Updates in Postmastectomy Radiation

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KEYWORDS

• Mastectomy • Postmastectomy • Radiation • Clinical risk factors
• Locoregional failure

KEY POINTS

- Locoregional failure rates after postmastectomy radiation have decreased in the modern era because of multiple factors.
- In patients with 1 to 3 positive nodes, additional clinical and pathologic risk factors must be considered when recommending treatment.
- Postmastectomy radiation is recommended in certain patients with node-negative disease who have high-risk features.
- Increased use of neoadjuvant chemotherapy in early breast cancer creates clinical challenges in patient selection for postmastectomy radiation, and increasing data suggest that response to treatment may be used to tailor locoregional therapy recommendations in selected patients.

Radiation therapy has been used for decades to eradicate occult microscopic disease in the postmastectomy chest wall and draining regional nodal basins, thereby decreasing locoregional failure (LRF) and even improving survival end points in select patients.

Many of the historic data clinicians use to guide the use of postmastectomy radiation therapy (PMRT) includes patients treated in the 1970s and 1980s, an era in which LRF was substantially higher than it is now. Since the publication of the landmark randomized studies showing the benefits of PMRT, there has been a marked decrease in LRF among patients with breast cancer after mastectomy because of multiple factors.[1–4] These factors include improved diagnostic and staging tools, earlier stage at diagnosis, improved surgical techniques, and increasingly effective systemic therapies. In light of this, this article provides updates on recommendations regarding PMRT based on contemporary data.

Disclosure: The authors have nothing to disclose
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Surg Oncol Clin N Am 26 (2017) 383–392
http://dx.doi.org/10.1016/j.soc.2017.01.010
surgonc.theclinics.com

PMRT FOR 1 TO 3 POSITIVE NODES

The use of PMRT in the setting of 4 or more positive lymph nodes has been broadly accepted because of the high risk of LRF in this population; however, controversy remains regarding the utility of PMRT in patients with 1 to 3 positive nodes. The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) updated their meta-analysis on the role of PMRT in 2014.[1] The meta-analysis included 22 trials and 8135 patients with breast cancer between 1964 and 1986 who were randomly assigned to receive chest wall and regional nodal radiotherapy after mastectomy and axillary dissection. A subset analysis of 1133 patients with 1 to 3 positive nodes who had received systemic therapy showed a LRF rate of 21% without irradiation and 4.3% with PMRT at 10 years ($P<.001$). The 10-year rate for any recurrence, either local or distant, was 45.5% without radiation and 33.8% with radiation ($P<.001$). Moreover, breast cancer mortalities were 49.4% and 41.5% ($P = .01$) without radiation and with radiation, respectively. These data support the benefit of PMRT in preventing both LRF and overall recurrence, as well as improving breast cancer mortality. Although these numbers are clearly supportive of the benefits of PMRT, most patients included in the EBCTCG analysis were included in randomized trials conducted in the 1970s and 1980s and broadly grouped patients by nodal stage but not other more recently elucidated risk factors for recurrence such as receptor status, age, lymphovascular invasion (LVI), grade, and other pathologic features.[2–4] In the current era, rates of LRF seem to be considerably lower than the rates mentioned earlier, and are understood to vary substantially with risk factors for recurrence. The trend toward lower rates of LRF in more recent years is highlighted in a study from the MD Anderson Cancer Center in which a cohort of 1027 patients with T1 to T2 breast cancer with 1 to 3 positive lymph nodes treated with mastectomy and systemic therapy with or without PMRT were analyzed by treatment era.[5] Specifically, those treated in an early era (1978–1997) were compared with those treated in a later era (2000–2007). In the early cohort, PMRT was observed to decrease 5-year rates of LRF from 9.5% to 3.4% ($P = .028$). However in the later cohort, PMRT did not seem to significantly decrease rates of LRF, and 5-year rates of LRF without PMRT were only 2.8%. Overall in modern series, rates of LRF in patients treated with mastectomy and systemic therapy without radiation generally range from 4% to 23% (with most studies ranging from 4% to 10%) depending on risk factors.[5–8]

Several contemporary retrospective studies have highlighted the significance of specific risk factors for recurrence in determining the utility of PMRT in patients with 1 to 3 positive nodes. Moo and colleagues[9] published a retrospective analysis of 1331 patients with T1 to T2 tumors with 1 to 3 positive nodes who underwent mastectomy with or without PMRT. The overall rate of LRF in the no-PMRT group was 4.3%. On a multivariate analysis of patients in the no-PMRT group, both age less than or equal to 50 years and lymphovascular invasion (LVI) were significantly associated with increased risk of LRF, suggesting that these factors warrant consideration of PMRT in this cohort. Similarly, Yildirim and Berberoglu[8] published a study of patients with T1 to T2 tumors with 1 to 3 positive nodes who were observed without PMRT, and the overall rate of LRF was 4.3% at a median follow-up time of 70 months. On multivariate analysis, age less than or equal to 35 years, LVI, and ratio of positive nodes greater than 15% were the most important prognostic factors for LRF. Moreover, patients with 2 or 3 of the risk factors mentioned earlier had a LRF rate of 23%, compared with 2.7% among those who had only 1 risk factor. Both these studies highlight the importance of individual clinical-pathologic risk factors when evaluating the benefit of PMRT in patients with 1 to 3 positive nodes.