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Reproductive Late Effects after Hematopoietic Stem Cell Transplant in Pediatric, Adolescent and Young Adult Cancer Survivors

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Abstract

As advancements in cancer treatment such as Hematopoietic Stem Cell Transplant (HSCT) continue to improve the survival rates of pediatric, Adolescent and Young Adult (AYA) cancers, a growing number of survivors are living to their reproductive years. Many of these patients will experience the adverse impact that oncology care can have on reproductive potential such as infertility, gonadal insufficiency, genital graft-versus-host disease, uterine injury, psychosexual dysfunction and increased risks of breast and cervical cancer. Termed Late Effects (LE), these concerns may greatly impact patients' quality-of-life post-treatment and are therefore an essential component of developing comprehensive cancer treatment plans. There is expert consensus on how to screen for, prevent and treat many of the aforementioned LEs, however the recommended practices are rarely executed. As with other topics in oncofertility, educating providers and establishing standardized workflows which encourage interdisciplinary collaborations will go a long way towards widespread improvements in the quality of reproductive care offered to patients who receive HSCT. Here, we offer suggestions on how to promote the implementation of new and established standards of reproductive healthcare for young patients who receive HSCT and related treatments.

Keywords: Genital graft-versus-host disease • Gonadal insufficiency • Hematopoietic stem cell transplant • Hormone therapy • Oncofertility • Pediatric • Radiation-induced uterine injury • Reproductive late effects • Adolescent and Young Adult (AYA) cancer

Introduction

Historically, the impacts of oncologic interventions on reproductive function have been under appreciated, with little attention given to thoroughly investigating reproductive health concerns for many of the treatments available today. However, a growing body of evidence continues to identify reproductive late effects (LE), insults to gynecologic and urologic health resulting from oncology care. A 2021 study on two hundred seventy-eight childhood and adolescent cancer patients determined 77% of the cohort to have moderate-to-high risk of infertility, however only 9% underwent fertility preservation procedures, statistics similar to what other groups have reported. In many similar studies, patients reported that counseling on possible reproductive late effects mitigated regret and worry over fertility concerns post-care, further highlighting the importance of offering consultations to this population [1-3].

Description

While research is needed to understand the full extent of LEs, it is accepted that treatments may not only impact the reproductive organs directly, but also impact reproductive capacity through deleterious effects on endocrine function and pelvic anatomy. Many striking reports suggest that upwards of 50% of male and 67% of female childhood and AYA cancer survivors experience abnormal steroid hormone and/or gonadotropin levels at some point during or after oncology treatment regimens. Considering the essential role hormones play in development and fertility, there is an alarming potential for these treatments to impact one's health. In regards to HSCT, high-dose alkylator and radiation therapies administered during

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pre-transplant conditioning have been documented to cause infertility, gonadal insufficiency, genital graft-versus-host disease, uterine injury, psychosexual dysfunction and increased risks of breast and cervical cancer through both direct and indirect means. There is clearly a need to optimize reproductive healthcare in this population and implement standardized care into practice.

Groups have offered expert consensus through evidence-based guidelines for the prevention and management of gynecological complications which may arise from treatments administered during both autologous and heterologous transplantation. Embedded in guidelines broadly addressing fertility preservation for cancer patients, the American Society of Clinical Oncology (ASCO), American College of Obstetrics and Gynecology (ACOG) and European Society of Human Reproduction and Endocrinology (ESHRE) offer protocols and recommendations for meeting the reproductive health needs of these patients [4].

ACOG committee on adolescent health care, 2014; ESHRE guideline group on female fertility preservation, 2020). Other working groups have offered expert consenses in publications which address reproductive concerns specifically for HSCT patients. In regards to promoting the dissemination of this information, we recommend three measures one improve the reach of oncofertility education for emerging and established providers, two include fertility preservation standards as a quality measure for oncology care and three incorporate guideline concordant recommendations in the survivorship care plans [5-10].

