Circulating miRNAs signature in unstable abdominal aortic aneurysms with positive 18FDG-PET

Audrey Courtois
Disclosure of Interest

Speaker name: Courtois Audrey

- I have the following potential conflicts of interest to report:

  Grants from: FP7 European Program: "Fighting Aneurysmal Diseases"
  n° 200647
An uptake of FDG detected by PET/CT is observed in some AAA (Sakalihasan et al., EJVS, 2002)

In some cases, the FDG uptake site detected by PET/CT corresponds to the rupture site.

The FDG uptake site corresponds to the high peak wall stress site (Xu et al., EJVS, 2010)
Symptoms: accelerating growth, pain

Inflammation: inflammatory cells in the wall, cytokines (CCL18)

Matrix remodeling: MMP, collagen expression

Smooth muscle cells loss: α-SMA positive cells

Courtois et al., Journal of Nuclear Medicine, 2013
Courtois et al., Molecular Medicine, 2015
Potential biomarkers?

Circulating microRNA

small non-coding RNA
Stable in the blood
Correlated with some diseases
<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>A0 (n=35)</th>
<th>A+ (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>74 (68-79)</td>
<td>75 (68-81)</td>
</tr>
<tr>
<td>Gender distribution (M/F)</td>
<td>35/0</td>
<td>20/2</td>
</tr>
<tr>
<td>Aneurysm diameter (mm)</td>
<td>54 (50-62)</td>
<td>55 (51-59)</td>
</tr>
<tr>
<td>SUV</td>
<td>0.43 (0.35-0.62)</td>
<td>0.96 (0.87-1.09)***</td>
</tr>
<tr>
<td>Cardiovascular events</td>
<td>20/35</td>
<td>9/22</td>
</tr>
<tr>
<td>Hypertension</td>
<td>22/35</td>
<td>14/22</td>
</tr>
<tr>
<td>Smokers:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Current</td>
<td>12/35</td>
<td>7/22</td>
</tr>
<tr>
<td>- Former</td>
<td>20/35</td>
<td>12/22</td>
</tr>
<tr>
<td>COPD</td>
<td>16/35</td>
<td>7/22</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3/35</td>
<td>5/22</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>23/35</td>
<td>13/22</td>
</tr>
<tr>
<td>Statins</td>
<td>19/35</td>
<td>12/22</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>11/35</td>
<td>6/22</td>
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<tr>
<td>Calcium channel blocker</td>
<td>4/35</td>
<td>4/22</td>
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<tr>
<td>ACEI</td>
<td>4/35</td>
<td>2/22</td>
</tr>
<tr>
<td>NSAID</td>
<td>0/35</td>
<td>1/22</td>
</tr>
</tbody>
</table>

Uptake of FDG measured = Standardized Uptake Value (SUV) = SUV AAA/ SUV Liver
First experiment on plasma samples from A0 and A+ patients

A0

4 pools of samples

Realtime PCR for 380 miRNA

Comparison of miRNA expression

3 pools of samples

A+
- 9 miRNA were downregulated
- 8 miRNA were upregulated
6 miRNA were significantly modulated in A+ patients as compared to A0 patients
The ROC curves show the discriminating powerfull of the four downregulated miRNAs
And in the wall:

A0 (n=12)  A+ (n=9)

A+_{neg}  A+_{pos}

miR-99b-5p (A.U.)  miR-125b-5p (A.U.)  miR-204-5p (A.U.)

A0  A+_{neg}  A+_{pos}  A0  A+_{neg}  A+_{pos}  A0  A+_{neg}  A+_{pos}
- MMP13 is a validated target of miR-125b-5p and was previously showed to be increased in the A+pos site of aneurysm

![Graph A](image)

\[ r = -0.72 \]
\[ p = 0.003 \]

![Graph B](image)

\[ r = -0.63 \]
\[ p = 0.01 \]

- In the media of A+ patients, miR-125b-5p and miR-204-5p were significatively and negatively correlated with MMP13
CONCLUSION

- 17 circulating miRNA were modulated between A0 and A+ patients and 6 of them were validated by realtime PCR

- The 6 miRNA modulated were significantly correlated with the SUV (AAA/liver) while two miRNA were correlated with the diameter of AAA

- miR-125b-5p has the higher AUC calculated on ROC curves

- miR-99b-5p, miR-125b-5p and miR-204-5p were downregulated in the aneurysmal wall at the specific FDG uptake site

- MMP13, a validated target of miR-125b-5p involved in the progression of AAA, was negatively correlated with this miRNA and with miR-204-5p

miR-125b-5p could represente a new potential biomarkers of the degradation of AAA leading to rupture
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