Critical review of the murine AAA models

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Disclosure of Interest

Speaker name: Raphaël Coscas

• I have the following potential conflicts of interest to report:
  • Consulting: Medtronic, Bard, Abbott, Spectranetics, Terumo
  • Employment in industry
  • Shareholder in a healthcare company
  • Owner of a healthcare company
  • Other(s)

• I do not have any potential conflict of interest
Less open surgery and aortic specimens

Diagnosis and interventions at late disease stage

No clearly proven medical therapy

Experimental AAA Models
The ideal AAA model

- Thrombus
- Rupture
- Continuous growth
- Atherosclerosis
- Medial proteolysis
- Leucocyte infiltrate
Classifications of current AAA models

• Murine / Large animals
• Surgical / Chemical / Genetic
• Non dissecting / Dissecting
Intra-aortic Elastase Perfusion

Anidjar et al. Circulation 1990
MRI

Intraluminal thrombus

Thrombus

Neutrophils

Blood


Non dissecting

- Simple
- Thrombus
- ECM destruction

- Not constant
- No rupture
- Healing

- Porphyromonas Gingivalis injections
Healing at Day 21
Mesenchymal cells
Elastase +
*Porphyromonas*
*Gingivalis* injections
Adventitial elastase application

Useful in mice
Genetic modifications

Bhamidipati et al. Surgery 2012
Decellularized aortic xenograft

- Guinea pig ➔ Lewis rat
- Decellularization SDS
- ECM assessment

- Constant
- Thrombus
- ECM destruction
- Adaptive immunity

- Micro-surgery
- No rupture
- Healing

- Porphyromonas Gingivalis injections

Rupture induced through adaptive immunity activation

Calcium Chloride Application

- Simple
- Mice
- Intercellular Conductance
- Calcifications

- Moderate dilatation
- No atheroma
- No Thrombus
- No rupture
- Healing

Saccular Aneurysm

Calcifications

Free DNA

Fe^{++}

Fe^{+++}

H. Etienne, Coscas R, Michel JB et al., presented at the 2017 ESVS congress
Angiotensin II perfusion + High fat diet

- Apo E -/- Mice
- Dissecting aneurysm
  - Simple
  - Thrombus
    - Not constant
    - Suprarenal
    - Parietal thrombus
    - Healing

*Daugherty et al. J Clin Invest 2000*
β-aminopropionitrile administration

- « Lox » inhibitor
- ECM maturation
- Genetic model: « Blotchy Mouse »
- Family thoracic aneurysms

- Association with angiotensin II leads to Rupture

Maki et al. Circulation 2002
### AAA models vs. human AAAs

<table>
<thead>
<tr>
<th>Human Pathology</th>
<th>Aortic Elastase Perfusion</th>
<th>Xenograft</th>
<th>CaCl₂ Application</th>
<th>Angiotensin II Perfusion</th>
<th>BAPN</th>
<th>Saccular Model</th>
<th>MCR Agonist + Salt</th>
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<tbody>
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<td>Rupture</td>
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<td>Persistent growth</td>
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<td>Medial degeneration</td>
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<td>Leukocyte infiltration</td>
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BAPN indicates β-aminopropionitrile; CaCl₂, calcium chloride; ILT, intraluminal thrombus; IMT, intramural thrombus; and MCR, mineralocorticoid receptor.

*May occur very early.
†Observed when using decellularized grafts.
Conclusion

• The ideal AAA model has not been created yet

• Each model allows to study one part of the human pathophysiology

• Research should focus on models with continuous growth and/or rupture
9th International Meeting on Aortic Diseases

New insights into an old problem CHU Liège, APF

www.chuliege-imaa.be