Topics in oncofertility must first be integrated into medical education. Reaching providers with differing expertise is of utmost importance, as a high degree of coordination between oncology, urology, OB/GYN, primary care and internal medicine specialists is required for optimal care. Medical educators will need to offer oncofertility lessons to students and trainees which highlight not only topics relevant to the discipline, but also the tenents and benefits of multi-disciplinary collaboration. Beyond didactic instruction, offering research opportunities to emerging professionals who show interest in understanding reproductive LEs may greatly support not only the individual's career development, but the advancement of the field. As highlighted above, emerging evidence indicates there is much left to uncover in terms of screening and treatment of LEs which could greatly improve patient care and quality of life [11-13].

Oncofertility experts often experience care coordination as a major hurdle for implementing treatments due to the complexity of navigating healthcare systems, a problem enhanced as the size of the institution grows. Therefore, while all institutions providing oncology services should include fertility preservation standards as a measure of quality for oncology care, it is particularly important for large, comprehensive cancer centers to establish these operating procedures. Establishing systems which support providers, for example, by designating a patient navigator or nurse to guide patients and assist providers through these processes, helps institutions to achieve elevated levels of care (van den Berg; Whiteside). By setting comprehensive reproductive healthcare as a standard for all oncology patients and supplementing existing infrastructures to support patients and providers through workflows established to accomplish these care goals, leadership can encourage an improvement in the standard of care at their institutions [14-18].

In regards to our third suggestion, incorporating guideline concordant recommendations into the survivorship care plans, leveraging technology to standardize this process will be important. Patients should undergo thorough follow-up evaluations at least every six months for two years after HSCT. Examination should include a genital assessment, HPV and breast cancer screening and analysis of serum gonadotropins and sex steroid hormones to assess indicators of altered pubertal development and subfertility as per guidelines written by the American society of clinical oncology, children's oncology group and national comprehensive cancer network. Patients should be screened with appropriate clinical questionnaires such as the genital tract chronic graft-versus-host assessment and scoring form, sexual functioning questionnaire short form, Female Sexual Function Index (FSFI) and Sexual Health Inventory for Men (SHIM). Patients and caretakers should be educated on signs of reproductive health distress and encouraged to reach out to providers if any concerns arise. Every 1-2 years, bone mineral density evaluation by MOC-DEXA of the vertebral area and of the right and left femur should be repeated if abnormal. It may be possible to increase the duration between follow up visits if the improvement of symptoms meets appropriate expectations and as the chance of recurrence reduces over time [19,20].

Conclusion

There is a clear need to appreciate the impact of reproductive LEs on quality of life. LE's after HSCT are well described in the literature, yet implementation of evidence based recommendations for screening and treatment remain suboptimal. By improving the reach of oncofertility education, including fertility preservation as a standard measure of care quality and incorporating guideline concordant recommendations into survivorship care plans, we can contribute to elevating care in this population.

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Conflicts of Interest

No conflicts of interest or disclosures.

