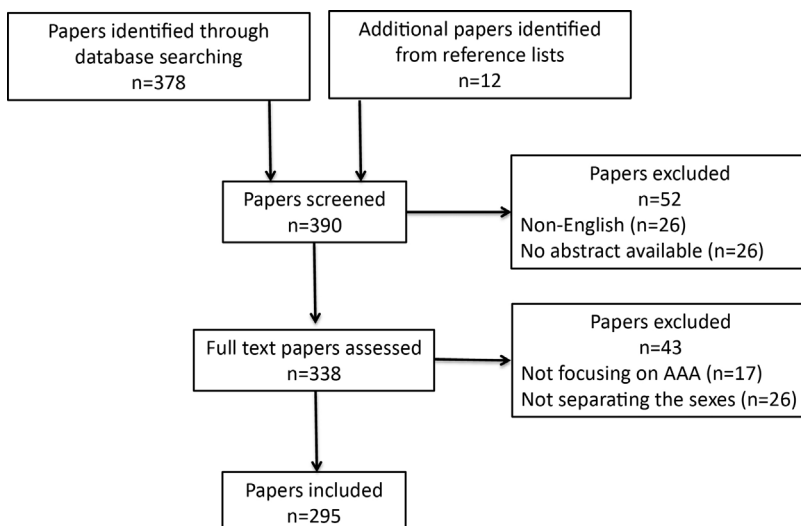


Fig. 2. Outcome of the systematic review of the literature.

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