IDENTIFYING RISK FACTORS FOR MENTAL HEALTH AND QUALITY OF LIFE AMONG CHILDHOOD CANCER SURVIVORS

Ph.D. Thesis Booklet

Márton Szabados M.D.

Translational Medicine Program

Pathological and Oncological Division

SEMMELWEIS UNIVERSITY

Supervisors:	Miklós Garami M.D., Ph.D.
Official reviewers:	Charlotte Demoor-Goldschmidt M.D., PhD. Alexandra Katalin Csernus M.D., PhD.
Head of the Complex Examination Committee:	Prof. Miklós Szabó M.D., Ph.D.
Members of the Complex Examination Committee	Eero Kajantie M.D., D.Sc. Klára Horváth, M.D., Ph.D. Prof. István Balogh M.D., D.Sc. Péter Fehérvári Ph.D.

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1. Introduction

1.1. Overview of the topic

The thesis focuses on the neuropsychological well-being and health-related quality of life (HRQoL) of children, adolescents, and young adults with cancer, with particular emphasis on childhood brain tumor patients and survivors. The studies investigate risk stratification according to tumor location and clinical, socioeconomic characteristics, as well as the necessary measuring infrastructure for a systematic, long-term, multidisciplinary follow-up strategy.

1.2. What is the problem to solve?

As survival rates for pediatric cancer continue to improve, attention has shifted toward the long-term physical and psychological consequences of the disease and its treatment. Beyond well-documented physical late effects, childhood cancer survivors frequently experience anxiety, depression, and impaired health-related quality of life (HRQoL). Despite their clinical relevance, these psychological outcomes are often underrecognized and insufficiently monitored in routine survivorship care.

Survivors of pediatric brain tumors represent a particularly vulnerable group, as cognitive and psychosocial sequelae may arise from the combined effects of the disease. However, risk factors for affective disorders, such as the association between tumor location and the prevalence of anxiety and depression remains unclear.

Systematic assessment of HRQoL is essential for capturing patient related outcomes and guiding targeted interventions, yet prior to this work, there was a lack of validated HRQoL instrument was available for adolescent and young adult cancer patients in Hungary.

1.3. What would be the impact of our research results?

These studies provide an empirically grounded framework for the development of a multidisciplinary, long-term follow-up system in Hungary that systematically assesses HRQoL using a validated, culturally adapted instrument and incorporates tumor-related and psychosocial risk factors into routine monitoring.

2. Objectives

2.1. Study I. – Association of Tumor Location with Anxiety and Depression in Childhood Brain Cancer Survivors: A Systematic Review and Meta-analysis

The aim of this meta-analysis was to examine how brain tumor location relates to the prevalence of anxiety and major depression, to support earlier diagnosis and targeted psychological interventions.

2.2. Study II. – Study Title - The Hungarian Cross-cultural Adaptation of the MMQL-AF for Measuring Quality of Life in Adolescents with Cancer

The aim of this study was to validate the Hungarian version of the MMQL and support the development of a robust long-term follow-up system for children with cancer and survivors in Hungary. A secondary goal was to examine clinical and psychosocial factors influencing HRQoL.

3. Methods

3.1. Study I.

The systematic review and meta-analysis were conducted in accordance with the PRISMA guidelines and methodological recommendations of the Cochrane Handbook and was prospectively registered in PROSPERO (CRD42022370756). A comprehensive literature search was performed across five databases (MEDLINE, Embase, CENTRAL, Scopus, and Web of Science) up to November 22, 2022, supplemented by citation tracking. Studies involving childhood brain tumor survivors were included if tumor location (supratentorial or infratentorial) and either diagnostic data or standardized measures of anxiety and depression were reported. Data extraction and risk of bias assessment (QUIPS-2) were conducted independently by two reviewers. Random-effects meta-analyses were performed to estimate pooled prevalence and symptom severity, with subgroup analyses based on tumor location. Heterogeneity was assessed using Cochran’s Q and I^2 statistics, and analyses were conducted using R.

3.2. Study II.

The Minneapolis–Manchester Quality of Life instrument - Adolescent Form (MMQL-AF) was translated and culturally adapted into Hungarian following standardized cross-cultural adaptation procedure. The study was authorized by the Scientific and Research Ethics Committee of the Health Science Council. Adolescents and young adults aged 13–20 years with cancer were recruited from the Pediatric Center of Semmelweis University, along with age-matched healthy controls. Participants completed self-administered questionnaires, with a subset completing a retest within two weeks to assess test–retest reliability. Structural validity was evaluated using confirmatory factor analysis, internal consistency with Cronbach’s alpha, and test–retest reliability with intraclass correlation coefficients. Exploratory analyses examined associations between HRQoL and clinical, demographic, and socioeconomic factors.

4. Results

4.1. Study I.

The analysis included 42 eligible articles with a total number of 1071 patients. Relevant articles were cohort studies, cross-sectional studies, and case series. Based on the available data infratentorial brain tumor survivors had significantly higher scores on various assessment tools measuring anxiety (MRAW (raw mean scores): 36.24 [CI (confidence interval): 28.81–43.67]; versus MRAW: 23.21 (CI 0.91–45.51); $p = 0.02$, and depression (MRAW: 27.57 (CI 14.35–40.78) versus MRAW: 13.84 (CI 11.43–16.26); $p < 0.01$.

4.2. Study II

The MMQL-AF demonstrated acceptable reliability (Cronbach's alpha 0.73–0.90; ICC 0.78–0.96; RMSEA = 0.062; 90% CI: 0.055–0.069; CFI = 0.828; TLI = 0.814; SRMR = 0.079; GFI = 0.962) and strong concurrent validity with PedsQL scores. Cancer patients reported significantly lower HRQoL than healthy peers (mean 3.58 vs. 3.81; mean difference 0.23; 95% CI: 0.05–0.41; $p = 0.012$). No significant difference emerged between patients on active treatment and patients off treatment. Patients with bone, soft-tissue, or central nervous system tumors reported worse outcomes (p = 0.015). Positive parental relationships were strongly associated with a better outlook (p < 0.001).

5. Conclusions

This thesis demonstrates that affective disorders are common and clinically relevant late effect among survivors of childhood brain tumors. The findings support the incorporation of systematic psychological screening and long-term mental health monitoring into the standard follow-up care for all pediatric brain tumor survivors, particularly those with infratentorial tumors. The Hungarian MMQL-AF tool offers a systematic, patient-focused approach for recognizing unmet requirements and tracking HRQoL outcomes over time. Collectively, these findings call for the establishment of a risk-stratified, multidisciplinary survivorship model which includes psychological evaluation and quality-of-life assessment.

6. Bibliography

6.1. Publications related to the thesis:

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