Sex differences in abdominal aortic aneurysm

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Human Studies

- Men AAA prevalence: 1.3% 45-54 y, 12.5% 75-84 y.
- Women AAA prevalence: 0% (youngest) 5.2% (oldest).
- AAA is diagnosed about 10 years later in women than in men.
- Meta-analysis of female patients under surveillance for a small AAA (3.0-5.4 cm): 4x greater risk of rupture than men, although the growth rates of AAA were similar in both sexes.
- For a specific diameter: time until rupture is shorter in women than in men.
- The underlying mechanisms of sex differences in the prevalence and incidence as well as the natural history of AAA are not fully understood.

Go et al. Circulation 2014. Scott et al. Br J Surg 2002. Sweeting et al. Br J Surg 2012. Wilson et al. J Vasc Surg 2003.

Human Studies

- Women are at higher risk of death after AAA repair irrespective of patient- and hospital- related factors.
- Female sex (OR, 1.54;95% CI, 1.38-1.70) is associated with increased mortality which is more pronounced of iAAA (1.93;95% CI, 1.66-2.25) than rAAA (1.29;95% CI, 1.13-1.48).
- A systematic review and meta-analysis of sex- based differences (236 studies): female patients more likely to present with a rAAA (OR, 1,18;95% CI, 1.09-1.28) than male patients. The all cause mortality for those with an AAA (RR, 1.35,95% CI, 1.20-1.52) was higher for the women.

Tedjawirja et al. Br J Surg 2022.
Shimena et al. J Vasc Surg 2022.
Ho-Yan Lee et al. J Vasc Surg 2022.

Human Studies

- Female sex ↑ in hospital mortality, peri-procedural complication, and spinal cord ischemia after elective complex EVAR of pararenal AAA.
- Female patients higher incidence of transfusion, pulmonary and bowel complications, additional arterial injury, embolization, leading to renal and limb ischemia.
- Women with AAA 6.1 to 7cm: 3y cumulative inc of rupture of 12.8% (95%CI, 7.5-19.6%) vs 4.5% (95%CI, 3-6.5%) in men (p=0.002).

Behrendt et al. Ejves 2021.
Pouncey et al. Ejves 2021.
Lancaster et al. J Vasc Surg 2022.

