Assessment of Treatment Response by $^{18}$F-Fludeoxyglucose Positron Emission Tomography (FDG-PET) in Patients with Large Vessel Vasculitis (LVV)

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Large Vessel Vasculitis

Healthy

Takayasu’s arteritis

- Blocked R Subclavian
- Narrowed L Carotid
- Blocked L Subclavian
- Widened Pulmonary Artery
FDG-PET CT in Large Vessel Vasculitis

Progression of Vascular Inflammation
Study Objectives

• To study if change in treatment is associated with change in FDG-PET activity in LVV

• To determine if specific therapies for LVV impact vascular FDG uptake
Methods

- Patients with giant cell arteritis (GCA) or Takayasu’s arteritis (TAK) recruited into prospective, observational cohort of LVV

- FDG-PET/CT at 6-month intervals (256 matrix, 3mm slice, 2 hour uptake time)
Standardized Uptake Values (SUVs)

• Semi-quantitative analysis of vascular FDG uptake

• Limitations of SUV as measure of vascular FDG uptake
  – Values are machine specific
  – Cannot be compared longitudinally
Target to background ratio (TBR)

- \( TBR = \frac{SUV_{\text{max}} \text{ Aorta Region}}{SUV_{\text{mean}} \text{ Liver}} \)

- Standardized uptake values (SUVs):
  - Ascending aorta and arch
  - Descending aorta
  - Liver (background)

- Change in TBR in each aortic region calculated between interval visits
<table>
<thead>
<tr>
<th>Treatment Status between Interval Visits</th>
<th>Criteria for Treatment Status Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased</td>
<td>Increase in average daily prednisone over past 7 days by $\geq 5$ mg</td>
</tr>
<tr>
<td>Decreased</td>
<td>Decrease in average daily prednisone over past 7 days by $\geq 5$ mg</td>
</tr>
<tr>
<td>Unchanged</td>
<td>Change in average daily prednisone over past 7 days by $&lt; 5$ mg</td>
</tr>
</tbody>
</table>
## Results

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total number of patients</strong></td>
<td>20</td>
</tr>
<tr>
<td><strong>GCA and TAK</strong></td>
<td>14 and 6</td>
</tr>
<tr>
<td><strong>Total number of visits</strong></td>
<td>49</td>
</tr>
<tr>
<td><strong>Patients treated with Glucocorticoids (GC)</strong></td>
<td>15 (75%)</td>
</tr>
<tr>
<td><strong>Patients treated with methotrexate (MTX)</strong></td>
<td>10 (50%)</td>
</tr>
<tr>
<td><strong>Patients treated with other DMARD/biologic</strong></td>
<td>8 (40%)</td>
</tr>
<tr>
<td><strong>Increased treatment</strong></td>
<td>11 visit intervals</td>
</tr>
<tr>
<td><strong>Decreased treatment</strong></td>
<td>5 visit intervals</td>
</tr>
<tr>
<td><strong>No change in treatment</strong></td>
<td>11 visit intervals</td>
</tr>
</tbody>
</table>

*Simultaneous decrease in GC with increase of DMARD over 2 treatment intervals excluded from analysis.*
Change in TBR of Aorta Among the 3 Treatment Categories

**Descending Aorta**
- **Increase in treatment**: 1.97, 1.58
- **Decrease in treatment**: 1.15, 1.36
- **No change in treatment**: 1.51, 1.51

**Median TBR values**
- **First Visit**: 1.73, 1.5, 1.18, 1.3
- **Follow up Visit**: 1.47, 1.48

**NS**: Not significant

**Increasing TBR in the Descending Aorta**
- **p = 0.01**

**Ascending Aorta (AAo) and Arch of Aorta**
- **Increase in treatment**: 1.97, 1.58
- **Decrease in treatment**: 1.15, 1.36
- **No change in treatment**: 1.51, 1.51

**Median TBR values**
- **First Visit**: 1.73, 1.5, 1.18, 1.3
- **Follow up Visit**: 1.47, 1.48

**NS**: Not significant
Regional Differences in Vascular FDG uptake with Treatment

6 months into treatment
Treatment with Methotrexate and Glucocorticoids is Associated with Reduced FDG-PET Vascular Activity

<table>
<thead>
<tr>
<th>TBR in specific aortic region</th>
<th>Variables</th>
<th>Correlation Coefficient</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Descending Aorta</td>
<td>MTX</td>
<td>-0.67</td>
<td>0.01</td>
</tr>
<tr>
<td>Descending Aorta</td>
<td>GCs</td>
<td>-0.40</td>
<td>0.03</td>
</tr>
<tr>
<td>Ascending Aorta and Arch</td>
<td>MTX</td>
<td>-0.42</td>
<td>0.16</td>
</tr>
<tr>
<td>Ascending Aorta and Arch</td>
<td>GCs</td>
<td>-0.22</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Multivariable regression: Change in GC dose and change in MTX dose independently associated with change in TBR of descending aorta.
Effect of Prednisone

71 yo man with GCA
Treated with tapered prednisone over 6 months
Effect of Methotrexate Alone

Before

After
Combined Effect of Prednisone and Methotrexate

Before

After
Discussion
Evidence for Efficacy of Methotrexate in Large Vessel Vasculitis

- Conflicting evidence about efficacy in three RCTs
  - Trials only used clinical features as outcome measures
- Methotrexate reduced vascular FDG uptake
- Imaging based outcomes may provide unique and complimentary opportunities to assess drug efficacy
Limitations

• Small cohort

• Unable to assess correlation of DMARDs (other than methotrexate) and biologics on vascular FDG uptake
Conclusions

• Change in treatment is associated with change in vascular FDG uptake

• Dynamic change in PET activity is dependent on the region of the aorta

• Methotrexate and prednisone can reduce vascular FDG uptake

• FDG-PET might be useful to monitor vascular disease activity as an outcome measure in clinical trials of LVV
Acknowledgment