Arrhythmia Burden in Patients with Indolent Lymphoma

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Introduction
Indolent Non-Hodgkin lymphomas (NHL) comprise a heterogeneous group of diseases including marginal zone lymphoma (MZL), lymphoplasmacytic lymphoma (LPL), small lymphocytic lymphoma/chronic lymphocytic leukemia (SLL/CLL), and follicular lymphoma (FL). These compose a heterogeneous group of disorders that frequently measures survival in years due to the long natural history of these diseases. Frequency and morbidity of cardiac arrhythmias in patients with indolent lymphoma is unknown, but recent observations note that arrhythmias are an increasing problem. Due to advances in treatment for indolent NHL with emergence of novel therapeutics, combined with an aging population and a long natural history, understanding of arrhythmia burden in indolent NHL with emergence of novel therapeutics is an area of research with important implications for patients undergoing active treatment as well as for long term lymphoma survivors.

Objectives
• Define the rate of arrhythmic events and sudden cardiac death in patients with indolent lymphoma during management

Methods
• Adult patients 18 years or older with indolent NHL treated at the University of Rochester Wilmot Cancer Institute between 2013-2019 were included in the Cardio-Oncology Lymphoid Malignancies Database and analyzed.
• Cardiac arrhythmias including ventricular arrhythmias (VT/VF), atrial arrhythmias (atrial fibrillation (afib)), flutter, SVT and atrial tachycardia), and bradyarrhythmias were identified using ICD-10 codes.
• Kaplan-Meier survival analysis was used to assess cumulative probability of arrhythmia.

Results

<table>
<thead>
<tr>
<th>Subtype of Indolent Lymphoma</th>
<th>Arrhythmia Incidence</th>
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<tbody>
<tr>
<td>CLL</td>
<td>38 (22%)</td>
</tr>
<tr>
<td>FL</td>
<td>53 (32%)</td>
</tr>
<tr>
<td>MZL</td>
<td>27 (16%)</td>
</tr>
<tr>
<td>LPL</td>
<td>17 (10%)</td>
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</tbody>
</table>

- Population: Male 522, Female 396
- Most common arrhythmia: Atrial fibrillation in 81 patients (9%)
- During median follow up of 24 months, 168 patients (18%) developed a new or recurrent arrhythmia.
- Overall, there were 80 (9%) deaths. Ten deaths were related to cardiovascular diseases; of which 8/10 (80%) were from sudden cardiac death.


Conclusions
• This real-world cohort demonstrates that patients with indolent lymphoma could have an increased risk of cardiac arrhythmias that is possibly exacerbated by treatment.
• Atrial fibrillation was the most common arrhythmia identified in this study and appears increased compared to the incidence in the general age matched population (1-1.8 per 100 person-years).
• Surprisingly, of 80 deaths, 8 (10%) were attributed to sudden cardiac death.
• This data set contributes important information that can help identify patients at increased risk of cardiovascular morbidity and mortality that can impact treatment.
• Prospective monitoring in these patients may better define the incidence and associated risks of arrhythmias.

Limitations and Future Directions
• Patients who have CLL are commonly treated with ibrutinib, which has a known side effect of Afib in up to 9% of patients.
• 63 patients out of 168 patients identified to have an arrhythmia were known to have a prior history of arrhythmia.
• Future directions will focus on risk factors for arrhythmias, subset analysis by histologic subtype, other factors affecting rates of arrhythmia, and developing an approach to prevent and treat arrhythmias in this patient population.

References