



A Comprehensive Study of Childhood Cancer and the Condition of Muscles

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DESCRIPTION

Skeletal muscle is essential for physical health and metabolic integrity, with sarcopenia (progressive muscle mass loss and weakness) being a risk factor for ageing and chronic disease. In the general population, loss of lean mass and muscle quality (force generation per unit of muscle) is associated with fatigue, weakness, and slowed walking speed, eventually interfering with the ability to maintain physical independence and influencing participation in social roles and quality of life. Muscle mass and strength deficits are also documented during childhood cancer treatment, and these frequently persist into adult survivorship, contributing to an ageing phenotype in this vulnerable population.

Although several treatment exposures appear to increase the risk of muscle mass and strength loss that persists after therapy, the pathophysiology underlying poor muscle quantity and quality in childhood cancer survivors is poorly understood. This is due in part to a lack of access to paediatric and adult survivor muscle tissue samples, as well as the difficulties associated with non-invasive investigative approaches for muscle assessment. Understanding the mechanisms of injury responsible for both initial and persistent dysfunction is important because muscle accounts for just under half of the body's mass and is essential for movement, metabolism, and metabolic health.

The goal of this study is to provide an overview of the available evidence describing associations between childhood cancer, treatment, and muscle outcomes, as well as to identify gaps in current knowledge. Increased childhood cancer survival rates are a direct result of significant therapeutic and diagnostic advances made in recent decades. Today, the expected 5-year survival rate for childhood cancer is greater than 85%. As the number of childhood cancer survivors grows, so does the number of studies aimed at identifying risk factors for limitations in physical function, adverse health outcomes, and reduced quality of life in long-term survivors. Skeletal muscle health in the general population is a clinical indicator of metabolic disease and fall risk.

In children, poor muscle health is linked to impaired mobility and early mortality, while low muscle mass and fitness are linked to metabolic risk. Muscle strength is a powerful predictor of insulin sensitivity and metabolic risk in both children and adolescents. During a critical period of physiological development, children with cancer receive aggressive chemotherapy and radiation treatment. Survivors may experience treatment-related musculoskeletal side effects. Although there has been a lot of focus on bone health, the acute and long-term effects of childhood cancer and treatment on muscle health have not been thoroughly studied.

The human body contains over 600 muscles, which account for 40% of total body mass. Muscle serves a number of health and functional functions throughout the lifespan. It is the mechanical machinery of daily movement that protects other organs from trauma. Muscle is the most abundant source of protein in the body and the primary reservoir of amino acids used by other tissues for regeneration and repair. Furthermore, it is a key site for glucose homeostasis, energy mobilization, and even acts as a secretory organ, releasing factors into circulation with autocrine and paracrine effects. Muscle that is in good condition is resilient; it is strong, flexible, abundant, and adaptable.

Muscle quality and function are the primary indicators of muscle health, incorporating the long-term effects of factors such as diet, exercise, and disease. Muscle fitness combines muscle quantity and quality with neurological coordination to provide a measure of functional capacity, which is expressed as strength, endurance, and power. Given that key muscle development occurs early in life, at a time when childhood cancer patients are subjected to aggressive chemotherapy and radiotherapy treatments, they are particularly vulnerable to early declines in muscle health, which may contribute to adverse outcomes later in life.

Muscle quality and function are both impaired in childhood cancer patients and survivors. However, the pathophysiologic mechanisms underlying these impairments are poorly understood. This is due in part to limited research access to

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muscle tissue samples, as well as challenges associated with non-invasive investigative approaches for muscle assessment. Given the importance of muscle to mobility, cardio-metabolic health, and quality of life, identifying treatment and diagnostic risk factors for muscle impairments will undoubtedly improve functional outcomes for both patients and long-term survivors. The goal of this study is to provide an overview of the evidence describing associations between childhood cancer, treatment, and muscle outcomes, as well as to identify gaps in current knowledge.

It is estimated that 15,590 children and adolescents under the age of 19 will be diagnosed with cancer by 2020. 241 Long-term

morbidity and mortality associated with late-term treatment effects will burden these children in survivorship; nearly two-thirds of childhood cancer survivors have at least one chronic health condition 30 years after diagnosis. 6 Muscle is involved in many of these conditions, and loss of mass and strength is still being reported. Children with cancer frequently have poor muscle health and function, which can deteriorate with treatment and persist into survivorship, increasing the risk of decreased physiologic reserve, insulin resistance, and exercise intolerance.