RESEARCH LETTER

Single- vs Multiple-Fraction Radiotherapy for Bone Metastases From Prostate Cancer

Palliative radiotherapy, comprising 1 or more fractions (ie, treatments) of daily radiation, is the mainstay of treatment for painful bone metastases. In 2005, a US-based randomized trial demonstrated no difference in pain relief between single- and multiple-fraction radiotherapy for uncomplicated bone metastases, confirming results from international trials.1,2

The Choosing Wisely campaign advocates single-fraction treatment for bone metastases.3 We examined whether single-fraction treatment has been incorporated into routine clinical practice for Medicare beneficiaries with prostate cancer and at what cost savings.

Methods | The Surveillance, Epidemiology and End Results (SEER)-Medicare database links patient data collected by SEER cancer registries to longitudinal Medicare claims.4 We selected patients aged 65 years or older with prostate cancer and identified bone metastases (International Classification of Diseases, Ninth Revision, diagnosis code 198.5) and subsequent courses of radiotherapy from January 1, 2006, through December 31, 2009.

For each patient, we identified the initial outpatient course of radiotherapy following the first diagnosis of bone metastases (index course) and ascertained the dates and number of radiotherapy fractions based on Medicare claims for radiation delivery (Medicare reimburses each radiotherapy fraction individually). Gaps between fractions of 14 days or longer were presumed to indicate new courses of radiotherapy.

Total and radiotherapy-related health care expenditures were calculated from the amount reimbursed by Medicare from the inpatient, outpatient, and physician/supplier component files from 15 days before the initial radiotherapy treatment date to 30 days posttreatment and were adjusted for inflation to 2009. Radiotherapy-related expenditures were calculated by summing Current Procedural Terminology codes between 77261 and 77999.5

We classified patients into single- or multiple-fraction treatment groups. We compared prognosis between the groups by evaluating survival estimates (palliative radiotherapy is not associated with survival improvements). We compared mean expenditures using analysis of variance. In sensitivity analysis, we restricted the cohort to patients without prior complicating events, including radiation, bone surgery, cord compression, or pathologic fracture.

Analyses were conducted using Stata version 12.1 (StataCorp). Statistical significance was set at .05 and all tests were 2-sided. The study was approved with a waiver of informed consent by the University of Pennsylvania institutional review board.

Results | Of 3050 patients, the median age was 78 years (interquartile range, 73-83 years), 85% were white, and 82% had 2 or more comorbid illnesses. Of these patients, 3.3% (95% CI, 2.7%-3.9%) had single-fraction radiotherapy and 50.3% (95% CI, 48.5%-52.1%) received more than 10 fractions (Table). In a sensitivity analysis restricted to 2028 patients without prior complicating events, 3.8% (95% CI, 3.0%-4.6%) had single-fraction radiotherapy.

Unadjusted median survival following the index radiotherapy course was lower in the single- compared with the multiple-fraction treatment group (5.0 months [95% CI, 3.6-10.5 months] vs 11.9 months [95% CI, 11.2-12.7 months], respectively; log-rank \( P = .001 \)). Among patients who survived more than 6 months, 51.7% (1076/2080) received subsequent radiation treatment (no significant difference between groups, \( P = .47 \)).

Mean 45-day radiotherapy-related expenditures were 62% lower for patients treated with single relative to multiple fractions ($1873 for single vs $4967 for multiple fractions; difference, $3094 [95% CI, $2107 to $4081]; \( P < .001 \)). Mean 45-day total health care expenditures were $13,112 for single and $11,702 for multiple fractions (difference, $1409 [95% CI, −$568 to $3386]; \( P = .16 \)). Mean 45-day total expenditures were substantially for patients who received single-fraction treatment because they were closer to death and using other medical services.

Discussion | Despite evidence demonstrating comparable pain relief for single-fraction treatment, only 3.3% of Medicare beneficiaries with bone metastases from prostate cancer received single-fraction treatment. Patients who received single-

### Table. Radiotherapy for Bone Metastases From Prostate Cancer, 2006 to 2009

<table>
<thead>
<tr>
<th>No. of Radiotherapy Fractions</th>
<th>Medicare Beneficiaries, No. (%) [95% CI]</th>
<th>Expenditures, Mean (95% CI), $</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>101 (3.3) [2.7-3.9]</td>
<td>1873 (903-2843)</td>
</tr>
<tr>
<td>2-5</td>
<td>395 (13.0) [11.8-14.1]</td>
<td>4967 (4787-5147)*</td>
</tr>
<tr>
<td>6-10</td>
<td>1020 (33.4) [31.8-35.1]</td>
<td>11,702 (11,343-12,062)*</td>
</tr>
<tr>
<td>11-20</td>
<td>1177 (38.6) [36.9-40.2]</td>
<td></td>
</tr>
<tr>
<td>&gt;20</td>
<td>357 (11.7) [10.6-12.8]</td>
<td></td>
</tr>
</tbody>
</table>

* These values are the mean expenditures for 2 through 20 or more radiotherapy fractions.
fraction radiotherapy had poorer prognoses, perhaps reflecting the perception that single-fraction treatment should be reserved for patients with limited life expectancy or poor performance status. However, single-fraction treatment has substantial benefits for patient-centric palliative care, including greater quality of life and convenience, reduced travel time, and lower treatment costs.

We were unable to differentiate complicated from uncomplicated bone metastases (though sensitivity analyses to address this limitation revealed similar results). In addition, Medicare claims data cannot differentiate retreatment from treatment of another anatomic site.

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