References

1. Afify, Z, P. J. Shaw, A. Clavano-Harding and C. T. Cowell. "Growth and Endocrine Function in Children with Acute Myeloid Leukaemia after Bone Marrow Transplantation Using Busulfan/Cyclophosphamide." *Bone Marrow Transplant* 25 (2000): 1087-1092.
2. Anazodo, Antoinette Catherine, Sumin Choi, Christina Signorelli and Sarah Ellis, et al. "Reproductive Care of Childhood and Adolescent Cancer Survivors: A 12-Year Evaluation." *J Adolesc Young Adult Oncol* 10 (2021): 131-141.
3. Anazodo, Antoinette, Paula Laws, Shanna Logan and Carla Saunders, et al. "How Can we Improve Oncofertility Care for Patients? a Systematic Scoping Review of Current International Practice and Models Of Care." *Hum Reprod Update* 25 (2019): 159-179.
4. Appiah, Leslie C, Molly Moravek, Holly Hoefgen and Seth Rotz, Krista Childress, et al. "Reproductive Late Effects after Hematopoietic Stem Cell Transplant in Pediatric, Adolescent and Young Adult Cancer Survivors." *Pediatr Blood Cancer* 70 (2023): e30551.
5. Barata, Anna and Heather Jim. "Quality of Life Assessment after HSCT For Pediatric and Adults." (2019): 251-256.
6. Bastings, LÖ. Baysal, CCM. Beerendonk, J. IntHout and MAF. Traas, et al. "Deciding About Fertility Preservation after Specialist Counselling." *Hum Reprod* 29 (2014): 1721-1729.
7. Buxbaum, Nataliya P, Cemre Robinson, Ninet Sinaii and Alexander Ling, et al. "Impaired Bone Mineral Density in Pediatric Patients with Chronic Graft-Versus-Host Disease." *Biol Blood Marrow Transplant* 24 (2018): 1415-1423.
8. Couto-Silva, A. C, C. Trivin, E. Thibaud and H. Esperou, et al. "Factors Affecting Gonadal Function after Bone Marrow Transplantation during Childhood." *Bone Marrow Transplant* 28 (2001): 67-75.
9. Gebauer, Judith, Claire Higham, Thorsten Langer and Christian Denzer, et al. "Long-Term Endocrine and Metabolic Consequences of Cancer Treatment: A Systematic Review." *Endocr Rev* 40 (2019): 711-767.
10. Guida, Maurizio, Maria Antonietta Castaldi, Rosa Rosamilio and Valentina Giudice, et al. "Reproductive Issues in Patients Undergoing Hematopoietic Stem Cell Transplantation: An Update." *J Ovarian Res* 9 (2016): 1-8.
11. "Keyser, Erin A. and Sloane W. Berger-Chen. "Gynecologic Issues in Children and Adolescent Cancer Patients and Survivors." *Obstet Gynecol* 132 (2018): E67-E77.
12. Kaneva, Kristiyana, Laura Erickson, Erin Rowell and Sherif M. Badawy. "Fertility Preservation Education for Pediatric Hematology-Oncology Fellows, Faculty and Advanced Practice Providers: A Pilot Study." *Pediatr Hematol Oncol* 39 (2022): 68-73.
13. Kim, Jayeon, Allison M. Deal, Ursula Balthazar, Laxmi A. Kondapalli and Clarisa Gracia, et al. "Fertility Preservation Consultation for Women with Cancer: Are We Helping Patients Make High-Quality Decisions?." *Reprod Biomed Online* 27 (2013): 96-103.
14. Knapp, Caprice A and Gwendolyn P. Quinn. "Healthcare Provider Perspectives on Fertility Preservation for Cancer Patients." *Cancer Treat Res* (2010): 391-401.
15. Li, Zhuoyan, Prerna Mewawalla, Pamela Stratton and Agnes SM Yong, et al. "Sexual Health in Hematopoietic Stem Cell Transplant Recipients." *Cancer* 121 (2015): 4124-4131.
16. Loren, Alison W, Pamela B. Mangu, Lindsay Nohr Beck and Lawrence Brennan, et al. "Fertility Preservation for Patients with Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update." *J Clin Oncol* 31 (2013): 2500-2510.
17. Morris, Charles A, Danielle Cabral, Hailu Cheng and Jeffrey N. Katz, et al. "Patterns of Bone Mineral Density Testing: Current Guidelines, Testing Rates and Interventions." *J Gen Intern Med* 19 (2004): 783-790.
18. Murphy, Jeanne, Mary McKenna, Suzanne Abdelazim and Minoo Battiwalla, et al. "A Practical Guide to Gynecologic and Reproductive Health in Women Undergoing Hematopoietic Stem Cell Transplant." *Biol Blood Marrow Transplant* 25 (2019): e331-e343.
19. Orio, Francesco, Giovanna Muscogiuri, Stefano Palomba and Bianca Serio, et al. "Endocrinopathies after Allogeneic and Autologous Transplantation of Hematopoietic Stem Cells." *Sci World J* (2014): 282147.
20. Ranjith, Saanthwana and Apoorva Dave. "Filling the Gaps in Oncofertility Care by Addressing Challenges Faced by Patients and Providers." *Cureus* 15 (2023).

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