

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

C Wei^{1,2,3}, R Cox^{2,4}, KJ Bradley^{2,5}, R Elson^{1,4}, MCG Stevens^{2,4}, EC Crowne^{1,2}

1. Department of Paediatric Endocrinology & Diabetes, Bristol Royal Hospital for Children, U.K.; 2. University of Bristol, U.K.; 3. Department of Paediatric Endocrinology, St George's Hospital, London; 4. Department of Paediatric Oncology, Bristol Royal Hospital for Children, U.K.; 5. Department of Endocrinology and Diabetes, Bristol Royal Infirmary, U.K

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) ≥ 1.7 mmol/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%

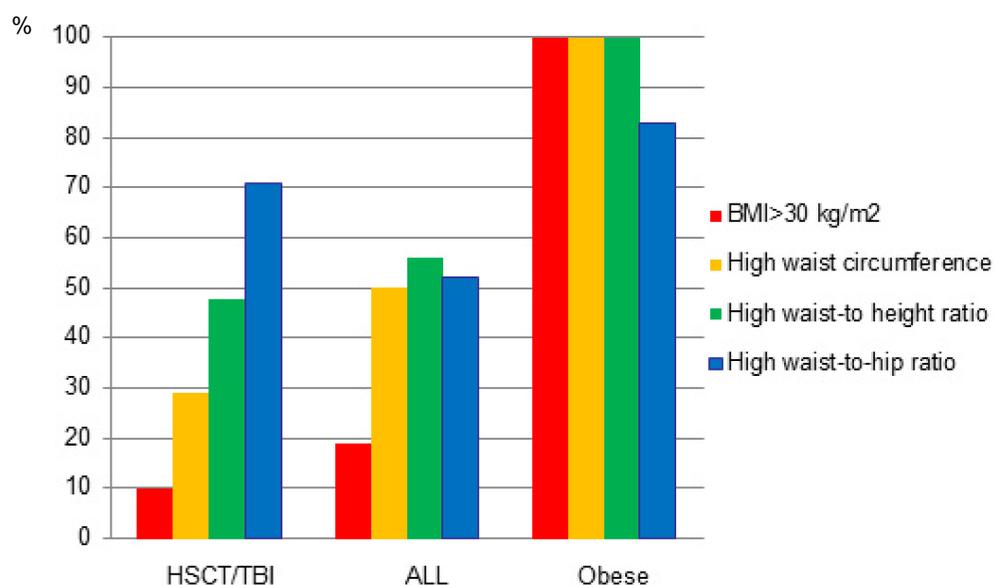
Approval: Regional Research Ethics Committee

Results

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

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

Figure 1: Central adiposity represented by different clinical methods



In the HSCT/TBI Group, the percentage of patients with central adiposity was higher when this was defined by the waist-to-height or waist-to-hip ratios compared with BMI or waist circumference. This difference was not observed in obese controls.

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

Group Definition	HSCT/TBI 1	ALL 2	Obesity 3	Odds ratios (CI) p values 1 vs. 2	Odds ratios (CI) p values 1 vs. 3
Standard IDF: central adiposity defined by ↑ waist circumference	4/21 (19%)	3/30 (10%)	5/30 (16.7%)	2.1 (0.4-10.7) p=0.40	1.2 (0.3-5.0) p=0.82
Modified IDF: central adiposity defined by ↑ waist-to-height ratio	8/21 (38%)	4/30 (13%)	5/30 (16.7%)	4.0 (1.0-15.8) p=0.047	3.1 (0.8-11.3) p=0.09
Modified IDF: central adiposity defined by ↑ waist-to-hip ratio	9/21 (43%)	3/30 (10%)	5/30 (16.7%)	6.8 (1.5-29.4) p=0.011	3.7 (1.0-13.6) p=0.044

The prevalence of metabolic syndrome in the BMT/TBI survivors was higher when central adiposity was defined using raised waist-to-height and waist-to-hip ratios than the measured waist circumference.

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 underestimates 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.

Acknowledgements: C Wei's clinical research fellow post was generously funded by the IPSEN clinical research fellowship. Consumables were funded by the BSPED research Award, David Telling Research funds, Peel Medical research award, NIHR feasibility & sustainability funds

