



Original article

Omission of radiotherapy in elderly women with early stage metaplastic breast cancer

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ABSTRACT

Purpose: Multiple studies have evaluated the omission of radiation therapy (RT) in elderly women with invasive carcinoma; no studies to date have assessed this question for metaplastic breast cancer (MBC). This study is the only known study describing national practice patterns and addressing the impact of RT versus observation on survival in elderly women with T1-2N0 MBC.

Methods: The National Cancer Data Base was queried (2004–2013) for women aged ≥ 70 years with T1-T2N0 MBC that underwent lumpectomy. Multivariable logistic regression ascertained factors associated with RT administration. Kaplan-Meier analysis evaluated overall survival (OS) between patients treated with or without postoperative RT. Cox proportional hazards modeling determined variables associated with OS. Propensity matching was performed in order to address indication bias.

Results: Of 547 total patients, 176 (32%) underwent observation, and 371 (68%) received postoperative RT. Temporal trends revealed that withholding RT steadily declined over the studied time period. RT delivery was less likely in patients not undergoing hormonal therapy or those ≥ 80 years old. In both the overall population and following propensity matching, delivery of RT was associated with higher OS ($p < 0.001$ for both). On Cox multivariate analysis, poorer OS was independently associated with advancing age, higher T stage, high-grade disease, and omitting postoperative RT ($p < 0.05$ for all).

Conclusions: Although level I evidence exists to omit RT in select elderly women, this is the only study evaluating this notion for MBC. These results do not support the routine withholding of RT in T1-2N0 MBC owing to the independent association with worse survival.

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1. Introduction

Level I evidence has existed for over a decade demonstrating that omission of postoperative radiation therapy (RT) in select T1-2N0, elderly women with invasive carcinoma is safe and results in acceptably low local recurrence rates without a detriment in overall survival (OS) [1–3]. Although the age threshold has varied based on the trial, including 50 [1], 70 [2], and 65 [3], none of these trials examined outcomes for patients with metaplastic breast cancer (MBC).

MBC is a rare but aggressive form of breast cancer with distinct histopathologic and molecular characteristics [4,5]. Although MBC

is frequently triple-negative, its prognosis is independently poorer than that of an invasive ductal triple-negative counterpart, likely due to other pathologic and molecular factors contributing to a high propensity for local-regional relapse [6–8] and relative resistance to systemic treatments [4,5].

There are limited investigations, none prospectively performed, illustrating management of this rare neoplasm [9–13]. As such, there are many unresolved aspects of management, including whether elderly patients should be treated by extrapolation of the aforementioned trials of RT omission, or whether all patients undergoing lumpectomy should receive postoperative RT. The present study, performed with the large, contemporary National Cancer Data Base (NCDB), is the only known study of MBC that evaluates management specifically in the elderly population. The goals of this investigation were to ascertain national practice patterns and temporal trends of management, along with the effect of omitting RT on survival.

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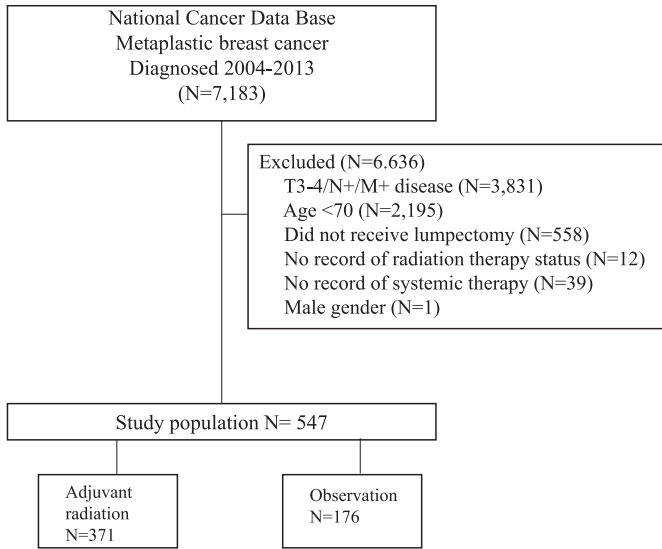


Fig. 1. Patient selection diagram.

