Background

- COPD is a well known risk factor for aneurysmal rupture
  under ultrasound surveillance. UK SAT Participants. Brown LC and Powell JT

- However, spirometry studies in the Viborg study showed
  all screening diagnosed AAA had obstructive pulmonary
doctor.

- Lindholt JS, Jørgensen B, Kletter NA, Henningsen EW. Systemic levels of cotinine and
  elastase, but not pulmonary function, are associated with the progression of small

- Only 13% used bronchodilators, indicating only a small
  fraction of AAA patients have some component of
  reversible obstructive pulmonary disease (ROPD).

- Use of bronchodilators was associated with transient
  increased growth rate, while the FEV1/expected FEV1
  ratio were not
  – indicating other still unknown important mechanisms

Methods and material

3 step translational research

- 1. VIVA: Subgroup study of all participants from the
  population-based randomized Viborg Vascular (VIVA)
screening trial (615 AAA and 18.238 controls).

- 2. DCCS: Population-based, Danish, nationwide, case-
  control study included all patients with a first-time
  admission for rAAA and up to five age- and sex-
matched AAA controls without rupture in Denmark
  from 1996-2012 (N=4,747 rAAA and 17,272 intact AAA)

- 3. Experimental angiotensin II AAA mice +/- ovalbumin
  sensitization and challenge to develop allergic lung
  inflammation (ALI)

Pharmacoepidemiological results

VIVA trial

- In the VIVA trial, anti-asthma medication showed
  45% significantly increased risk of AAA regardless of
  adjustment for smoking or other risk factors
  (Crude OR=1.45, Adj. OR=1.46).

- YKL-40 were significant higher in AAA patients
  compared to controls, and among users of
  bronchodilators compared to non-users

<table>
<thead>
<tr>
<th></th>
<th>AAA</th>
<th>Controls</th>
<th>P-value</th>
<th>Use of Bronchodilator</th>
<th>No-use of Bronchodilator</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>YKL-40</td>
<td>19.12±1.55</td>
<td>14.97±1.72</td>
<td>0.001</td>
<td>0.001 (1.01-2.85)</td>
<td>0.001 (1.01-2.85)</td>
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</tbody>
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DCCS: Pharmacoepidemiological results

- No disclosures
Results 2

- Simultaneous production of acute lung inflammation in AAA mice
- - doubled abdominal aortic diameter
  - increased macrophage and mast cell content, and arterial SMC loss a.o.
- ALI also increased plasma IgE, reduced plasma interleukin-5, and increased bronchioalveolar total inflammatory cell and eosinophil accumulation.

Results 3

- Intraperitoneal administration of an anti-IgE antibody* suppressed AAA lesion formation and reduced lesion inflammation, plasma IgE, and bronchioalveolar inflammation.

* Commercially available

CONCLUSIONS

Pharmacoepidemiological population-based studies showed reversible obstructive pulmonary disease as Asthma - especially recent active asthma - significantly increases risk of AAA and AAA-rupture.

An association between ALI and AAA in Ang-II–induced AAA mice was established. Mice with ALI from an inhaled allergen showed significantly enhanced AAA progression, before, during, or after AAA induction.

These translational findings document and furnish novel links between airway disease and AAA, two common diseases that share inflammatory aspects opening a potential novel treatment.