

BJOG-22-0767.R1 Multimorbidity warrants a proactive management of pregnancy in cancer survivors

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Invited mini-commentary on BJOG-22-0767.R1

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The population of adolescent and young adult (AYA) cancer survivors grows steadily owing to increasing survival rates around the world. Their reproductive health including infertility, as well as adverse pregnancy outcomes, has therefore become a significant area of interest.

In this large retrospective cohort study of Desai et al. (Desai et al. BJOG), the authors show an increased risk of premature birth and severe maternal morbidity in AYA survivors. Almost one third of these increased risks were mediated by maternal comorbidities. It is important to note that while the cancer survivors in this commercially insured population already had a fifty percent higher mean Maternal Comorbidity Index (1.8 vs 1.2), it is very well possible that comorbidity is even higher in the population insured via, for example, Medicaid. The International Guideline Harmonization Group has identified specific adverse pregnancy related outcomes that are known to be increased in childhood, adolescent and young adult cancer survivors, in order to characterize the population that will benefit specifically from a preconception consultation and pregnancy surveillance (van der Kooi et al. American Journal of Obstetrics and Gynecology, 2021. Volume 224, pages 3-15). As multimorbidity is common in this population, understanding specific treatment-related risks and its effect on the course of pregnancy is key in optimal clinical management.

Desai et al. report in their cohort of AYA cancer survivors a twofold increased prevalence of assisted reproductive technology (ART) use, but observed no modification of the risk on perinatal outcomes due to ART. This is reassuring, as the rapid growth in survival and fertility preservation will further increase the number of women with cancer that reproductive medicine units are caring for.

For individualized preconception consultation and pregnancy surveillance, more data is needed on the, perhaps dose-related, association between chemotherapy and radiotherapy and adverse pregnancy outcomes. Desai et al. report that prior chemotherapy but not radiation was associated with higher comorbidity index. Unfortunately, their insurance data does not provide specifics of the chemotherapy with regard to type and dosage. The subsequent observed increase in preterm births could be a consequence of anthracyclines resulting in peripartum cardiomyopathy and possibly iatrogenic prematurity, but also of alkylating agents resulting in loss of elasticity or vascularization. The lack of an association of radiotherapy with comorbidity index, or with preterm birth, is surprising, as an earlier meta-analysis showed an increased risk of premature delivery in cancer survivors treated with radiotherapy (RR 2.27, 95%-CI 1.34 – 3.82) (van der Kooi et al. European Journal of Cancer, 2019. Volume 111, pages 126 – 137) and abdominal radiotherapy was asso-

ciated with an increased risk of premature delivery in childhood cancer survivors (RR 1.70, 95%-CI 1.21 - 2.38) (Reulen et al. Journal of the National Cancer Institute, 2017. Volume 109).

The growing body of evidence emphasizes the need for preconception and prenatal surveillance as well as individualized pregnancy surveillance in AYA cancer survivors. Maternal comorbidity, previous anthracycline therapy, radiotherapy and possibly other chemotherapeutic agents warrant informed medical management to prevent and manage adverse pregnancy outcomes in this population that remains vulnerable with regard to the full breadth of their reproductive health.

Truncated citations

- 1 Desai et al. BJOG.
- 2 van der kooi et al. American Journal of Obstetrics and Gynecology, 2021. Volume 224, pages 3-15.
- 3 van der Kooi et al. European Journal of Cancer, 2019. Volume 111, pages 126 – 137.
4. Reulen et al. Journal of the National Cancer Institute, 2017. Volume 109