Altered fatty acid profile of periprostatic adipose tissue in prostate cancer patients: an MR spectroscopic study

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Target Audience: Results presented in this study will be of interest to a wide variety of audience - clinical oncologists specializing in prostate cancer, cancer biologists investigating the role of adipose in promoting cancers, scientists studying metabolism in obesity, and MR spectroscopists.

Purpose: Obesity is considered to be an adverse prognostic factor for prostate cancer (PCa). Several clinical studies suggest that periprostatic adipose tissue (PPA) may promote PCa growth, and elevated adiposity shows a positive association with more aggressive disease. In a study using transrectal ultrasonography, increased thickness of the PPA was positively associated with both the overall presence of PCa and the presence of high grade disease [1]. However, the molecular mechanism by which increased adiposity stimulates PCa progression remains unclear. We hypothesized that in addition to its increased mass, the composition of adipose tissue in the tumor microenvironment might be a prognostic marker for PCa aggressiveness.

Experimental Methods:

Tissue collection: PPA and SQA were collected from 30 PCa patients undergoing radical prostatectomy. Patient/tumor characteristics were as follows: range of body mass index (BMI) 21.0-40.5 (9 subjects BMI <25 (lean), 12 subjects BMI 25-30 (overweight), and 9 subjects BMI>30 (obese)); Gleason pattern: 52.5% (3+3), 35% (3+4), and 12.5% (4+3); 12.8% had extracapsular extension (ECE) which signifies aggressive PCa. MR Spectroscopy: PRESS localized proton MR spectra were acquired from 1xL voxels in the adipose specimens on a 14.1T Bruker Avance imaging spectrometer without water suppression using TR 40s, TE 7.5ms, spectral width 8000Hz and 16k complex points. FIDs were Fourier transformed after applying 2.5Hz exponential multiplication filter.

Data Analysis: Peak integrals of FA functional groups, corrected for T2 relaxation time, were measured from the spectra. The fractions of saturated (fS), mono-unsaturated (fM), poly-unsaturated (fU), and total unsaturated (fT) FA were calculated as described in literature [2]. The following FA ratios were compared between PPA and SQA: mono-unsaturated to saturated FA (fM/fS), poly-unsaturated to saturated FA (fU/fS), and total unsaturated to saturated FA (fT/fS). The corresponding receiver operating characteristic (ROC) curves were compared against pathologically determined ECE by using the area under the curve (AROC) and computing the 95% confidence intervals (CI) based on percentile boot strap samples.

Table 1. Fatty acid profile of PPA and SQA tissues in prostate cancer patients

<table>
<thead>
<tr>
<th>BMI Gr.</th>
<th>PPA</th>
<th>SQA</th>
<th>p-value</th>
<th>PPA</th>
<th>SQA</th>
<th>p-value</th>
<th>PPA</th>
<th>SQA</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25</td>
<td>1.26±0.12</td>
<td>1.34±0.09</td>
<td>0.65</td>
<td>0.90±0.07</td>
<td>0.95±0.06</td>
<td>0.57</td>
<td>2.16±0.16</td>
<td>2.29±0.13</td>
<td>0.56</td>
</tr>
<tr>
<td>25-30</td>
<td>1.39±0.13</td>
<td>1.46±0.16</td>
<td>0.74</td>
<td>0.94±0.08</td>
<td>0.94±0.07</td>
<td>0.99</td>
<td>2.33±0.24</td>
<td>2.40±0.22</td>
<td>0.81</td>
</tr>
<tr>
<td>&gt;30</td>
<td>1.60±0.16</td>
<td>1.17±0.07</td>
<td>0.03</td>
<td>1.30±0.26</td>
<td>0.81±0.06</td>
<td>0.09</td>
<td>2.93±0.28</td>
<td>1.99±0.12</td>
<td>0.05</td>
</tr>
</tbody>
</table>

ROC analysis of data from all PCa patients revealed that several differential MRS measures of FA composition (Δ) between PPA and SQA have potential for predicting pathologically determined ECE, a marker for aggressive PCa, as shown by their AROC and 95% CI (given in parentheses): ΔfM/fS 0.83 [0.66 – 0.98], ΔfU/fS 0.92 [0.81 – 0.99], ΔfP/fS 0.84 [0.68 – 0.98] and ΔfT/fS 0.16 [0.02 – 0.32]. Values of AROC closer to 1 or 0 indicate high predictive potential.

Discussion: Bioenergetic demands and increased membrane synthesis in PCa progression might be responsible for the altered FA profile in the PPA. Elevated fM/fS seen in obese patient PPA is consistent with increased activity of fatty acid desaturases, such as stearoyl-CoA desaturase-1, which moderates signaling processes related to cell proliferation, survival and malignant transformation to cancer [3]. Our ROC analysis suggests that alterations in FA composition of the PPA relative to SQA might be useful in developing a marker for aggressive PCa. Men within an active surveillance program currently require repeated biopsies for evaluation of their cancer. A non-invasively measured MRS marker for aggressive PCa has the potential to improve the accuracy of differentiating indolent from aggressive PCa and thereby eliminate unnecessary biopsies that cause trauma to the patient.

Conclusions: Lipid metabolism is altered in the vicinity of the tumor in PCa. FA profile of the PPA in obese PCa patients might represent a unique metabolic microenvironment permissive to cancer progression. Our results suggest that in vivo MRS may have potential for developing noninvasive biomarkers for aggressive PCs which will benefit men participating in active surveillance programs.

References:


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