**Introduction**

- Despite remarkable advancements in surgical technique, particularly in the endovascular space, no pharmacologic therapy has successfully slowed or halted abdominal aortic aneurysm (AAA) growth.1
- Aortic vascular smooth muscle cells (VSMCs) are innervated by the abdominal aortic plexus and the aortic wall is subject to three principle hemodynamic forces: 1) wall shear stress, 2) hydrostatic pressure, and 3) relative wall strain.2
- Biomechanical strain induces changes in VSMC phenotype, gene and protein expression, as well as apoptosis. [2] Aortic wall homeostasis is thus balanced, in part, by biomechanical forces derived from sympathetic nervous system (SNS) innervation and subsequent derangement may play a fundamental role in the aortic wall degeneration seen in AAA.

**GOAL:**
Investigate the relationship between SNS dysregulation and abdominal aortic wall morphology to further elucidate the mechanism of AAA pathogenesis and expansion.

**HYPOTHESIS:**
Dysfunction of sympathetic innervation to the abdominal aortic smooth muscle is an important factor to the onset of aortic dilatation and progression of aneurysmal disease.

**Methods**

**Animals:** ApoE KO mice, male, age 12-weeks

**Procedures:**
- Subcutaneous osmotic mini-pump implantation (ALZET Model 1004) for continuous Angiotensin II (AngII) infusion
- Intraperitoneal (IP) injection of 6-hydroxydopamine (6-OHDA) or buffer control

**Results**

Double denervation reduces survival in comparison to AngII and late denervation.

**Control**
- -
- -

**AngII Group**
- + -
- -

**Late Denervation Group**
- - +
- -

**Double Denervation Group**
- + +
- +

Systemic denervation, when paired with AngII infusion, induces greater max aortic diameter in surviving mice.

**Control**
- -
- -

**AngII**
- + -
- -

**Double Denervation**
- + +
- +

**Conclusions**

1. **Mortality:** Double denervation, when paired with AngII infusion, is associated with increased aortic-related mortality
2. **Aortic Diameter:** Double denervation, when paired with AngII infusion, is associated with greater aortic diameter in surviving mice
3. **Nerve Fiber Density:** Aortas from control ApoE-/- mice demonstrate low nerve fiber count with subsequent increase after AngII infusion
4. **Denervation:** Systemic denervation is achievable with IP 6-OHDA and double denervation confers sustained effects through aneurysm model timeline (28 days)

**Impact:**
Solidifying the connection between the SNS and AAA pathogenesis will provide a pivotal platform to investigate future pharmacologic, cellular, and even surgical therapies for AAA. Modulation of aortic sympathetic innervation remains a promising strategy with potential for cardiovascular disease broadly.

**Future Directions**
Systemic sympathetic denervation can be achieved via IP injection of 6-OHDA, however there is evidence of neural regeneration at two weeks.

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**References**