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Recommended Citation
Jackson, Teaka; Peterson, Sarah; Favreau-Lessard, Amanda; Burgess, Joanne; Bosworth-Farrell, Susan; Kramer, Robert S.; Sawyer, Douglas B.; Ryzhov, Sergey; and Robich, Michael P., "Potential of vascular endothelial growth factor as a biomarker of coronary artery disease in subjects undergoing CABG surgery" (2019). Maine Medical Center. 690. https://knowledgeconnection.mainehealth.org/mmc/690

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Potential of vascular endothelial growth factor as a biomarker of coronary artery disease in subjects undergoing CABG surgery

Teaka Jackson¹,², Sarah M. Peterson³, Amanda J. Favreau-Lessard¹, Joanne Burgess⁴, Susan Bosworth-Farrell⁴, Robert S. Kramer¹,⁴, Sergey Ryzhov¹, Douglas B. Sawyer¹,⁴, Michael P. Robich¹,⁴

Introduction

- Coronary artery disease (CAD) causes local hypoxia due to reduced blood flow
- Hypoxic conditions are known to induce vascular endothelial growth factor (VEGF) production, a key contributor to angiogenesis
- The purpose of this study was to determine the potential of VEGF as a marker of myocardial stress in subjects with CAD undergoing coronary artery bypass grafting (CABG) surgery

Methods

- Research was performed in accordance with study protocols approved by Maine Medical Center Institutional Review Board
- The study cohort consisted of plasma samples from 73 patients undergoing CABG surgery at Maine Medical Center (MMC) in Portland, ME
- Plasma samples were collected prior to operation (pre-op), during surgery, and 4-8, 24 and 96 hours following surgery
- VEGF concentration was determined using a DuoSet enzyme-linked immunosorbent assay (ELISA) kit (R&D Systems, sensitivity range 31.3-2000 pg/mL)
- Undetectable levels of VEGF (<31.3 pg/mL) were assigned a concentration equal to one-half of the lowest calibration point (15.6 pg/mL)
- All statistical analyses were performed in GraphPad Prism and a p-value <0.05 was considered statistically significant

Study Timeline

Blood collection, plasma preparation, collection of clinical data
ELISA

Results

Figure 1. Determining concentration of VEGF in plasma samples

Left: Representative VEGF ELISA plate. Lane 1 contains standard concentrations, and lanes 2 through 6 contain subject plasma samples

Table 1. Demographic data of VEGF expressors is not significantly different from those with undetectable levels

<table>
<thead>
<tr>
<th>Study Subject Demographics</th>
<th>VEGF Expressors</th>
<th>Undetectable</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>11</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Age*</td>
<td>66±10</td>
<td>63±11</td>
<td>0.47</td>
</tr>
<tr>
<td>Female</td>
<td>5 (45%)</td>
<td>20 (40%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Male†</td>
<td>6 (55%)</td>
<td>30 (60%)</td>
<td></td>
</tr>
<tr>
<td>BMI*</td>
<td>31±7.9</td>
<td>30±8.4</td>
<td>0.5</td>
</tr>
<tr>
<td>BMI≥30</td>
<td>32.3±7.5</td>
<td>30.6±5.4</td>
<td>0.18</td>
</tr>
<tr>
<td>Aortic cross clamp time (min)*</td>
<td>85±28</td>
<td>92±30</td>
<td>0.55</td>
</tr>
<tr>
<td>CPR time (min)*</td>
<td>100±89</td>
<td>105±55</td>
<td>0.66</td>
</tr>
<tr>
<td>Smoking history†</td>
<td>8 (73%)</td>
<td>36 (72%)</td>
<td>0.15</td>
</tr>
<tr>
<td>HbA1c%</td>
<td>7.0±1.9</td>
<td>6.7±1.8</td>
<td>0.67</td>
</tr>
<tr>
<td>EF&lt;50%†</td>
<td>33 (30%)</td>
<td>21 (40%)</td>
<td>0.49</td>
</tr>
</tbody>
</table>

*mean subjects BMI=body mass index, CPB=cardiopulmonary bypass, HbA1c=hemoglobin A1c, CPR=cardiopulmonary resuscitation, ED=ejection fraction

Conclusion

- Plasma levels of VEGF are characterized by interindividual variability
- Individual VEGF expression appears to vary in response to CABG surgery
- CABG surgery did not induce changes in the level of circulating VEGF, limiting its potential use as a biomarker of cardiometabolic stress in CABG patients

Future Directions

- Determine Hypoxic Inducible Factor 1α (a transcription factor for VEGF) expression by ELISA
- Investigate the biological activity of VEGF in CAD patients
- Examine potential relationships with cytokine, and clinical data and outcomes
- Understand if patient subpopulations (diabetes, heart failure) have varying VEGF levels and if they are impacted clinically

Acknowledgements

- Maine Economic Improvement Fund in support of T. Jackson
- The MMCRI-USM internship program

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