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Clinical Investigation

Nomogram for Predicting the Risk of Locoregional Recurrence in Patients Treated With Accelerated Partial-Breast Irradiation

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Summary

Accelerated partial-breast irradiation (APBI) is a treatment option in appropriately selected patients with early-stage breast cancer. Although societal guidelines have been formulated to stratify patients into risk groups, they do not take into consideration the impact of multiple risk factors on clinical outcomes. We have created an easy-to-use nomogram that predicts for locoregional failure in patients treated

Purpose: To develop a nomogram taking into account clinicopathologic features to predict locoregional recurrence (LRR) in patients treated with accelerated partial-breast irradiation (APBI) for early-stage breast cancer.

Methods and Materials: A total of 2000 breasts (1990 women) were treated with APBI at William Beaumont Hospital (n = 551) or on the American Society of Breast Surgeons MammoSite Registry Trial (n = 1449). Techniques included multiplanar interstitial catheters (n = 98), balloon-based brachytherapy (n = 1689), and 3-dimensional conformal radiation therapy (n = 213). Clinicopathologic variables were gathered prospectively. A nomogram was formulated utilizing the Cox proportional hazards regression model to predict for LRR. This was validated by generating a bias-corrected index and cross-validated with a concordance index.

Results: Median follow-up was 5.5 years (range, 0.9-18.3 years). Of the 2000 cases, 435 were excluded because of missing data. Univariate analysis found that age <50 years, pre-/perimenopausal status, close/positive margins, estrogen receptor negativity, and high grade were associated with a higher frequency of LRR. These 5 independent covariates were used to create adjusted estimates, weighting each on a scale of 0-100. The total score is identified on a points scale to obtain the probability of an

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Conflict of interest: none.

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with APBI in the off-protocol setting.

LRR over the study period. The model demonstrated good concordance for predicting LRR, with a concordance index of 0.641.

Conclusions: The formulation of a practical, easy-to-use nomogram for calculating the risk of LRR in patients undergoing APBI will help guide the appropriate selection of patients for off-protocol utilization of APBI. © 2015 Elsevier Inc.

Introduction

Accelerated partial-breast irradiation (APBI) is emerging as a safe and viable treatment option for appropriately selected women with early-stage breast cancer (1-3). Although several randomized trials comparing APBI with the current standard of care, whole-breast irradiation (WBI), are completed or are currently accruing, there have been multiple societies that have made recommendations regarding the utilization of this treatment technique off-protocol, taking into account a variety of clinical and pathologic factors (4-7). The American Society for Radiation Oncology (ASTRO) released a consensus statement in 2009 that stratified patients according to risk groups based on factors including age, BRCA status, tumor size, margin status, presence of lymphovascular space invasion, estrogen receptor (ER) status, histology, multifocality, nodal status, extensive intraductal component, and the use of neoadjuvant therapy (7).

Although these recommendations provide clinicians with guidelines for treatment, there are limitations associated with these societal-based recommendations. Although individual factors in these guidelines have been associated with local recurrence (8-12), studies have demonstrated that these guidelines fail to consistently stratify patients by local recurrence risk (13, 14). It is also important to point out that these guidelines are now outdated 5 years, with new data available for updating.

Currently there is a paucity of data integrating multiple risk factors to predict outcomes in patients with early-stage breast cancer. A nomogram developed at Memorial Sloan-Kettering Cancer Center evaluated factors associated with local failure after breast-conserving therapy in patients with ductal carcinoma in situ (DCIS) (15). The applicability of this nomogram remains limited owing to the confines of their patient cohort, nearly half of whom did not receive adjuvant radiation therapy, despite its proven benefit in decreasing risk of local failure even in patients with very favorable disease (16-18). Thus, the availability of a tool that identifies patients at higher risk of local failure would be useful for aiding in the clinical decision-making process of adjuvant radiation therapy, allowing clinicians to identify patients for whom APBI would be most beneficial. Therefore, the purpose of this study was to use our long-term clinical experience with APBI to develop a nomogram that will account for clinical and pathologic characteristics that may stratify patients by ipsilateral breast locoregional recurrence (LRR) to determine the most appropriate patients for treatment with APBI.

Methods and Materials

Patient characteristics

The study cohort consisted of 2000 cases (1990 patients, 10 with bilateral breast cancer) treated with a lumpectomy followed by APBI for early-stage breast cancer at William Beaumont Hospital (WBH n = 551) and the American Society of Breast Surgeons MammoSite Registry Trial (ASBrS; n = 1449). Patient characteristics and clinical outcomes were combined and analyzed using clinical–pathologic definitions and outcome calculations that have been previously described (19, 20). This study was approved by the WBH institutional review board (HIC no. 2013-449).

WBH cohort

Patients were treated between June 1995 and May 2013. Treatment techniques included multiplanar interstitial catheters (n = 98), balloon-based brachytherapy with either MammoSite (Hologic, Bedford, MA) or Contura (SenoRx, Aliso Viejo, CA) devices (n = 240), and 3-dimensional conformal radiation therapy (n = 213). Brachytherapy dosing was via low-dose-rate (50 Gy over a 96-hour period at 0.52/Gy/h) or high-dose-rate (32-34 Gy in 8-10 fractions) implants. Forty-five patients were treated on 1 of 2 in-house protocols delivering 28 Gy in 4 twice-daily fractions using high-dose-rate brachytherapy. Three-dimensional conformal radiation therapy was delivered to a total of 38.5 Gy in 10 fractions. Patients enrolled on the ASBrS MammoSite Registry Trial were removed from the WBH cohort to avoid data redundancy.

American Society of Breast Surgeons cohort

The ASBrS MammoSite Registry Trial evaluated outcomes from patients treated with the MammoSite single lumen brachytherapy device. This was a collaborative group registry from 97 institutions. Patients were treated between May 2002 and July 2004, all of whom received adjuvant APBI via the MammoSite single lumen device to a total dose of 34 Gy in twice-daily fractions. Demographic and clinical information, along with follow-up data for clinical outcomes, was gathered prospectively. Margin status was defined as "negative" if more than 2 mm from the tumor margin, "close" if the margin was <2 to ≥ 0.01 mm, and "positive" if there was tumor at the margin. More detailed information regarding the trial's enrollment criteria, data collection/management, treatment techniques, statistical analyses, and follow-up protocols have been published previously (21, 22, 23).