Male and female aortas 14 days after elastase perfusion

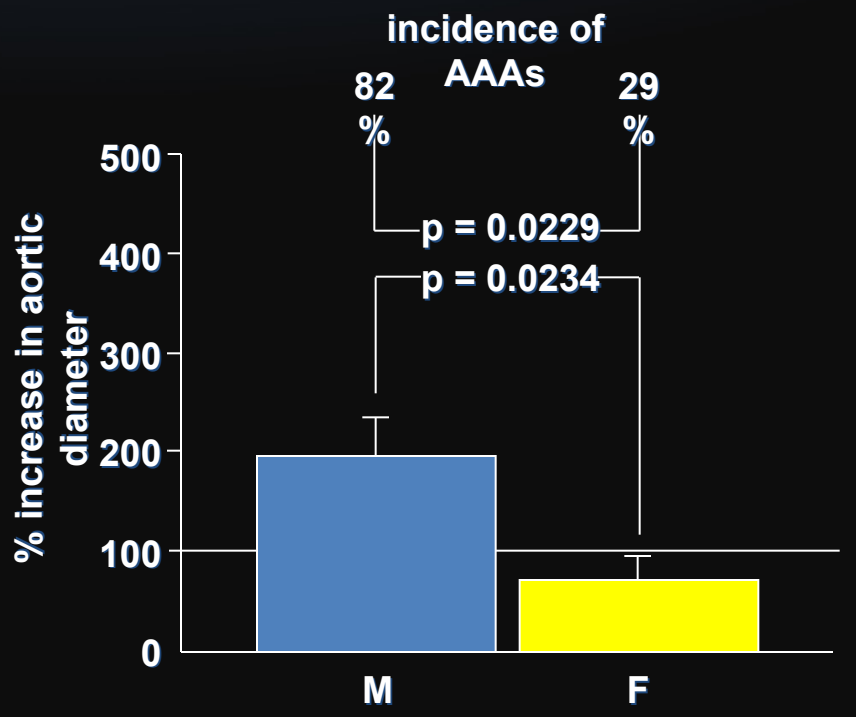
15 male mices

15 female mices

elastase - perfusion

one week AAA measurements

two weeks AAA measurements



Gorav et al, ATVB;2004

Estradiol-treated male aortas subjected to elastase perfusion

male mices

13 → 17 β-estradiol

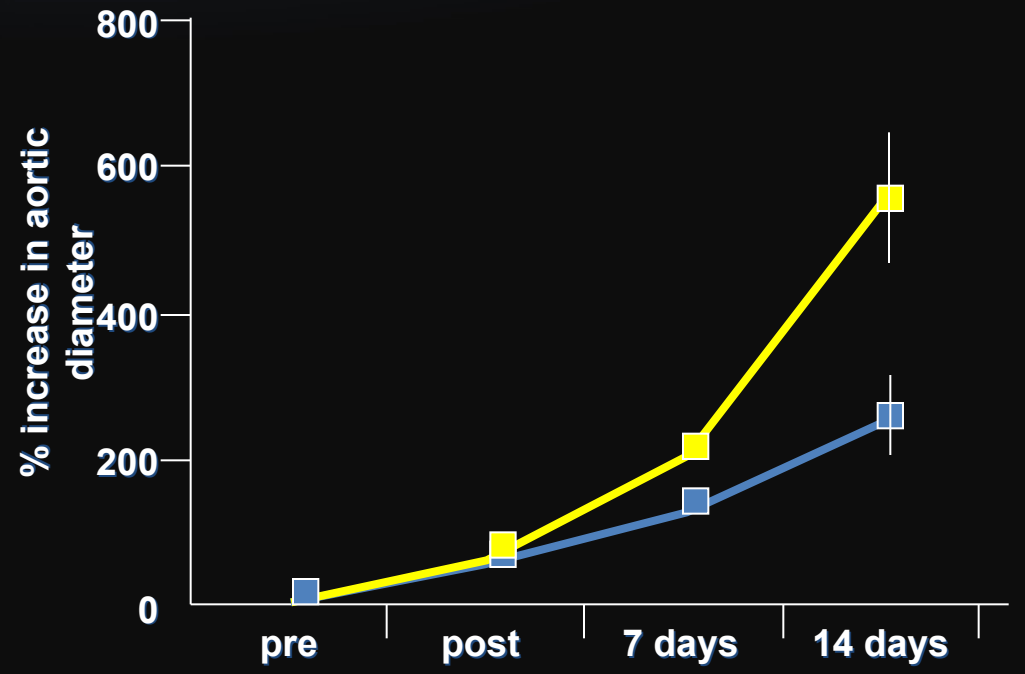
13 → CONTROL

21 days

elastase - perfusion

one week
AAA measurements

two weeks
AAA measurements



Gorav et al, ATVB;2004

Animal Studies

- Consistent sexual dimorphism with much greater inc of AAA in males.
- Gonadectomy studies: clear effect of removal of testes in reducing AAAs, while removal of ovaries minimal effect.
- Dimorphism: attribution to both hormonal and chromosomal influences.
- Recent studies: protection of females with 2 X chromosomes from AngII-induced AAAs.
- The absence of a 2nd X chromosome promotes AngII-induced AAAs.

Sawada et al. ATVB 2022.

Conclusion

- Males and females with AAAs (human and animal studies): significant epidemiological, biomechanical, and pathophysiological differences.
- **Sex steroids** likely play an important role in mediating sex differences in AAA through **regulation of the ECM** and the **inflammation of aneurysmal wall.**
- Female sex hormones regulate certain cytokines, chemokines, and other proteins with the majority consisting of members of MAPKs, such as AKT, JNK, ERK, and as a result they inhibit the expression and activity of certain MMPs, especially MMP2 and MMP9, providing a **protective role** in aneurysm formation.
- Female sex hormones: direct **anti-oxidant** effect, generation of **nitric oxide**, prevention of **apoptosis.**
- Despite of the many detrimental effects of testosterone, some studies revealed that androgens exert **atheroprotective** effects against cardiovascular disease at least in the elderly people, mediated by the androgen receptors.
- Lower levels of testosterone had harmful effect on AAA and on the cardiovascular system in men.