The Effect of Aggressive Blood Pressure Control on the Recurrence of Atrial Fibrillation after Catheter Ablation

Substrate Modification with Aggressive Blood Pressure Control: SMAC-AF

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Background

Radiofrequency catheter ablation for atrial fibrillation has become an important therapy for AF, however recurrence rates remain high.

Background

• Recurrent AF may be due to recovery of conduction in the antral region of the pulmonary veins OR the presence of an arrhythmogenic atrial substrate, that is not modifiable by ablation alone

• Hypertension is the most common worldwide risk factor associated with the development of AF

Clinical Question

Does aggressive blood pressure (BP) lowering prevent recurrent atrial fibrillation (AF) after catheter ablation in a population at high risk for recurrent AF?
Methods

Randomized, parallel, open-label, clinical trial with blinded endpoint evaluation in thirteen centers in Canada

Inclusion

• Baseline blood pressure > 130/80 mm Hg in clinic
  – Two measurements taken 5 minutes apart if in sinus, four measurements if in AF
• Symptomatic paroxysmal or persistent atrial fibrillation
• Refractory or intolerant of at least one Class I or III antiarrhythmic medication
• Scheduled to undergo catheter ablation

Exclusion

• Known moderate to severe renal dysfunction
• Prior intolerance to an angiotensin-receptor II antagonist
• Prior ablation for AF
• Persistent AF (> 1 year)
• Other non-cardiovascular medical condition making 1 year survival unlikely
Randomization
1:1 allocation

Aggressive BP treatment:
Target BP <120/80 mm Hg

Standard BP treatment

Upstream Therapy Delivered
0-6 months prior to ablation

Ablation
3 months Blanking Period

Guideline-directed Therapy

Ablation

Outcome

Follow-up minimum 12 months, maximum 30 months from randomization
Aggressive BP Treatment

Step 1 – Quinapril, 20-40 mg po od 40 mg
Step 2 – Hydrochlorothiazide 12.5 mg po od
Step 3 – Atenolol 50 mg po od
Step 4 – Norvasc 2.5-10 mg po od
Step 5 – Terazosin 1 mg po od

Standard BP Treatment

Treatment recommended to referring physician to treat according to the Canadian Hypertension Guidelines; no changes made by the study team

Follow-up

Both arms: q 3 months in Year 1, q 6 months until end
Transtelephonic monitoring: 2x/week q 3 months
Symptomatic transmissions post-ablation: palpitations, shortness of breath, dizziness, reduced exercise tolerance, chest pain
Outcomes

• **Primary outcome:**
  – time to symptomatic AF/atrial tachycardia (AT)/atrial flutter (AFL) lasting > 30 seconds more than 3 months post ablation

• **Secondary outcomes:**
  – Any recurrent AF/AT/AFL 3 months post ablation
  – Any recurrent AF/AT/AFL post randomization
  – Visits to the emergency department and hospitalizations for atrial arrhythmia
  – Recurrent ablation therapy
Results

Randomized (n=184)

Allocation

Aggressive BP treatment (n=92)
- Received AF catheter ablation (n=88)
- Did not receive AF catheter ablation (n=4)

Standard BP treatment (n=92)
- Received AF catheter ablation (n=85)
- Did not receive AF catheter ablation (n=7)

Follow-Up

Lost to follow-up (1 death, 1 lost to follow up)

Lost to follow-up (n=2)

Analysis

Analysed (n=88)

Analysed (n=85)
### Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Aggressive BP Treatment (N=92)</th>
<th>Standard BP treatment (N=92)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59.9±8.2</td>
<td>60.2±9.3</td>
</tr>
<tr>
<td>Women –no. (%)</td>
<td>21 (22.8%)</td>
<td>28 (30.4%)</td>
</tr>
<tr>
<td>Caucasian –no. (%)</td>
<td>91 (98.9%)</td>
<td>91 (98.9%)</td>
</tr>
<tr>
<td>Body Mass Index**</td>
<td>31±6.0</td>
<td>31.6±6.0</td>
</tr>
<tr>
<td>Persistent</td>
<td>41 (44.6%)</td>
<td>39 (42.4%)</td>
</tr>
<tr>
<td>Time since AF diagnosis (months)†</td>
<td>30.3 (15.1,64.0)</td>
<td>28.8 (14.6,67.3)</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>142.9±11.0/84.9±8.5</td>
<td>142.2±12.6/84.3±8.5</td>
</tr>
<tr>
<td>Hypertension</td>
<td>70 (76.1%)</td>
<td>70 (76.1%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>15 (16.3%)</td>
<td>10 (10.9%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>2 (2.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Prior TIA/Stroke</td>
<td>4 (4.4%)</td>
<td>3 (3.3%)</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>23 (25.0%)</td>
<td>13 (14.1%)</td>
</tr>
<tr>
<td>CHA$_2$DS$_2$VaSc Score (mean±SD)</td>
<td>1.6±1.1</td>
<td>1.6 ±1.1</td>
</tr>
<tr>
<td>Left atrial size, parasternal long axis - mm</td>
<td>41.7±6.0</td>
<td>41.9±7.1</td>
</tr>
</tbody>
</table>
Blood Pressure

