Nicotine is a regulator of segmental aortic stiffening –
Implications for AAA development

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I have the following potential conflicts of interest to report:

☐ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

☑ I do not have any potential conflict of interest
Segmental aortic stiffness contributes to AAA development and progression

Segmentally stiff aorta
Homogeneous aorta

Diastole
Systole
Tissue glue

Artificial vascular stiffening adjustment utilizing tissue-glue-application to the proximal adjacent segment of AAA during PPE surgery

Porcine Pancreas Elastase -> mice

28 days follow-up

Gene expression in murine aneurysm

Raaz U et al. Circulation. 2015
The burden of nicotine in AAA disease

Hypothesis:

Nicotine (e-cigarettes) causes different vascular stiffness development in the abdominal (AS) and thoracic (TS) aortic segment and enhances segmental aortic stiffness (SAS)

Implications for Abdominal Aortic Aneurysm Susceptibility?

**Mouse model - setup**

**Function:**
- Ultrasound: -> global aortic stiffness by PWV
- Pressure-myography: -> segmental aortic stiffness

**流程图:**
- nicotine implantation
- 40 days
- Ultrasound

**TS**
**AS**
Nicotine increases pulse wave velocity (global aortic stiffness marker) and primarily affects the abdominal (AS) rather than the thoracic aortic (TS) aortic segment.

**Conclusions**
- Nicotine primarily stiffens the AS vs. TS.
- We conclude that the difference in stiffness development for TS and AS may in part explain nicotine’s role in promoting AAA.

Wagenhaeuser MU et al. Front. Physiol. 2018
Similar elastin degradation in the abdominal and the thoracic aortic segment – higher elastin baseline content in the thoracic aortic segment

Wagenhaeuser MU et al. Front. Physiol. 2018
Nicotine up-regulates MMP-2/-9 in the aortic wall and increases MMP activity

Conclusions

- Nicotine up-regulates mmp-2/9 gene and protein expression and enhances overall mmp activity in the TS and AS.
- Although nicotine uniformly upregulates MMP expression in the aorta, the lower basal elastin content of the abdominal aorta may render this segment particularly susceptible to stiffening effects.

Wagenhaeuser MU et al. Front. Physiol. 2018
MMP-2/-9 inhibition normalizes global aortic stiffness

Conclusions

• MMP-2/9 inhibitor is effective to contain MMP activation and arterial stiffening in nicotine-treated mice.

Wagenhaeuser MU et al. Front. Physiol. 2018
Overall Conclusion - summary

• Nicotine enhances aortic PWV *in vivo*.

• Nicotine up-regulates mmp-2/9 gene and protein expression and enhances overall mmp activity in the TS and AS.

• Nicotine primarily stiffens the AS vs. TS.

• Although nicotine uniformly upregulates MMP expression in the aorta, the lower basal elastin content of the abdominal aorta may render this segment particularly susceptible to stiffening effects.

• We conclude that the difference in stiffness development for TS and AS may in part explain nicotine’s role in promoting AAA.

• MMP-2/9 inhibitor is effective to contain MMP activation and arterial stiffening in nicotine-treated mice.
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