Are Sinus Node Dysfunction and Pacemaker Implantation more common in patients with non-ablated Atrial Fibrillation?

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Objective

- Assess association between Sick Sinus Syndrome and Atrial fibrillation.

- Assess the affect of different variables on relationship between atrial fibrillation and pacemaker implantation.
Background:

- Short period of atrial fibrillation induces electrical remodeling of the atria with lowering of threshold and refractoriness*.

- Pacing induced atrial fibrillation induces sinus node dysfunction and negatively affecting intra-atrial conduction and atrial refractoriness.

- Chronic atrial fibrillation is associated to significant damage to the sinus node, peri sinus tissue and sinus nodal artery.

- Rate control strategies allow persistence of the atrial fibrillation with controlled ventricular rate, it is theoretically expected that the chronic underlying atrial fibrillation will induce sinus node dysfunction over a sufficient time.

Sick sinus syndrome

Sick Sinus Syndrome is a *clinical syndrome* characterized by chronic sinoatrial (SA) node dysfunction,

- Sinus Bradycardia
- Sinus node arrest
- Sinus node exit block
- Bradycardia-Tachycardia Syndrome
**Symptoms:**

- lightheadedness,
- presyncope,
- syncope,
- Palpitations:
  - Chronotropic incompetence
  - Dyspnea
- worsening chest discomfort

*Prior to any testing beyond an ECG, a thorough evaluation should be performed for potentially reversible causes*
Atrial Fibrillation:

- Most common chronic arrhythmia
- Annual cost of approximately 16 billion dollars.
- Complicates cardiopulmonary disease processes and many of these are increasing in prevalence, including hypertension, obesity and obstructive sleep apnea.
- Incidence and prevalence of atrial fibrillation has increased.
Methods:

- Retrospective cohort study of patients that underwent permanent pacemaker implantation at Mercy Hospital of Buffalo in one year.

- Demographics of sample. Indication of pacemaker, presence or absence Atrial fibrillation. If atrial fibrillation was present then categorized into two categories. Persistent and paroxysmal.

- After excluding cases that did not meet the inclusion criterion. Indications for pacemaker were reclassified into sick sinus syndrome and non sick sinus syndrome.

- Chi sq. test and phi cramer test were used for categorical variables. Binary multivariable Logistic regression was used to assess affect of different variables. Independent t test was done to calculate difference between continuous variables.
Inclusion Criterion:

- All consecutive patients presenting to South Buffalo Mercy Hospital for permanent pacemaker implantation within the period of one year 2012 to 2013.

Exclusion Criteria:

- Biventricular pacemaker for heart failure
- Pacemaker implantation for Vasovagal syncope or Hypersensitive Carotid Sinus syncope
- Pacemaker implantation after cardiac transplant.
- Pacemaker implantation for AV block immediately after Acute Myocardial infarction.
- Pacemaker Implantation after any valvular surgery.
Total cases with Pacemaker: 482

Cases included in analysis: 469

Cases Excluded: 13

Sick Sinus Syndrome: 323
- sinus exit block
- Sinus Pauses
- sinus Bradycardia
- Bradycardia-tachycardia Syndrome

Atrioventricular Blocks: 110
- Type II second degree
- 3rd Degree
- Bi and trifascicular block

Symptomatic Atrial Fibrillation: 13

Missing data: 20

Cases Excluded: 13
Results:
Mean = 75.37
Std. Dev. = 12.852
N = 462
Sick sinus syndrome was found to be significantly more in atrial fibrillation patient as compared to non-atrial fibrillation patients, 88% vs. 57% (p<0.05)

## Chi Square test

<table>
<thead>
<tr>
<th></th>
<th>No Sick Sinus Syndrome</th>
<th>Sick Sinus Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial Fibrillation</td>
<td>93</td>
<td>124</td>
</tr>
<tr>
<td>No Atrial Fibrillation</td>
<td>25</td>
<td>184</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>df</th>
<th>Sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>50.742&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1</td>
<td>&lt;0.00005</td>
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<tr>
<td>Phi Cramer test</td>
<td>0.345</td>
<td>NA</td>
<td>&lt;0.00005</td>
</tr>
</tbody>
</table>
Binary Logistic Model:

\[ \ln \left( \frac{p}{1-p} \right) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 \ldots \]

with and

\( x_1 = \) age (years),
\( x_2 = \) A.Fib (yes/No)
\( X_3 = \) Gender (Male/Female)
\( p = \) probability (proportion) of \( y=1 \), where \( y = \) Probability of having Sick Sinus Syndrome
\( \text{so } \left( \frac{p}{1-p} \right) = \text{ODDS of Sick Sinus Syndrome} \)

\[ \ln (\text{odds of sick Sinus Syndrome}) = \beta_0 + \beta_1 (\text{AGE}) + \beta_2 (\text{Gender}) + \beta_3 (\text{Presence of AFib}) \]
The slope estimate for Atrial Fibrillation is $\beta = 1.723$

- An estimated $\ln(\text{odds ratio})$ of Sick Sinus Syndrome for AFib patient to Non Afib Patient, who are of the same age and Sex. i.e adjusted association between Sick Sinus Syndrome and Atrial Fibrillation.