Systolic blood pressure (mmHg) vs. Months
- Aggressive group: 135.4±15.7 mm Hg
- Standard group: 123.2±13.2 mm Hg

Diastolic BP (mmHg) vs. Months
- Aggressive group: 80.8±10.2 mm Hg
- Standard group: 76.7±11.4 mm Hg

p<0.001 between groups
p=0.082 between groups

26% of patients in the aggressive group experienced hypotension
Primary Outcome: Time to recurrent symptomatic AF/AT/AFl 3 months post ablation

Hazard Ratio 0.94
95% CI (0.65, 1.38)
p = 0.763

Months of Follow-up

No. at Risk
Standard BP Treatment: 85 84 57 45 38 32 25 23 19
Aggressive BP Treatment: 88 88 61 52 37 33 28 24 21
## Secondary Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Aggressive BP Treatment (n=92)(%)</th>
<th>Standard BP Treatment (n=92)(%)</th>
<th>Hazard Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AF/AT/AFI 3 months post ablation*</td>
<td>62 (70.5)</td>
<td>54 (63.5)</td>
<td>1.12 (0.78,1.62)</td>
</tr>
<tr>
<td>AF/AT/AFI post randomization</td>
<td>81 (88.0)</td>
<td>79 (85.9)</td>
<td>1.00 (0.74,1.37)</td>
</tr>
<tr>
<td>AF-related emergency department visits**</td>
<td>25 (27.1)</td>
<td>23 (25.0)</td>
<td>1.08 (0.66,1.77)</td>
</tr>
<tr>
<td>AF-related hospitalizations</td>
<td>9 (9.8)</td>
<td>10 (10.9)</td>
<td>1.11 (0.47,2.62)</td>
</tr>
<tr>
<td>Recurrent ablation therapy*</td>
<td>22 (25.0)</td>
<td>25 (29.4)</td>
<td>0.81 (0.46,1.43)</td>
</tr>
</tbody>
</table>

*n=88 in the aggressive BP treatment group, n=85 in the standard BP treatment group

**Including visits to ED for hypotension
<table>
<thead>
<tr>
<th>Variable</th>
<th>95% CI and Hazard Ratio</th>
<th>P value for interaction</th>
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</thead>
<tbody>
<tr>
<td>Age &gt; 61 yr</td>
<td></td>
<td>0.013</td>
</tr>
<tr>
<td>&lt; 61 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>0.539</td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body Mass Index &gt;31 kg/m²</td>
<td></td>
<td>0.996</td>
</tr>
<tr>
<td>&lt;31 kg/m²</td>
<td></td>
<td></td>
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<tr>
<td>Type of AF: Persistent</td>
<td></td>
<td>0.399</td>
</tr>
<tr>
<td>Paroxysmal</td>
<td></td>
<td></td>
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<tr>
<td>Baseline BP &gt;140 mmHg</td>
<td></td>
<td>0.022</td>
</tr>
<tr>
<td>&lt;140 mmHg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHADS$_2$ score &gt;2</td>
<td></td>
<td>0.241</td>
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<tr>
<td>&lt;2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left atrial size &gt;42mm</td>
<td></td>
<td>0.591</td>
</tr>
<tr>
<td>&lt;42mm</td>
<td></td>
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</table>
Limitations

• Patients in the standard treatment group were well treated
• Duration of therapy prior to ablation was a median of 3.5 months and may not have resulted in adequate effect
• Only BP was controlled, other risk factors were not addressed systematically
• Significant atrial remodelling had occurred from long-standing hypertension and frequent paroxysms of AF that was no longer reversible
Conclusion

• This duration of aggressive BP treatment in patients with AF undergoing catheter ablation, did not result in a reduction of atrial arrhythmias after ablation.

• Upstream blood pressure lowering for AF will require further study in randomized clinical trials to better understand its potential benefit in prevention of recurrent AF.