Baseline Lipid Values in Patients Referred for Cardiac Rehabilitation with Atherosclerotic Cardiovascular Disease

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Introduction
A number of lipid parameters, including low density lipoprotein cholesterol (LDL-C), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and non-high density lipoprotein cholesterol (non-HDL-C) are currently used in atherosclerotic cardiovascular disease (CVD) risk assessment and treatment decisions. Although many of the clinical guidelines promote using calculated LDL-C in risk assessment, non-HDL-C is a more sensitive predictor of CVD morbidity and mortality in a CVD-free population than LDL-C.** Non-HDL-C can be easily calculated by subtracting HDL-C from TC, and is not influenced by high triglycerides, unlike calculated LDL-C. The focus on LDL-C may leave certain high-risk subgroups with continued elevated levels of non-HDL-C vulnerable to an adverse cardiac event, even while on statin therapy. Patients with known CVD and previous events are considered to be at highest residual risk for recurrent CVD events.** It is recommended that this population receive high-intensity statin treatment, aggressive lifestyle modification, and cardiac rehabilitation (CR) if available.** There is clearly a growing body of evidence for the usefulness of non-HDL-C as a marker of CVD risk. However, there are few studies that demonstrate the potential differences in predictive accuracy for the most commonly used lipid measures, especially in the high risk CR patient population.

Purpose
This study evaluates which lipid measures were better predictors of CVD in patients subsequently enrolled in CR.

Study Design
Baseline, off-treatment lipid measurements from subjects enrolled in 3 CR programs in central Pennsylvania between 11/2012 and 8/2015 aged 26-89 with known CVD were retrospectively obtained and analyzed (n=328). Off-treatment lipid measures within 5 years prior to the time of initial CVD diagnosis were obtained. Patients were age and sex matched to appropriate controls (n=328) without evidence of CVD or statin use (Table 1). Statistical analysis utilizing SAS 9.4 (SAS Institute, Cary, NC) included a logistical regression model of the overall population and gender subgroups to compare lipid parameters to the overall lipid parameter as an outcome (n=566). A two-sample t-test was used to compare the means of each lipid value. Graph was made utilizing R version 3.2.3 software.

Results

Table 2: Baseline lipid values

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Total</th>
<th>Patients</th>
<th>Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>Overall</td>
<td>189.4 (47.1)</td>
<td>183.7 (37.4)</td>
<td>p=0.09</td>
</tr>
<tr>
<td></td>
<td>Men</td>
<td>192.0 (49.9)</td>
<td>179.8 (37.5)</td>
<td>p=0.007</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>157.6 (45.8)</td>
<td>137.1 (38.9)</td>
<td>p=0.04</td>
</tr>
</tbody>
</table>

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Table 3: Predictive Value of Lipid Markers

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Overall (n=328)</th>
<th>Patients (n=328)</th>
<th>Controls (n=328)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>0.524</td>
<td>0.497</td>
<td>0.519</td>
<td>p=0.09</td>
</tr>
<tr>
<td></td>
<td>0.612</td>
<td>0.589</td>
<td>0.583</td>
<td>p=0.001</td>
</tr>
<tr>
<td></td>
<td>0.612</td>
<td>0.589</td>
<td>0.583</td>
<td>p=0.001</td>
</tr>
</tbody>
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Conclusions
- LDL-C, HDL-C, and non-HDL-C are independently associated with risk of CVD development and there are significant differences in the baseline values of patients and controls.
- Non-HDL-C was a slightly better predictor based on the higher c-statistic and gender subgroup analysis in which LDL-C no longer was a significant predictor
- Mean baseline values, while statistically significant, are not dramatically elevated.

Implications
- Non-HDL-C is a slightly better or at least equivalent predictor of CVD risk compared to LDL-C in this high risk group. Further studies with greater power are needed to illustrate these differences in the CR population
- Lipid control is important in CVD prevention, but a dramatically elevated LDL-C may not be seen in many patients presenting with CVD
- Non-HDL-C has the benefit that it is not affected by triglyceride levels while LDL-C calculated using the Friedewald Formula is affected by triglycerides and may not correlate accurately with atherosclerotic cholesterol.

References: