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Report

Late Effects Surveillance Recommendations among Survivors of Childhood Hematopoietic Cell Transplantation: A Children's Oncology Group Report

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A B S T R A C T

Hematopoietic cell transplantation (HCT) is an important curative treatment for children with high-risk hematologic malignancies, solid tumors, and, increasingly, nonmalignant diseases. Given improvements in care, there are a growing number of long-term survivors of pediatric HCT. Compared with childhood cancer survivors who did not undergo transplantation, HCT survivors have a substantially increased burden of serious chronic conditions and impairments involving virtually every organ system and overall quality of life. This likely reflects the joint contributions of pretransplantation treatment exposures and organ dysfunction, the transplantation conditioning regimen, and any post-transplantation graft-versus-host disease (GVHD). In response, the Children's Oncology Group (COG) has created long-term follow-up guidelines (www.survivorshipguidelines.org) for survivors of childhood, adolescent, and young adult cancer, including those who were treated with HCT. Guideline task forces, consisting of HCT specialists, other pediatric oncologists, radiation oncologists, organ-specific subspecialists, nurses, social workers, other health care professionals, and patient advocates systematically reviewed the literature with regards to late effects after childhood cancer and HCT since 2002, with the most recent review completed in 2013. For the most recent review cycle, over 800 articles from the medical literature relevant to childhood cancer and HCT survivorship were reviewed, including 586 original research articles. Provided herein is an organ system–based overview that emphasizes the most relevant COG recommendations (with accompanying evidence grade) for the long-term follow-up care of childhood HCT survivors (regardless of current age) based on a rigorous review of the available evidence. These recommendations cover both autologous and allogeneic HCT survivors, those who underwent transplantation for nonmalignant diseases, and those with a history of chronic GVHD.

INTRODUCTION

Hematopoietic cell transplantation (HCT) has long been an important curative treatment for children with high-risk

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Table 1
Overview of Late Effects, Organized by Treatment Exposures Commonly Seen among Survivors of Childhood HCT

Exposure	Late Effect*
HCT experience in general	• Dental abnormalities • Renal toxicity • Hepatic toxicity • Low bone mineral density • Avascular necrosis • Increased risk of second cancers • Adverse psychosocial/quality of life effects • Mental health disorders, risk behaviors • Psychosocial disability due to pain, fatigue
Transplantation conditioning	
Alkylating agent	• Cataract (busulfan) • Pulmonary fibrosis (busulfan) • Renal toxicity • Urinary tract toxicity • Gonadal dysfunction • Therapy-related AML/MDS • Bladder cancer
Epipodophyllotoxin	• Therapy-related AML/MDS
DNA interstrand crosslinking agents (ie, platinum/heavy metal)	• Ototoxicity • Renal toxicity • Gonadal toxicity
TBI†	• Neurocognitive deficits • Leukoencephalopathy • Cataract • Dental abnormalities • GH deficiency • Hypothyroidism, thyroid nodule • Pulmonary toxicity • Breast tissue hypoplasia • Cardiac toxicity • Renal toxicity • Gonadal dysfunction • Uterine vascular insufficiency • Diabetes • Dyslipidemia • Musculoskeletal growth problems • Second cancers
Pretransplantation exposures, not listed above	
Anthracycline/anthraquinone	• Cardiac toxicity • Therapy-related AML/MDS
Bleomycin	• Pulmonary toxicity
Cytarabine	• Neurocognitive deficits • Leukoencephalopathy
Methotrexate	• Neurocognitive deficits • Leukoencephalopathy • Renal toxicity • Low bone mineral density
Corticosteroid	• Cataract • Low bone mineral density • Avascular necrosis
Cranial radiation†	• Neurocognitive deficits • Leukoencephalopathy • Cerebrovascular disease • Cataract • Craniofacial abnormalities • Dental abnormalities, xerostomia • Growth hormone deficiency • Hypothyroidism, thyroid nodule • Increased obesity • Precocious puberty • Brain tumor
Spinal radiation (in addition to cranial dose)	• Cardiac toxicity • Scoliosis/kyphosis, musculoskeletal problems

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