Body composition by computed tomography scan as a predictor of chemotherapy toxicity in patients with renal cell carcinoma

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Identification of biomarkers associated with cancer outcome or treatment related toxicity is a challenge.

Several recent studies demonstrate an association between severe skeletal muscle depletions (sarcopenia) and excess chemotherapy toxicity (Baracos et al 2010, Prado et al 2008)

CT = considered a gold standard method used to assess body composition

Renal cell carcinoma (RCC) patients have a strikingly heterogeneous weight and BMI-potential source of variation in drug concentration and metabolism

Sex specific cut offs for sarcopenia =55.4 cm$^2$/m$^2$ males and 38.9 cm$^2$/m$^2$ females (Prado et al 2008)

Aims

- Describe skeletal muscle tissue and adipose tissue in a cohort of patients with renal cell carcinoma

- Study the effect of sarcopenia (at the start of chemotherapy) on chemotherapy toxicity

- Determine what percentage of patients are sarcopenic and establish if low muscle mass is a key predictor of chemotherapy toxicity and efficacy
Methods

- Retrospective analysis of prospectively collected data

- **Inclusion criteria:** Adult (male and female) patients > 18 years with metastatic clear cell renal cell carcinoma between 2007-2012, ECOG 0-1 and treated with Sunitinib (50mg)

- Participating hospitals: Mercy University Hospital, St Vincent's University Hospital Dublin, Cork University Hospital

- Two consecutive CT images - taken within ±30 days before or after the initiation of cycle 1

- Lumbar vertebral landmark (L3) was selected

- Fat free mass was calculated using pre determined regression equations by Mourtzakis et al 2008
### Demographics

<table>
<thead>
<tr>
<th>Category</th>
<th>Total (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>43</td>
</tr>
<tr>
<td>Females</td>
<td>12</td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>64 (10.6)</td>
</tr>
<tr>
<td>Hospital</td>
<td></td>
</tr>
<tr>
<td>Dublin, n (%)</td>
<td>21 (38.1)</td>
</tr>
<tr>
<td>Cork, n (%)</td>
<td>34 (61.8)</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td></td>
</tr>
<tr>
<td>Average (range)</td>
<td>28.6 (19.9-41.4)</td>
</tr>
<tr>
<td>Sarcopenia, n (%)</td>
<td>18 (33)</td>
</tr>
<tr>
<td>Dose limiting toxicity (DLT), n (%)</td>
<td>40 (73)</td>
</tr>
</tbody>
</table>
Sarcopenia and BMI

- Normal weight: 33% Sarcopenia, 56% BMI
- Overweight: 27% Sarcopenia, 44% BMI
- Obese: 40% Sarcopenia, 0% BMI
Results

Male
BMI 27
Non sarcopenic (63.5cm$^2$/m$^2$)
DLT > 6 months

Male
BMI 27
Sarcopenic (52.7cm$^2$/m$^2$)
DLT < 6 months
## Toxicities

### in < 6 months vs. > 6 months

<table>
<thead>
<tr>
<th></th>
<th>DLT in &lt; 6months</th>
<th>DLT in &gt; 6months</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=29</td>
<td>n=26</td>
<td></td>
</tr>
<tr>
<td>Skeletal Muscle L3 area (cm²)</td>
<td>151.5</td>
<td>173.7</td>
<td>0.019</td>
</tr>
<tr>
<td>Skeletal muscle L3 index (cm²/m²)</td>
<td>51.8</td>
<td>59.4</td>
<td>0.012</td>
</tr>
<tr>
<td>Total Fat Free Mass (FFM) (kg)</td>
<td>51.4</td>
<td>57.7</td>
<td>0.03</td>
</tr>
<tr>
<td>Adipose tissue index (cm²/m²)</td>
<td>132</td>
<td>127.9</td>
<td>NS</td>
</tr>
<tr>
<td>Dose Sunitinib mg/FFM</td>
<td>1.01</td>
<td>0.89</td>
<td>0.02</td>
</tr>
<tr>
<td>Number of Toxicities</td>
<td>4.4</td>
<td>2.3</td>
<td>0.002</td>
</tr>
</tbody>
</table>
Skeletal Muscle Mass (SMM) and Toxicity

SMM below the 25th centile vs. above the 75th centile

< 25th centile
(<44.8cm²/m²)

- n = 13
- DLT 92%
- DLT < 6 months 77%
- Number of toxicities = 5

> 75th centile
(>63.2cm²/m²)

- n = 14
- DLT 57%
- DLT in < 6 months 28%
- Number of toxicities = 2
Conclusion

- Sarcopenia is prevalent in patients with RCC
- It's an occult condition in patients with normal/high BMI
- Importance of muscle mass independent of weight or BMI
- Significant predictor of DLT
- Potential use of baseline body composition to predict toxicity