# Evaluation of Cardiovascular Risk Factors in Long-term Survivors of Brain Tumours who Received Cranial Irradiation

Leeds Centre for Diabetes and Endocrinology

Nikolaos Kyriakakis[1], Satish S. Kumar[1], Julie Lynch[1], Ramzi Ajjan[2], Adam Glaser[3], Georgina Gerrard[4], Carmel Loughrey[4] & Robert D. Murray[1]

[1]Leeds Centre for Diabetes and Endocrinology, St James's University Hospital, Leeds, UK
[2]Division of Cardiovascular and Diabetes Research, Leeds Institute of Cardiovascular and Metabolic Medicine (LICAMM), University of Leeds, Leeds, UK
[3]Paediatric Haematology & Oncology, Leeds General Infirmary, Leeds, UK
[4]Clinical Oncology, Leeds Cancer Centre, St James's University Hospital, Leeds, UK

## Introduction

Epidemiological data has shown childhood cancer survivors to have excess morbidity and mortality for at least 10-15yrs after establishing remission from the primary cancer. The Childhood Cancer Survivors Study (CCSS) in the USA reported survivors of more than 5 years (n= 20,227) to have a 10.8 fold excess in overall mortality [1]. Of interest was the standardised mortality rates for cardiac disease (SMR) was significantly elevated (SMR 8.2) [1]. Studies have shown that for long term survivors of brain tumours, the risk for cardiovascular disease is strongly increased due to dyslipideamia, central obesity, and elevated systolic blood pressure, particularly for those with associated growth hormone deficiency [2, 3, 4].

## Methods

We undertook a cross sectional study to assess cardiovascular risk in long-term survivors of brain tumours following cranial irradiation compared with healthy matched controls. The following cardiovascular markers were measured: full lipid profile, fasting glucose and parameters of body composition. Basal anterior pituitary hormone profile and dynamic pituitary tests (ITT or GST) were also undertaken in the patient group. IGF-I and thyroid function tests were performed in the control group. Patients were recruited from the outpatient clinics in the Department of Endocrinology at the Leeds Teaching Hospitals NHS Trust, while the control group consisted of healthy volunteers, derived from the Leeds Teaching Hospitals Staff .

## Results

36 patients (mean age 30.9 13.9 years) and 36 controls (mean age 31.5 13.4 years) were assessed. The male:female ratio was 1.4:1 for the patient group and 1.6:1 for the controls. The mean age of the patients at the time of diagnosis was 22.1 16.1 years. 17 patients (47.2%) had child-onset primary brain tumours, while 19 patients (52.8%) were diagnosed during adulthood. All patients were treated with cranial radiotherapy (cXRT) (mean dose 50.0 8.6Gy, mean number of fractions 28 5.3), 28 patients (77.8%) had surgery and 15 patients (41.7%) received chemotherapy.

Evidence of hypopituitarism was present in 91.7% (33/36) of patients, while only 3 patients (8.3%) had entirely normal pituitary function. All patients with hypopituitarism had either severe (24/36, 66.7%), or partial growth hormone deficiency (GHD) (9/36, 25%). LH/FSH, ACTH and TSH deficiencies were present in 16.7%, 11.1% and 5.6% of patients respectively. Clinically significant ACTH deficiency requiring glucocorticoid replacement was present in only 5.6% of patients.

**Table 1.** Summary of clinical characteristics for the patients group (N=36). Results are presented as absolute numbers of patients. Numbers in brackets represent percentages. Numbers in years represent mean values with their standard deviations.

| Characteristic | Patients (%) | Characteristic | Patients (%) |
|---|---|---|---|
| **Gender** | | Age at diagnosis (yrs) | 22.1±16.1 |
| Male | 21 (58.3%) | Age at the time of the study (yrs) | 30.9±13.9 |
| Female | 15 (41.7%) | **Time of brain tumour onset** | |
| **Type of tumour** | | Child-onset | 17 (47.2%) |
| Glioma | 16 (44.4%) | Adult-onset | 19 (52.8%) |
| Medulloblastoma | 12 (33.3%) | **Anterior pituitary hormone deficits** | |
| Pineal tumour | 5 (13.9%) | Severe GHD | 24 (66.7%) |
| Other primary brain tumour | 2 (5.6%) | Partial GHD | 9 (25%) |
| Unclassified | 1 (2.8%) | LH/FSH deficiency | (16.7%) |
| **Therapeutic interventions** | | ACTH deficiency | (11.1%) |
| Surgery | 28 (77.8%) | TSH deficiency | (5.6%) |
| Cranial radiotherapy | 36 (100%) | **Other endocrinopathies** | |
| Mean dose (Gy) | 50.0±8.6 | Primary hypothyroidism | 4 (11.1%) |
| Mean number of fractions | 28±5.3 | Primary hypogonadism | 1 (2.8%) |
| Chemotherapy | 15 (41.7%) | Precocious puberty | 1 (2.8%) |

## Results (cont'd)

Regarding other endocrinopathies, 4 patients (11.1%) had primary hypothyroidism, 1 patient (2.8%) had primary hypogonadism and 1 patient (2.8%) had precocious puberty. The clinical characteristics of the patient group are summarised in Table 1.

