Getting to the Heart of the Matter

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A current area of debate in oncology is the potential overdiagnosis and overtreatment of breast cancer, with ductal carcinoma in situ (DCIS) at the center of the controversy. Over 60,000 women are diagnosed with DCIS annually, comprising about 20% of all breast cancer diagnoses (1). Many of these women are treated with lumpectomy and radiotherapy (RT), based upon the results of the randomized trials of lumpectomy with or without RT demonstrating a statistically significant reduction in preinvasive and invasive events following RT (2–4). Among those who choose not to be treated with RT, the actual magnitude of developing an invasive event is unclear but has been estimated to be anywhere from 14–50% depending upon patient selection. Unfortunately, biomarkers have yet to reproducibly identify those lesions that will undergo malignant progression and those that will not. Therefore, the dilemma leading to overdiagnosis and overtreatment of DCIS persists.

For these reasons, many patients with DCIS will still need treatment, so clearly defining the potential risks of RT (along with the benefits) is crucial. Additionally, because patients with node-negative invasive disease are also treated with RT fields and techniques similar to those used for DCIS, understanding the risks from RT has an even greater impact.

In this issue of the Journal, Dr. Boekel and colleagues present a large registry study, including essentially all patients in the Netherlands with DCIS as their first neoplasia diagnosed before age 75 years, from 1989 through 2004. Through the Netherlands Cancer Registry (NCR), over 10,000 patients were identified and cross-linked to the Cardiac Intervention Registry, which captures data on all heart interventions, to the Statistics Netherlands Registry for cause of death, and to the Dutch Hospital Data Registry for hospital discharge diagnosis codes. The authors found that with a median follow-up of ten years, there was no overall difference in cardiovascular disease (CVD) risk comparing the 2,899 patients treated with surgery and RT vs the 7,466 patients treated with surgery alone. There was also no difference in CVD risk in patients treated with RT by laterality. However, interestingly, when a history of CVD within two years prior to DCIS diagnosis was considered, there was a 1.85 relative risk of a cardiac event in irradiated patients compared with the un-irradiated cohort. While this association was statistically nonsignificant, it is consistent with other reports that have noted patients with cardiac comorbidities to be at increased cardiac risk after RT (5). Thus, these patients must be watched carefully and managed appropriately.

Understanding the potential for cardiac toxicity following RT is important for all cancer patients. However, for patients with indolent or highly curable disease, a better understanding of the late effects of RT treatment, including cardiac toxicity, could have a profound impact as they consider their treatment options. Radiation-associated heart disease has been an area of research for over 20 years but recently was highlighted in an article by Darby and colleagues, which suggested increased cardiac risk as early as five years following breast cancer RT even with low doses of radiation to the heart (5). While this is an important study and one truly worthy of attention, the methodology did not allow patient-specific dose estimates to be calculated, which is particularly problematic when trying to estimate low dose cardiac exposures. The patients in this series were treated from 1958 to 2001, largely without CT-based planning, so heart doses were modeled based on a “typical” virtual patient. While this was a pragmatic approach, individual anatomy could not be considered. Since heart dose can vary dramatically based on the heart location of each patient, modeling may have resulted in inaccurate dose estimates.

So how can we continue to move forward and build upon the work by Darby et al. to acquire more accurate data on cardiac effects from radiation and to also minimize cardiac exposure whenever possible? How can we “get to the heart of the matter”? First, in CT-based treatment planning, it is essential to note the exact position of the heart relative to the breast for radiation planning and to allow precise dose calculations. Second, the heart must be contoured consistently. Without guidance, there is great variation in a seemingly simple task. To address contouring inconsistencies across disease sites, radiation oncology consensus atlases have been developed. For the heart, we created an atlas including expertise of cardiologists and cardiac radiologists and with it demonstrated more consistent calculation of heart doses (6). It has subsequently been validated by nine observers in Denmark and the UK and has been incorporated into the new Danish national guidelines (7). Additional work still remains to disseminate guidelines more widely. Finally, once we have accurate data, transfer between different vendor-specific treatment planning systems must be made easier so that we can pool actual cardiac dose data and link with cardiac outcomes.

What can we do in the meantime? Overall, cardiac risk following RT has been decreasing over time (8), likely due to increased emphasis of minimizing radiation dose to the heart, as well as improving technology for treatment planning and delivery while optimizing the care of cardiac comorbidities. We have at our disposal the ability to sculpt both high and low dose regions and deliver treatment with even greater precision. Furthermore, when
the heart is close to the RT field, maneuvers such as deep inspiration breath hold have been shown to displace the heart posteriorly away from the breast, thus reducing heart dose. Should maximal efforts to minimize cardiac exposure be incorporated into treatment planning for every patient undergoing breast RT where the heart is in close proximity to the radiation field? Absolutely! Although the paper by Boekel and colleagues suggests that consideration of dose to the heart following breast radiation delivered in the modern era may not be necessary, follow-up was short. Until we have more long-term data suggesting a safe dose threshold below which no cardiac toxicity is seen, we must err on the side of caution and always strive to minimize cardiac exposure. We have come a long way, and the results of Boekel et al. are indeed encouraging. Take heart—both cure and cardiac protection are achievable goals.

References

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