Sudden death and cardiomyopathy associated with LMNA in the Nova Scotia Duck Tolling Retriever

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Introduction

Dilated cardiomyopathy (DCM) is the most common cardiomyopathy in humans and is characterized by dilation of the left ventricle and decreased systolic function of the heart. Individuals with DCM develop heart failure, arrhythmias and are at risk for premature and sudden death. DCM has a prevalence of one in 400 individuals, with 20-48% of those cases being familial DCM (FDCM). Human FDCM often has a dominant mode of inheritance, but a recessive mode of inheritance has been documented as well (FDCM). DCM has also been reported in certain dog breeds and has been associated with genes that encode structural proteins of the cardiac myocyte. FDCM has not been reported in the Nova Scotia Duck Tolling Retriever (NSDTR).

Genome Wide Association Study and Whole Genome Sequencing

- We hypothesize that a guanine deletion in the LMNA gene causes a frameshift mutation which impairs the processing of prelamin to mature Lamin A but does not impair processing of mature Lamin C. Loss of Lamin A leads to DCM and sudden death in the NSDTR.
- Genotyping of 300 NSDTR revealed a carrier frequency of 8.7%.
- Future genetic testing of the LMNA deletion can be used to reduce the incidence of DCM in NSDTR.

Pedigrees

<table>
<thead>
<tr>
<th>WM (kg)</th>
<th>LVId</th>
<th>LVIds</th>
<th>LVIDn (normal &lt;1.7)</th>
<th>Fractional Shortening (normal &gt;25%)</th>
<th>LA/Ao (normal &lt;1.6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affected</td>
<td>11.3k</td>
<td>3.9cm</td>
<td>3.4cm</td>
<td>1.9</td>
<td>13.5%</td>
</tr>
<tr>
<td>Affected</td>
<td>15.4k</td>
<td>4.5cm</td>
<td>3.6cm</td>
<td>2.0</td>
<td>20%</td>
</tr>
<tr>
<td>Sibling</td>
<td>17.6k</td>
<td>3.6cm</td>
<td>1.7cm</td>
<td>1.6</td>
<td>53%</td>
</tr>
<tr>
<td>Parent</td>
<td>19.5k</td>
<td>2.8cm</td>
<td>1.9cm</td>
<td>1.2</td>
<td>35%</td>
</tr>
<tr>
<td>Parent</td>
<td>16.3k</td>
<td>3.3cm</td>
<td>1.6cm</td>
<td>1.4</td>
<td>54%</td>
</tr>
</tbody>
</table>

References


Acknowledgments

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