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Survival after partial breast brachytherapy in elderly patients with nonmetastatic breast cancer

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ABSTRACT

BACKGROUND: Despite growing utilization of accelerated partial breast irradiation using brachytherapy (APBI-Brachy) for elderly breast cancer patients, there are limited data from randomized Phase III trials to support its routine use. This study uses population-based data to examine whether APBI-Brachy results in comparable survival rates compared with whole breast irradiation (WBI).

METHODS: A sample of 29,647 female patients diagnosed with nonmetastatic breast cancer in 2002–2007 treated with breast-conserving surgery and radiotherapy was identified in the Surveillance, Epidemiology, and End Results Program-Medicare data set. Log-rank tests, Cox proportional hazards models, instrumental variable analysis, and subgroup analysis were used to study the comparative effectiveness of APBI-Brachy and WBI.

RESULTS: During a median followup of 3.6 and 4.8 years, 123 (7.7%) and 3438 (13.6%) patients died after APBI-Brachy and WBI, respectively. Recurrence-free survival ($p = 0.9711$) and overall survival rates ($p = 0.0551$) did not differ significantly between the two radiation modalities. After accounting for tumor characteristics, patient characteristics, community factors, and comorbidities, the recurrence-free survival (hazard ratio, 1.05; 95% confidence interval, 0.90–1.23; $p = 0.5125$) and overall survival (hazard ratio, 0.87; 95% confidence interval, 0.72–1.04; $p = 0.1332$) rates were still not significantly different between patients treated with APBI-Brachy and WBI.

CONCLUSION: Partial breast brachytherapy and WBI resulted in similar recurrence-free and overall survival rates in this cohort of elderly breast cancer patients, even after adjustment for the more favorable characteristics of patients in the former group. These findings will need to be confirmed by the randomized trials comparing these modalities.

Keywords: Brachytherapy; Breast-conserving therapy; Accelerated partial breast irradiation; Breast carcinoma; Effectiveness

Introduction

Radiation therapy has played an important role in improving survival and local control rates among female breast cancer patients in multiple randomized trials (1). Whole breast irradiation (WBI) has been recommended for patients with early stage cancers after breast-conserving surgery (BCS) in practice guidelines (2–4). However, WBI involves a 4–7-week course of daily treatment, depending on the schedule chosen. It has been suggested that this burden is an important cause of lack of adherence for receiving appropriate adjuvant radiation therapy (5). Accelerated partial breast irradiation (APBI) is an alternative to WBI, which significantly decreases the number of patient visits and thus could potentially reduce the incidence of radiation therapy omission after BCS. In contrast to 16–36 fractions of radiotherapy in WBI, APBI usually involves twice-daily treatments for more than 5 days. Accelerated partial breast irradiation using brachytherapy (APBI-Brachy) is a procedure in which physicians

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place catheters or a balloon applicator inside the breast to deliver radiation to the operative cavity and surrounding tissue using a radioactive isotope. APBI-Brachy has become an increasingly popular alternative to WBI in the United States (6).

Despite its increasing utilization, the use of APBI-Brachy as the sole radiation treatment after BCS remains controversial. Recent clinical trials found that APBI-Brachy provides similar local control rates compared with WBI (7–11). However, a recent population study using Medicare claims data found that APBI-Brachy is associated with a twofold increased risk for subsequent mastectomy compared with WBI in elderly patients (12). Their study was criticized by the American Brachytherapy Society for not controlling for important tumor characteristics (13). The results of large Phase III randomized trials being conducted in North America and Europe, which compare WBI to APBI, will take many more years to emerge (14).

We, therefore, feel that an immediate need exists for a population-based study to compare the effectiveness of APBI-Brachy with that of standard WBI. We used the linked Surveillance, Epidemiology, and End Results Program (SEER)-Medicare database to examine this issue after accounting for tumor, patient, and comorbidity factors. Instrumental variable analyses and subgroup analyses were used in this study to control for the selection bias in the observational data (15, 16). Instrumental variable analysis mimics the key feature of randomization by finding a variable that affects treatment assignment but has no independent effect on outcomes. Subgroup analyses analyzed the survival outcomes among the patients that fit most closely into the ''suitable'' category of the American Society for Radiation Oncology (ASTRO) consensus guidelines.

Methods

Data source

Data for this study were taken from the linked SEER-Medicare database. The SEER-Medicare data reflect the linkage of two large population-based sources of data that provide detailed information about Medicare beneficiaries with cancer. The current SEER-Medicare database 2011 edition contains SEER registry information for patients with a first breast cancer diagnosed between 2002 and 2007 and Medicare claims of those patients from 2001 to 2009. Patients' census tract information and sociodemographic information of patients' census tract are also included. The SEER program of the National Cancer Institute currently collects and publishes cancer incidence and survival data from 18 population-based cancer registries covering approximately 28% of the U.S. population (17). SEER regions include the states of California, Connecticut, Hawaii, Iowa, Louisiana, New Jersey, New Mexico, Utah; multicounty areas of Atlanta and rural Georgia and Detroit; and American Indians/Alaska Natives in Arizona and Alaska. Medicare is the primary health insurer for 97% of the population aged 65 years and older. The Medicare program is likely to have complete claims information for patients not enrolled in a health maintenance organization and has therefore, been used extensively in cancer care research. The SEER-Medicare data have also been used to study recurrence and survival among breast cancer patients (18–20).

The Pennsylvania State University Institutional Review Board approved this study, and the National Cancer Institute, Centers for Medicare & Medicaid Services, and individual SEER cancer registries approved data requests. This article was reviewed by the SEER-Medicare program to ensure the confidentiality of patients and providers in SEER areas.

Cohort selection

A sample of 26,931 female patients aged 65 years or older was identified. We limited the analysis to those most likely to have complete claims, namely patients who had continuous Medicare Part A and Part B enrollment and no enrollment in a health maintenance organization from diagnosis through death or to the end of this study (December 31, 2009). The cohort was restricted to patients who underwent radiotherapy within 6 months after their last BCS. Patients who died and who had a secondary diagnosis of cancer or subsequent mastectomy within this 6-month period were excluded because they may have elevated risk

Table 1
Claims codes used to classify treatment modalities

Procedures	*ICD-9* procedure codes	CPT/HCPCS codes
WBI	9221–9226, 9228, 9229	77427, 77431–77432, 77401–77409, 77411–77414, 77416, 77418, 77470, 77499, 77520, 77522–77523, 77525, 77750, 77789, 77790
Brachytherapy	9227	19296–19298, 77326–77328, 77761–77763, 77776–77778, 77781–77784, Q3001, C9714–C9715
BCS	8520–8523, 8525	2002–2006: 19110, 19120, 19125, 19160, 19162 2007–2008: 19110, 19120, 19125, 19301, 19302
Chemotherapy	9925	96400–96549, Q0083–Q0085, J8520, J8521, J8530, J8540, J8560, J8597, J8610, J8999; J9000–J9999 but excluding J9003, J9165, J9175, J9202, J9209, J9212–J9226, J9240, J9395

CPT = Current Procedural Terminology; HCPCS = Healthcare Common Procedure Coding System; *ICD-9* = *International Classification of Diseases, Ninth Revision*; WBI = whole breast irradiation; BCS = breast-conserving surgery.