Diagnosing the metabolic syndrome in survivors of childhood haematopoietic stem cell transplantation and total body irradiation

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Background

- Young adult survivors of childhood HSCT/TBI survivors have an increased cardiometabolic risk.
- The International Diabetes Federation (IDF) defines the metabolic syndrome as:
  - Central adiposity using increased waist circumference or body mass index (BMI)
  - Plus 2 additional features from the following:
    - ↑ Triglycerides (TG) >1.7mmol/L
    - ↓ HDL (M<1.03mmol/L, F<1.29mmol/L)
    - ↑ Blood Pressure (BP): SBP>130, DBP>85 mmHg
    - ↑ Fasting glucose (FG) >5.6 mmol/L or known diabetes.
- The metabolic syndrome may be under reported in HSCT survivors who may not have raised BMI and/or waist circumference.

Aim

- To identify appropriate clinical methods to assess central adiposity in order to identify the Metabolic Syndrome in HSCT/TBI survivors.

Method

Participants 3 Groups (aged 16-26):
- Group 1: BMT/TBI ALL survivors diagnosed at <18 yrs, in remission ≥3 yrs (n=21, 11M)
- Group 2: Standard chemotherapy treated ALL survivors diagnosed at <18 yrs in remission ≥3 yrs (n=31, 13M)
- Group 3: subjects with simple obesity (n=30, 10M)

Assessments
- BP
- Auxology: height, weight, waist & hip circumferences
- Blood tests: Fasting glucose and Oral glucose tolerance test, HDL, TG

Cut-offs for metabolic syndrome components
- ↑ Body Mass index (weight/height²) > 30kg/m²
- ↑ Waist-to-height Ratio: raised >0.5
- ↑ Waist-to-hip ratio: raised >0.8 female, >0.9 male
- ↑ BP, ↑ FG, ↑ TG, ↓ HDL as per IDF criteria
- Diabetes (WHO criteria): 120 minute glucose >11.1 mmol/L

Statistics: Odds ratios, confidence intervals, significance 5%

Discussion and Conclusions

- HSCT have a high cardiometabolic risk without overt obesity
- BMI and uncorrected waist circumferences do not identify central adiposity in HSCT/TBI survivors.
- The standard IDF criteria of the metabolic syndrome underestimate HSCT/TBI survivors with increase metabolic risk.
- The waist-to-hip ratio is more representative of central adiposity allowing identification of metabolic syndrome and risk in HSCT/TBI survivors, and may be useful in routine clinic follow-up in these patients.

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Table 1: Prevalence of hypertension, dyslipidaemia and impaired FG/diabetes in each group as per IDF criteria

<table>
<thead>
<tr>
<th>Group</th>
<th>HSCT/TBI</th>
<th>ALL</th>
<th>Obesity</th>
<th>Odds ratios (CI) p values 1 vs. 2</th>
<th>Odds ratios (CI) p values 1 vs. 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑SBP or DBP</td>
<td>4/21 (18%)</td>
<td>4/31 (13%)</td>
<td>6/30 (20%)</td>
<td>1.6 (0.35-7.2) p=0.55</td>
<td>0.94 (0.23-3.9) p=0.93</td>
</tr>
<tr>
<td>↓HDL</td>
<td>12/21 (57%)</td>
<td>8/30 (27%)</td>
<td>16/30 (53%)</td>
<td>3.7 (1.1-12.0) p=0.003</td>
<td>1.2 (0.4-3.6) p=0.79</td>
</tr>
<tr>
<td>↑TG</td>
<td>10/21 (48%)</td>
<td>3/30 (10%)</td>
<td>4/30 (13%)</td>
<td>8.2 (1.9-35.5) p=0.005</td>
<td>5.9 (1.5-23.0) p=0.001</td>
</tr>
<tr>
<td>↑ FG or diabetes</td>
<td>2/21 (9.5%)</td>
<td>0/30 (0%)</td>
<td>0/30 (0%)</td>
<td>7.8 (0.36-172) p=0.20</td>
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</tr>
</tbody>
</table>

Table 2: Prevalence of metabolic syndrome using standard and modified IDF criteria.

<table>
<thead>
<tr>
<th>Group</th>
<th>Definition</th>
<th>HSCT/TBI</th>
<th>ALL</th>
<th>Obesity</th>
<th>Odds ratios (CI) p values 1 vs. 2</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Standard IDF: central adiposity defined by ↑ waist circumference</td>
<td>4/21 (19%)</td>
<td>3/30 (10%)</td>
<td>5/30 (16.7%)</td>
<td>2.1 (0.4-10.7) p=0.40</td>
<td>0.94 (0.23-3.9) p=0.93</td>
<td></td>
</tr>
<tr>
<td>Modified IDF: central adiposity defined by ↑ waist-to-height ratio</td>
<td>8/21 (38%)</td>
<td>4/30 (13%)</td>
<td>5/30 (16.7%)</td>
<td>4.0 (1.0-15.8) p=0.047</td>
<td>1.2 (0.3-5.0) p=0.82</td>
<td></td>
</tr>
<tr>
<td>Modified IDF: central adiposity defined by ↑ waist-to-hip ratio</td>
<td>9/21 (43%)</td>
<td>3/30 (10%)</td>
<td>5/30 (16.7%)</td>
<td>6.8 (1.5-29.4) p=0.011</td>
<td>3.7 (1.0-13.6) p=0.044</td>
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</tbody>
</table>

The prevalence of metabolic syndrome in the BMT/TBI survivors was higher when central adiposity was defined using waist-to-height or waist-to-hip ratios compared with BMI or waist circumference. This difference was not observed in obese controls.