Thyroid function tests and IGF-I values were within the normal limits for all individuals in the control group. No significant difference was found in the TSH (p=0.2) and free T4 (p=0.4) values between patients and controls.

Total and LDL-cholesterol were significantly higher in patients compared with controls (5.3 1.1mmol/L vs 4.6 1.0mmol/L, p=0.007 and 3.1 0.8mmol/L vs 2.7 0.9mmol/L, p=0.011 respectively). Body composition analysis showed patients had significantly elevated waist circumference (93.9 15.6cm vs 80.3 10.9cm, p<0.001), waist-hip ratio (0.88 0.08 vs 0.82 0.08, p<0.001), fat mass (FM) and FM% (24.0 12.2kg vs 15.7 6.6kg, p=0.003 and 29.6 9.7% vs 22.1 8.3%, p<0.001), truncal FM and truncal FM% (13.0 6.7kg vs 8.2 3.7kg, p=0.004 and 29.4 10.0% vs 21.0 8.1%, p<0.001) and summative (suprailiac, infrascapular, biceps, triceps) skinfold thickness (75.7 32.3mm vs 42.5 16.4mm, p<0.001) when compared with controls. No differences were found in the HDL, triglycerides, glucose, BMI and lean body mass between the two comparison groups. Results of the markers of cardiovascular risk in the patient and control group are summarised in Table 2.

**Table 2.** Fasting lipid profile, plasma glucose, body composition and skinfold thickness results in patients with child and adult onset brain tumours (N=36) and in the control group (N=36). Data are shown as mean values with their standard deviation. P-value <0.05 is considered statistically significant.

| Parameter | Patients | Controls | P-value | Parameter | Patients | Controls | P-value |
|---|---|---|---|---|---|---|---|
| | | | | **Bioimpedence** | | | |
| Age (years) | 30.9±13.9 | 31.5±13.4 | 0.624 | Fat Mass (kg) | 24.0±12.2 | 15.7±6.6 | **<0.001** |
| **Lipid and Glucose profile** | | | | Fat Mass % | 29.6±9.7 | 22.1±8.3 | **<0.001** |
| Total cholesterol (mmol/L) | 5.3±1.1 | 4.6±1.0 | **0.007** | Lean Body Mass (kg) | 54.1±13.5 | 54.0±12.0 | 0.96 |
| LDL cholesterol (mmol/L) | 3.1±0.8 | 2.7±0.9 | **0.011** | Truncal Fat Mass (kg) | 13.0±6.7 | 8.2±3.7 | **<0.001** |
| HDL cholesterol (mmol/L) | 1.6±0.6 | 1.4±0.4 | 0.14 | Truncal Fat Mass % | 29.4±10.0 | 21.0±8.1 | **<0.001** |
| Triglycerides (mmol/L) | 1.7±2.7 | 1.1±0.5 | 0.17 | Truncal Lean Body Mass (kg) | 29.3±6.7 | 31.4±9.2 | 0.29 |
| Fasting glucose (mmol/L) | 4.8±0.8 | 4.8±0.4 | 0.6 | **Skinfolds (mm)** | | | |
| | | | | Suprailiac | 21.1±10.7 | 10.6±5.1 | **<0.001** |
| BMI | 27.2±6.4 | 24.1±3.3 | 0.1 | Infrascapular | 22.5±9.9 | 13.9±6.2 | **<0.001** |
| Waist (cm) | 93.9±15.6 | 80.3±10.9 | **<0.001** | Biceps | 13.6±5.8 | 8.4±4.2 | **<0.001** |
| Waist/Hip ratio | 0.88 | 0.82 | **<0.001** | Triceps | 18.4±9.2 | 10.1±5.2 | **<0.001** |
| | | | | Summative | 75.7±32.3 | 42.5±16.4 | **<0.001** |

## Conclusions

Our results show that cancer survivors following cranial irradiation demonstrate an adverse lipid and body composition profile, which may contribute to the increased cardiovascular risk of these patients. The high prevalence of hypopituitarism in the patient group may explain at least partially the alterations observed in the cardiovascular risk markers.

### References

1. **Mertens AC, Yasui Y, Neglia JP, et al.** 2001 Late mortality experience in five-year survivors of childhood and adolescent cancer: the Childhood Cancer Survivor Study. J Clin Oncol 19:3163-72
2. **Heikens J, Ubbink MC, van der Pal HP, et al.** 2000 Long term survivors of childhood brain cancer have an increased risk for cardiovascular disease. Cancer 88:2116-21
3. **Meacham LR, Gurney JG, Mertens AC, et al.** 2005 Body mass index in long-term adult survivors of childhood cancer: a report of the Childhood Cancer Survivor Study. Cancer 103:1730-9
4. **Talvensaari KK, Lanning M, Tapanainen P, Knip M** 1996 Long-term survivors of childhood cancer have an increased risk of manifesting the metabolic syndrome. J Clin Endocrinol Metab 81:3051-5

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Nikolaos Kyriakakis
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