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Breast cancer radiotherapy and cardiac risk: The 15-year paradox!

Breast cancer is the leading cause of morbidity and mortality in women in the developed world and its incidence in the developing world is on the rise. Management of breast cancer requires a multimodality approach and an integration of the services of surgery, radiotherapy (RT), and chemotherapy. Recent reports have shown not only the established two-thirds reduction in local recurrence when RT is used after mastectomy or breast conserving surgery (BCS), but also an overall survival benefit of around 5-10%.[1-4]

However, for the past two decades, radiation-induced heart disease (RIHD) has become a subject of increasing discussion in articles and editorials. A cohort of nearly 90,000 women was reported from the Swedish Cancer Registry with data on laterality of breast cancer and cardiac mortality.[5] In this study, mortality from cardiovascular diseases was higher in women with left-sided tumors. The latest Early Breast Cancer Trialists’ Collaborative Group (EBCTCG) analysis reported a significantly increased risk of cardiovascular morbidity in breast cancer patients. In a meta-analysis involving 23,500 patients, they reported an excess risk associated with use of RT ($P = 0.0001$).[4]

Another meta-analysis reported by Cuzick et al., involving 7,941 women, found that the standardized mortality ratio in breast cancer patients was greater for patients treated with RT as compared to controls.[6]

Interestingly, RIHD has links with another steadily emerging concept in breast cancer. After BCS, hypofractionated RT in breast cancer has gained ground, especially since a Canadian randomized trial demonstrated its efficacy in achieving disease-free overall outcomes as well as equivalence in cosmesis scores.[7] This approach is at present being vigorously pursued by the UK groups and a series of randomized trials are underway.[8]

Hypofractionation is an interesting concept in breast cancer patients and has two cardinal rationales: The first is the logistic rationale - the fact that the number of RT fractions in BCT is actually reduced by half can certainly make BCT more attractive and more acceptable for the patient and the doctor. The other rationale is the biological rationale - the fact that alpha/beta of breast cancer is less than 4 is being proposed by the UK trials. This means that breast cancer will be more sensitive to dose per fraction, and a higher dose per fraction will give a higher therapeutic ratio for breast cancer than conventional fractionation (2 Gy/day). This is important since it means that further improvement (albeit small) in local control rates may be possibly achieved by hypofractionation.

We had, however, written earlier about the hazards of increasing the dose per fraction in breast cancer without considering the cardiac effects.[9] Indeed, a second school of thought with inherent contradiction is doing the rounds. Some authors suggest using 1.8 Gy per fraction (less than conventional) to prevent cardiac morbidity in breast cancer.[10] A cardinal fact to be kept in mind in this regard is suggested by the recent EBCTCG analysis. It may take nearly 15 years of follow-up to decisively determine the full spectrum of cardiovascular effects post radiotherapy and all future trials would do well to keep this in mind.

On the other hand, it can be argued that current radiotherapy practice is very much different from the one practiced two decades back. Radiation oncologists, buoyed by the giant leaps in radiation oncology gadgets and technical innovations (e.g., high-precision linear accelerators, 3-D conformal therapy, intensity-modulated radiotherapy, and image-guided radiotherapy) are emphatic that the cardiovascular risk has considerably decreased. Also, there is an increasing trend for omission of the internal mammary field (which presumably increased the dose to the heart in the earlier reported series). Besides, the studies stating a significant cardiovascular risk too had their own flaws. For example, the Swedish study took no account of the volume of heart irradiated, preexisting cardiac morbidity, dose and fractionation, or the use of adjuvant chemotherapy that contains potentially cardiotoxic anthracycline. Similarly, the EBCTCG results and the meta-analysis by Cuzic are based on what would now be considered as poor...
radiotherapy techniques and poor fractionation schedules. Also, to the defense of the radiation oncologist, some trials have reported minimal morbidity post radiotherapy. Overgaard et al., in a more recent publication, have shown no excess cardiac deaths in patients followed up for over 10 years.[11] The combined analysis of the premenopausal and postmenopausal trials of the Danish Breast Cooperative Group has shown that the newer techniques of radiotherapy have reduced cardiac morbidity.[12] In a SEER study by Giordano, with each succeeding year after 1979, the hazard of death from ischemic heart disease for women with left-sided vs those with right-sided disease declined by 6% (HR = 0.94, 95% CI = 0.91-0.98), a standing testimony to the claims of the radiation oncologist.

Furthermore, in a recent SEER study, analysis of data on 16,270 patients reported no significant differences between patients with left-sided vs right-sided breast tumors in cardiac morbidity in patients who received RT.[14] Finally, the studies which demonstrated cardiac morbidity have used different doses and different parameters for cardiac morbidity and/or cardiac mortality assessment. The long-term follow-up required (> 15 year median follow-up) to unequivocally establish the cardiac risk with RT is unfortunately found wanting in most series. This has led to ambiguity in this rather important subject. Finally, the tools for measuring cardiac morbidity have been varied and been loosely applied. Some of these (such as perfusion studies) even show some reversibility over time.[15] No clinical studies in literature have assessed DVH comparisons of the dose received by the heart and the long-term risk of RIHD. It may also be difficult to determine (especially in single-arm studies) whether the cardiac morbidity was due to the natural course of events and factors such as hypertension, smoking, or diabetes or actually because of the effect of RT.

What should the present-day radiation oncologist do to avoid or minimize RIHD? Till definite clinical data is available, it would be prudent to spare the heart as much as possible. Possible strategies for this could involve keeping the heart away from the posterior edge of the tangential portal in conventional simulation. Similarly, in CT-based simulation, it would be proper to do contouring of the heart and take the cardiac DVH also into consideration while deciding the collimation or the wedge thickness. Treatment in the lateral decubitus or prone positions has been reported to give a lesser dose to the heart and can be employed in suitable situations.[16,17] Another option is to manipulate the medial and the lateral borders of the portals to achieve cardiac sparing. If the tumor is medially placed, it is the lateral border which is moved up and if the tumor is medial, then the medial border will be taken away from midline (towards the ipsilateral side). This technique does involve sparing a portion of the involved breast but the risk of such tumors to develop a far away local recurrence is extremely small, especially if the initial tumor size is small.[18,20] It would seem rational not to exceed a daily dose per fraction of more than 1.8-2 Gy in case it is not possible to avoid a significant portion of the heart in the treatment portals. Finally, patients should be advised to stop smoking and take appropriate medications to control their hypertension and diabetes.[21]

If, indeed, the current hypofractionated trials prove to cause excessive cardiac morbidity in due course of time, the smart radiation oncologist can still have the last laugh: he can say, “Oh! We no longer use those primitive techniques,” and the verdict will be postponed for a further 15 years!

REFERENCES

13. Giordano SH, Kuo YF, Freeman JL, Buchholz TA, Hortobagyi GN, Goodwin JS. Risk of cardiac death after adjuvant radiotherapy for