2. Materials & Methods

The NCDB is a joint project of the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society, which consists of de-identified information regarding tumor characteristics, patient demographics, and patient survival for approximately 70% of the US population [14–17]. All pertinent cases are reported regularly from CoC-accredited centers and compiled into a unified dataset, which is then validated. The NCDB contains information not included in the Surveillance, Epidemiology, and End Results (SEER) database, including details regarding

use of systemic therapy. The data used in the study were derived from a de-identified NCDB file (2004–2014). The American College of Surgeons and the CoC have not verified and are neither responsible for the analytic or statistical methodology employed nor the conclusions drawn from these data by the investigators. As all patient information in the NCDB database is de-identified, this study was exempt from institutional review board evaluation.

Inclusion criteria for this study were ≥70 year old women with newly-diagnosed, T1-2 N0 M0 MBC treated with lumpectomy. Records regarding use of RT and systemic therapy as well as vital status were required for inclusion in the study. Patients receiving either neoadjuvant or adjuvant chemotherapy were eligible for the present study. The International Classification of Disease (ICD)-0-3 codes included in the present study were 8560, 8562, 8570–8572, 8575, and 8980–8982, based on previously published studies that have included different variants of MBC [11]. In accordance with the variables in NCDB files, information collected on each patient broadly included demographic, clinical, and treatment data.

All statistical tests were two-sided, with a threshold of $p < 0.05$ for statistical significance, and were performed using STATA (version 14, College Station, TX). Multivariable logistic regression modeling ascertained characteristics predictive of RT administration. Survival analysis was per the Kaplan-Meier method, with group comparisons carried out with the log-rank test. Overall survival (OS) referred to the interval between the date of diagnosis and the date of death, or censored at last contact. Univariate analysis evaluated factors associated with overall survival; subsequently, Cox multivariate analysis included variables that were either significant or showed a strong trend to statistical significance on univariate analysis. The proportional hazards assumption was checked graphically using log-log plots.

To account for indication bias, propensity score matching was used to compare patients between groups. Propensity matching is a method that creates quasicase/control pairs using a retrospective

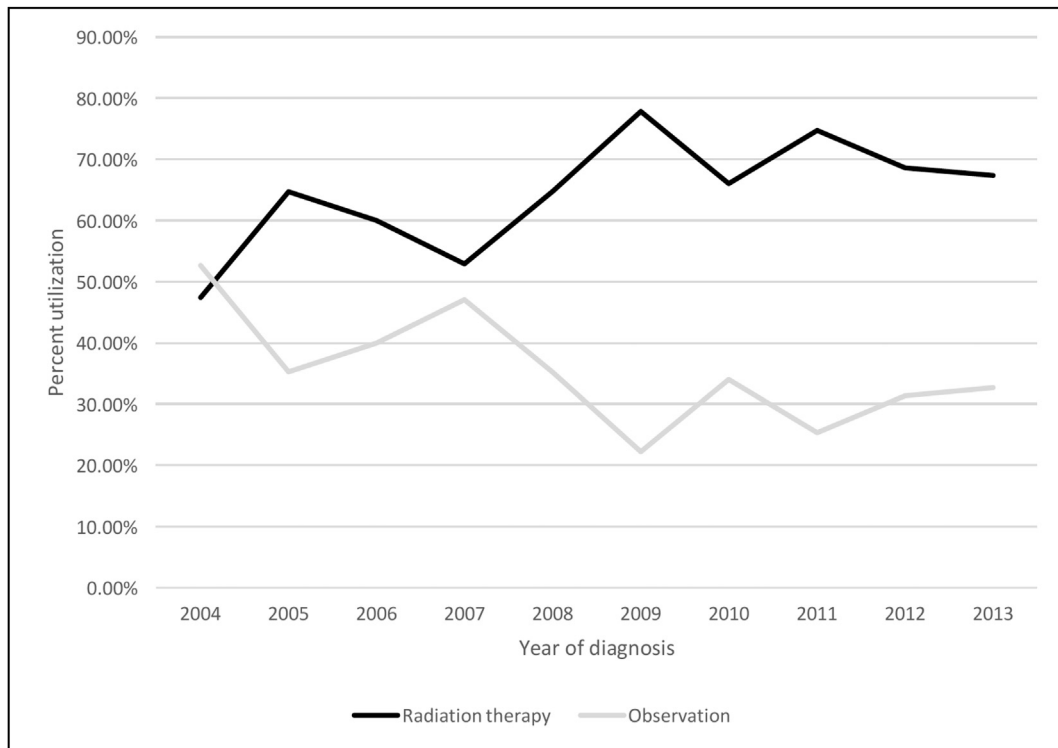


Fig. 2. Utilization of radiation therapy versus omission thereof over time.

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