The Effect of Age at Diagnosis of Type I Von Willebrand Disease on Diagnostic Lab Values: A Pediatric Perspective

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Project Overview

• Retrospective database review using the American Thrombosis and Hemostasis Network (ATHN) dataset

• Compare age at diagnosis and Ristocetin Cofactor and von Willebrand Antigen levels in patients with Type I von Willebrand disease
• Diagnosis of type I von Willebrand disease can be difficult due to multitude of factors that can affect von Willebrand factor antigen (vWF:Ag) and ristocetin cofactor (vWF:RCo) levels within an individual patient and between lab draws
Background

• The 2008 NHLBI guidelines for diagnosis of von Willebrand Disease recommended the use of the following levels for vWF:Ag and/or vWF:RCo for diagnosis of type I VWD.
  • <30 IU/dL = Type I vWD
  • 30-50 IU/dL = Low von Willebrand Factor
Background

Prior studies have shown age can affect vWF:Ag and vWF:RCo levels in healthy adults.

Changes in von Willebrand factor level and von Willebrand activity with age in type 1 von Willebrand disease

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Fig. 1. Baseline and Last VWF:Ag, VWF:RCo and FVIII for each patient.
Background
Aims

• **Primary Aim:**
  - Determine if age at diagnosis of type I von Willebrand disease correlates with VWF:Ag and VWF:RCo levels at diagnosis.
Aims

• **Secondary Aims:**
  
  • Determine if there is a difference in reason for testing (i.e. bleeding symptoms vs family history) between age strata

  • Number of patients that would be reclassified as low von Willebrand Factor according to the NHLBI 2008 guidelines titled “The Diagnosis, Evaluation and Management of von Willebrand Disease”
Methods

• **Inclusion Criteria**
  • Diagnosis (Type I vWD)
  • Sex
  • Age at diagnosis
  • Diagnostic Lab Values
    • vWF: Ag
    • vWF:RCo
    • Factor VIII:C
3815 patients were excluded from further review:
- 1423 no age at diagnosis
- 2392 incomplete lab record (vWF:Ag, vWF:RCo, Factor VIII:C)

2042 patients included in initial review

1570 patients included in statistical analysis

5857 patients with Type I (including Type IC) von Willebrand Disease extracted from ATHN dataset

472 patients were excluded from further review due to lab values outside of range to be included in analysis
Results

• An ANOVA (Analysis of variance) was completed to determine if there is a statistically significant difference between the mean vWF:Ag and vWF:RCo across the diagnosis age strata.

• The null hypothesis that the mean vWF:Ag levels were homogenous across diagnosis age strata was rejected (p< 0.001).

• The null hypothesis that the mean vWF:RCo levels were homogenous across diagnosis age strata was rejected (P=0.001).

• A post-hoc analysis was then performed comparing all possible pairs of means to determine if there is a statistically significant difference in mean vWF:Ag and vWF:RCo between strata.
Results

Mean Difference = 5.3 (CI 2.0-8.6)
Results

Mean Difference = 7.1 (CI 3.6-10.5)
**Results**

Mean Difference = 5.4 (CI 1.0-11.8)
Results

Mean Difference = 3.4 (CI 1.1-5.8)
Results

Mean Difference = 3.1 (CI 0.7-5.6)
## Results

Table 1: Association between testing reason and age at diagnosis

<table>
<thead>
<tr>
<th>Testing Reason</th>
<th>Strata 1 (0-2 years)</th>
<th>Strata 2 (3-10 years)</th>
<th>Strata 3 (11-20 years)</th>
<th>Strata 4 (21-30 years)</th>
<th>Strata 5 (30+ years)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding Symptom</td>
<td>33 (10.8%)</td>
<td>117 (20.2%)</td>
<td>152 (33%)</td>
<td>13 (14.4%)</td>
<td>14 (10.6%)</td>
<td>329 (21.0%)</td>
</tr>
<tr>
<td>Family History</td>
<td>49 (16.0%)</td>
<td>62 (10.7%)</td>
<td>29 (6.3%)</td>
<td>5 (5.6%)</td>
<td>13 (9.9%)</td>
<td>158 (10.1%)</td>
</tr>
<tr>
<td>Lab Screening</td>
<td>2 (0.7%)</td>
<td>9 (1.6%)</td>
<td>3 (0.7%)</td>
<td>1 (1.1%)</td>
<td>2 (1.5%)</td>
<td>17 (1.1%)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (1.3%)</td>
<td>7 (1.2%)</td>
<td>5 (1.1%)</td>
<td>1 (1.1%)</td>
<td>1 (0.8%)</td>
<td>18 (1.1%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>219 (71.3%)</td>
<td>385 (66.4%)</td>
<td>272 (59.0%)</td>
<td>70 (77.8%)</td>
<td>102 (77.3%)</td>
<td>1048 (66.8%)</td>
</tr>
<tr>
<td>Total</td>
<td>307</td>
<td>580</td>
<td>461</td>
<td>90</td>
<td>132</td>
<td>1570</td>
</tr>
</tbody>
</table>

Chi-Squared Test: $p < 0.001$
Results

Diagnostic Classification of Patients According to the 2008 NHLBI Guidelines

- 70% Type 1 von Willebrand Disease
- 30% Low von Willebrand Factor
Limitations

• **Core Data Elements**
  • Required data fields are minimal
  • Elements may have more than 1 way of entering the data

• **Discrepancy of Data Entered**
  • Several patients had diagnostic lab values entered that were not reflective of their diagnosis of Type I von Willebrand Disease
Future Research

- Should age at diagnosis be considered in the diagnosis of Type I vWD?
- Will need large prospective study evaluating vWF:Ag and vWF:RCo levels as patients increase in age (include pediatric patients)
Future Research

• Does puberty correlate with increased levels of vWF:Ag and vWF:RCo?