- Odds ratio estimate is $e^{1.73} \approx 5.6$; Afib patients in the sample have 460% greater odds of having Sick Sinus Syndrome and than non Afib patients in the sample of the same age and Sex.

- The 95% for the age adjusted odds ratio for males compared to females is $(e^{1.21}, e^{2.35}) \rightarrow (3.391, 9.257)$

<table>
<thead>
<tr>
<th></th>
<th>$\beta$</th>
<th>Standard Error</th>
<th>P value</th>
<th>Exp ($\beta$) Odds Ratio</th>
<th>95% C.I. for Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td>-0.001</td>
<td>0.009</td>
<td>0.904</td>
<td>0.999</td>
<td>0.982 - 1.016</td>
</tr>
<tr>
<td>AFIB(Yes/No)</td>
<td>1.723</td>
<td>0.256</td>
<td>0.000</td>
<td>5.602</td>
<td>3.391 - 9.257</td>
</tr>
<tr>
<td>GENDER(Male/Female)</td>
<td>-0.280</td>
<td>0.232</td>
<td>0.229</td>
<td>0.756</td>
<td>0.480 - 1.192</td>
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<tr>
<td>Constant</td>
<td>0.492</td>
<td>0.665</td>
<td>0.459</td>
<td>1.636</td>
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</tr>
<tr>
<td></td>
<td>$\beta$</td>
<td>Standard Error</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
</tr>
<tr>
<td>AGE</td>
<td>-0.015</td>
<td>0.021</td>
<td>0.476</td>
<td>0.985</td>
<td>0.944</td>
</tr>
<tr>
<td>GENDER (Male/Female)</td>
<td>-0.571</td>
<td>0.451</td>
<td>0.206</td>
<td>0.565</td>
<td>0.233</td>
</tr>
<tr>
<td>TYPE AFIB (PAROXYSMAL/PERSISTENT)</td>
<td>-0.343</td>
<td>0.450</td>
<td>0.446</td>
<td>0.709</td>
<td>0.293</td>
</tr>
</tbody>
</table>

In Atrial fibrillation patients after adjustment for Age and gender there is no statistically significant association between type of Atrial Fibrillation and Sick Sinus Odds ratio of 0.709 (CI 0.293-1.715).
Independent sample t test does not show statistically significant difference between average age of patients with and without Sick sinus syndrome 75.83 vs 74.17 (p= 0.815)
Independent sample t test shows no statistically difference between average age of patients with or without atrial fibrillation 73.82 vs. 76.27 (p= 0.045)
In patient less than 70 years of age adjusted odds of sick sinus syndrome was 4.88 (CI 1.8-13) times higher in Afib patient than non AFib patients.

In patient more than 70 years of age adjusted odds of sick sinus syndrome was 5.88 (CI 3.26-10.562) times higher in Afib patient than non A Fib patients. There difference is not statistically difference since there is overlap in confidence interval.
Discussion:

It is well defined fact that Sick sinus syndrome itself predisposes to atrial fibrillation.

- sinus bradycardia strongly facilitate the conditions for AF by increasing atria ectopy and dispersion of refractoriness

- SA nodes modulates the PV arrhythmogenesis center. This effect is lost in Sinus node dysfunction.

- certain mode of pacing as AAIR is more common than DDDR mode of pacing responsible for causing atrial fibrillation.
In our study, assumption was converse i.e., atrial fibrillation if present predated the diagnosis of sick sinus syndrome and pacemaker implantation.

- Long standing atrial fibrillation would result in electrophysiological and structural remodeling of the sinus node and would lead to sinus node dysfunction. When sinus node dysfunction is symptomatic, it leads to pacemaker implantation.

- Estimated likelihood of having sick sinus syndrome in atrial fibrillation patients was five times as compared to non-atrial fibrillation patients.

- Unlike other studies, age at implantation, gender, or type of atrial fibrillation were not found to be significant predictors for sick sinus syndrome.
Limitation of Study

- Selection and referral bias. It is not necessarily applicable on population without pacemaker who either has sinus node dysfunction and/or atrial fibrillation.

- Absolute of risk of sick sinus syndrome that would require longitudinal studies.

- No confounding or interaction effect from duration of atrial fibrillation, age at time of Atrial fibrillation, CHF, CAD, electrolytes, structural heart disease, medications.

- Missing data might bias our study results.
Conclusion:

- Our study suggest that atrial fibrillation increases likelihood of having sick sinus syndrome.

- In a case displaying signs of both SND and atrial fibrillation. It is difficult whether Atrial fibrillation develops as result of underlying Sinus node dysfunction or vice versa since we have evidence for both.

- The Sinus node dysfunction and atrial fibrillation are possible different reflection of same pathological process rather one dominating the other. It likely related to fibrosis.

- It is important to identify patient at risk of having sick sinus syndrome related bradycardia since it can lead to serious injury from fall and trauma.
Thanks

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John J Cai
Henri T. Woodman
&
Anam Butt