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JNCI J Natl Cancer Inst (2019) 111(11): djz063

doi: 10.1093/jnci/djz063
First published online April 9, 2019
Editorial

EDITORIAL

Colorectal Cancer Screening in Childhood Cancer Survivors

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Survivors of childhood, adolescent, and young adult cancer are at increased risk of developing subsequent colorectal cancers (CRCs) (1–4). Those who received abdominal radiotherapy or certain chemotherapeutic agents such as procarbazine (1,4) or platinum agents (1) for their first cancer are particularly at risk.

These findings in large cohorts of childhood, adolescent, and young adult cancer survivors have spurred the debate on whether (high-risk) survivors should be screened for CRC. However, there are several aspects of CRC screening for which current evidence is lacking in the population of childhood cancer survivors. For example, the trade-off between the potential benefits of CRC screening in terms of mortality and morbidity reduction and the potential harms such as distress and unnecessary diagnostic follow-up procedures or medical interventions due to false-positive findings (also considering the costs) is unclear.

In this issue of the Journal, Gini et al. provide important new insight into the balance between potential costs and benefits of colonoscopy-based CRC screening among childhood cancer survivors (5). The authors used a well-established screening simulation model (MISCAN-Colon) (6), which has been used previously to guide public health policy (7, 8). The model has been adjusted to reflect the elevated CRC risk of childhood cancer survivors based on risk estimates from the North American Childhood Cancer Survivors Study (CCSS) (1). Also, the elevated overall all-cause mortality of survivors in comparison with the general population was quantified using SEER-cancer registry data. The authors simulated 91 different screening strategies, with varying intervals and varying start and end ages of screening, in which measures of effectiveness (in terms of number of deaths prevented, mortality reduction, and life-years gained), resources (in terms of number of colonoscopies, total cost), and cost-effectiveness (ratio between additional costs and additional life-years gained) were calculated. The authors concluded that the optimal strategy among all survivors was to screen every 10 years from age 40 years to 60 years. This scenario averted 79.2% of CRC deaths and had a cost-effectiveness of $67 000 per life-year gained. Both in those treated with and without abdominopelvic radiotherapy, early initiation of screening was cost effective. One limitation the authors described was that they assumed the adherence to the screening was 100% in order to have unbiased estimates. This adherence rate is unlikely in a real-world scenario, as also shown in an evaluation of screening adherence in the CCSS population, where more than 70% of the survivors were not screened as recommended (9). Therefore, the population impact of the screening will be lower than estimated. Another important issue that the authors raised is that they only investigated screening by colonoscopy in their simulation study, because that is the preferred option in other high-risk populations. Alternative screening modalities, such as fecal occult blood testing, may constitute important alternative options in this particular population of survivors, and their value should be further investigated.

The US Preventive Services Task Force recommends colonoscopy-based CRC screening in the general population at ages 50–75 years, with an interval of every 10 years (10). It is important to evaluate whether screening among survivors should take place before the population-based screening programs start and whether screening should be more intensive at ages where population-based screening is in place. Although the results of the present study are an important contribution to existing data, there should be a note of caution for the results concerning survivors aged 50 years and older. The authors assumed a relative risk of 4.2 of CRC compared with the general population based on the standardized incidence ratios from the CCSS report (1). However, the majority of survivors in that report were younger than 50 years of age, with a large contribution of person-years prior to age 40 years. It is likely that the relative risk of CRC among survivors compared with the general population will be lower at older ages, as has been suggested for subsequent digestive cancers (3) and for any subsequent cancer (3,11,12), where partly substantial

Received: March 22, 2019; **Accepted:** April 3, 2019

decreases have been observed in the relative risk at higher attained ages. Moreover, the patients included in the CCSS study were diagnosed between 1970 and 1987, with decreases in administered radiotherapy dose and exposed volume of healthy tissues since. Albeit imprecise, the collective literature is suggestive of an association between levels of radiation exposure (13), which implies possibly lower CRC induction rates for more recently treated patients. Therefore, adequate stratification of risk groups according to treatment period may be necessary to avoid possible overscreening for those survivors treated in the 1990s and early 2000s and reaching their 30s and 40s in the upcoming years.

Currently, clinical practice guidelines addressing the surveillance for late effects in long-term survivors of childhood and young adult cancer have been published by several groups (14–18). There are differences in guidelines between countries with respect to recommendations for CRC screening among childhood cancer survivors. Only in the United States is active CRC screening recommended for childhood cancer survivors, with more intensive surveillance for those who received radiotherapy to the abdomen, pelvis, or spine or who received total body irradiation (14). International guideline development can help us to establish a common vision and integrated strategy for CRC surveillance in childhood and young adult cancer survivors throughout the world. The International Guideline Harmonization Group for late effects of childhood cancer is a worldwide endeavor to collaborate in guideline development. The main goal is to improve the quality and care of survivors of childhood, adolescent, and young adult cancers (19). The International Guideline Harmonization Group has planned to start this year with the development of a guideline on CRC surveillance based on the best available evidence on risk, diagnostic tests, and possible intervals for testing. This simulation study by Gini et al. is one piece of evidence towards the development of recommendations for CRC surveillance among childhood cancer survivors. To make balanced evidence-based recommendations about screening, further considerations of benefits and harms of screening and of possible screening modalities should be evaluated according to standard guideline development methods.

Notes

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The authors have no conflicts of interest directly related to this editorial.

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