



# Commentary on "Long-term endocrine sequelae after hematopoietic stem cell transplantation in children and adolescents"

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Advancements in treatment, along with enhanced supportive care have led to increased rates of survival among pediatric cancer patients.<sup>1)</sup> Every year in the United States, approximately 15,000 children between the ages of 0 and 19 are diagnosed with cancer, with over 85% surviving for at least 5 years.<sup>2)</sup> The majority of patients experience long-term survival, with over 500,000 in the United States and 30,000 in Korea.<sup>2,3)</sup> However, childhood cancer survivors undergo the long-term complications including endocrine disorders commonly.

Endocrine complications encompass growth failure, hypopituitarism, hypogonadism, hypothyroidism, diabetes mellitus, dyslipidemia, obesity, osteoporosis, adrenal insufficiency.<sup>2,4)</sup> A systematic review from 3 studies revealed that around 29.0% to 39.1% of childhood cancer survivors treated with cranial radiation therapy experienced growth hormone deficiency, with higher doses of cranial radiation associated with a higher risk.<sup>5)</sup> Shin et al.<sup>6)</sup> reported a one-year effect of growth hormone replacement without recurrence or occurrence of other tumors in 19 out of 24 growth hormone deficiency patients who survived childhood leukemia.

Childhood cancer survivors demonstrate decreased bone mineral density (BMD) relative to the general population, which can be attributed not only to chemotherapeutic treatments like glucocorticoids and radiation but also to factors like the cancer itself, hormonal insufficiency, inadequate nutrition, and reduced physical activity.<sup>7,8)</sup> Jang et al.<sup>9)</sup> emphasized the importance of evaluating BMD and monitoring the cumulative dose and duration of glucocorticoids for patients with secondary osteoporosis. According to clinical practical guidelines for optimizing bone health in Korean children and adolescents, sufficient intake of calcium and vitamin D, along with adequate body weight and physical activity, are recommended for childhood cancer survivors. Bisphosphates could also be helpful in increasing BMD.<sup>10)</sup>

The PanCareLIFE Consortium and the International Late Effects of Childhood Cancer Guideline Harmonization Group<sup>11)</sup> recommend counseling female childhood, adolescent, and young adult cancer patients who are at potential risk of infertility due to high-dose alkylating agents, ovarian radiotherapy, or hematopoietic stem cell transplantation (HSCT) about fertility preservation options such as oocyte or embryo cryopreservation and harvesting of ovarian tissue for cryopreservation.<sup>12)</sup> Before undergoing gonadotoxic chemotherapy or radiotherapy, testicular tissue cryopreservation is primarily offered to young male cancer patients. Moreover, Delgouffe et al.<sup>13)</sup> recommend testicular tissue banking for male patients requiring high-risk conditioning therapy before HSCT or bone marrow transplantation.

In this research,<sup>14)</sup> the authors studied 200 Korean childhood cancer survivors after HSCT and revealed that 67.5% of the patients experienced endocrine complications. Short stature and diabetes mellitus were prevalent among the prepubertal HSCT group, while hypogonadism and osteoporosis were more common among the pubertal HSCT group.<sup>14)</sup> Factors such as pubertal age at HSCT, female sex, and steroid use were identified as predictors of increased risk of endocrine complications. Another retrospective study from Spain involving 157 children post-HSCT presented similar risk factors for endocrinopathies including older age at HSCT, pubertal Tanner stage V, chronic graft-vs-host disease, direct gonadal therapy and specific treatments such as radiotherapy and steroids.<sup>15)</sup> Figueiredo et al.<sup>16)</sup> also reported similar results from a study of 152 Portuguese patients after HSCT during childhood. We need to plan

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customized surveillance strategies based on the characteristics of the childhood cancer survivors. While this study has the limitation of selection bias because 173 deceased patients were excluded, the extensive duration of the study makes the data significant.

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