EDITORIAL

Obstetrical Care in Survivors of Childhood Cancer: Utilization of Unique Linked Databases to Further Refine Consensus Guidelines

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With advances in treatment for childhood cancer over the last several decades, long-term survival rates are expected to exceed 80% (1). With the exception of those patients receiving total-body radiotherapy, radiotherapy directly to the ovaries, or high-dose alkylator chemotherapy as utilized in stem cell transplantation, many female survivors of childhood cancer will retain the capacity to become pregnant (2,3). The vast majority of the literature related to pregnancy and survivorship is focused on the ability to become pregnant or the impact of prior therapy on pregnancy outcomes such as miscarriages, stillbirths, and premature births (4,5).

There is less information available on the maternal risks in survivors who are able to maintain pregnancies. Much of the published data has been obtained from childhood cancer survivor cohort studies that have reported on the risks of pregnancy-related cardiomyopathy (6) or hypertension (7), or cancer registries linked to birth records (8) that have described other maternal conditions related to specific chemotherapy or radiation exposures. Cohort studies are advantageous in that they provide detailed information on the specific cancer treatment exposures, although they may be limited in obtaining detailed and comprehensive information on maternal outcomes secondary to a dependence on surveys of patient reports of long-term complications, as well as, in some cancer types, their relevance to more contemporary treated cohorts of childhood cancer survivors. Consensus guidelines have incorporated management recommendations based on the results of these studies, and in particular, referral of female survivors to high-risk maternal-fetal medicine programs is recommended, especially if treatment included anthracyclines or abdominal radiotherapy (9).

In this issue of the Journal, Reulen et al. report on the risk of developing pregnancy and labor complications in 2783 singleton pregnancies among 1712 female survivors of childhood cancer through linkage of population-based data from the British Childhood Cancer Survivor Study cohort with hospital inpatient and outpatient electronic health records from the Hospital Episode Statistics (HES) database in the United Kingdom (10). Utilization of the HES database also allowed comparison with risks observed in a large random sample of deliveries in the general population. Receipt of abdominal radiotherapy was associated with several pregnancy and labor complications. These survivors were more likely to have preterm delivery or low-birthweight infants, consistent with prior studies (5). Statistically significant risks for pregnancy-associated hypertension, gestational diabetes mellitus, and anemia were observed, especially for survivors of Wilms tumor treated with radiotherapy. Similar to reports in other Wilms tumor cohorts (7), hypertension was observed in nearly a quarter of Wilms tumor survivors receiving radiotherapy, but rates were not increased during pregnancy in those survivors with no history of abdominal radiotherapy. Gestational diabetes mellitus, a complication not previously linked to abdominal radiotherapy for childhood cancer, developed in 4.9% of survivors treated with radiotherapy, a rate statistically higher than observed in survivors treated without radiotherapy or in the general population (10).

As is the case with many population-based linked registry analyses, there are limitations as well as advantages with this approach. In addition to those highlighted by the authors, the survivor population is notable for Wilms tumor, comprising the largest proportion of survivors treated with abdominal radiotherapy (7.4%, vs 1.1% for the next largest group, Hodgkin lymphoma) (10). Given the potential for confounding factors specific to therapy for Wilms tumor (nephrectomy, specific adjuvant chemotherapy agents), the results may not be as
generalizable to other groups of survivors treated with abdominal radiotherapy. In addition, modern approaches for most childhood cancers have refined abdominal radiotherapy fields and doses, although the lack of statistically significant year-to-year variation in pregnancy and labor complications in this study suggests that risks persist, even in contemporary survivors. The linkage of this large population-based cohort with the comprehensive population-based inpatient, outpatient, and emergency hospital records has many strengths over existing cohort or hospital-based registry studies. However, the results of this study still do point toward the need for additional research, such as detailed normal tissue dosimetry studies of the kidneys and pancreas as a means of further understanding the impact of specific radiation doses on risk for development of pregnancy-associated hypertension and diabetes mellitus.

Of particular note, survivors treated without abdominal radiotherapy had similar rates of pregnancy or labor complications as the general population (10). Yet survivors, especially those with a history of bone tumors or treatment with abdominal radiation, were more likely to opt for elective cesarean section. Pregnancies in survivors treated with abdominal radiotherapy were not identified as high-risk pregnancies requiring greater supervision, compared with those survivors who had not received abdominal radiotherapy. These results suggest that there were not uniform practices in identifying survivors in need of referral to high-risk maternal-fetal medicine programs.

There continue to be disparities between consensus guidelines and what happens in clinical practice. As has been highlighted in the childhood cancer survivorship field, challenges in disseminating findings from survivorship research into the general population exist (9), and this extends into obstetrical care. Many female survivors may be unaware of the need for enhanced screening during pregnancy, especially as follow-up care at specialized survivor care centers declines considerably beyond the five-year post-treatment period (11).

The International Late Effects of Childhood Cancer Guideline Harmonization Group (http://www.ighg.org) is developing international evidence-based guidelines for the surveillance of chronic health problems in child, adolescent, and young adult cancer survivors. Guidelines led by experts in cancer survivorship and obstetrics have been published for the surveillance of premature ovarian insufficiency (12). Data from large population-based cohorts linked with hospital records provide critical contributions toward the refinement of evidence-based guidelines for the surveillance of obstetric complications. Even with the availability of guidelines, their use is inconsistent (13). With increasing numbers of female survivors of childhood cancer who retain the ability to become pregnant, the implementation of evidence-based guidelines for the surveillance of pregnancy and labor complications is even more critical.

Note
The authors have no conflicts of interest to disclose.

References