Background

- Skeletal-related events (SREs) are associated with an increased hazard of prostate cancer-specific mortality among men diagnosed with prostate cancer (PCa) and bone metastasis (BM).
- Information also is limited regarding the separate roles of components of SREs including pathological fracture (PF), spinal cord compression (SCC), and bone surgery (BS).

Objective

To estimate the hazard of PCa-specific and all-cause mortality associated with SREs, as a cluster of events as well as by component.

Methods

- We analyzed PCa-specific and all-cause mortality among elderly SEER-Medicare stage IV PCa patients diagnosed between 2000 and 2007.
- Treatment-related data from 1999 to 2009 were extracted from linked Medicare claims files.
- Patients were censored if they enrolled in an HMO or lost Part A and/or B enrollment or if they were alive at the end of the period (December, 2009).

Study inclusion and exclusion criteria:

- Continuous enrollment in Medicare Part A and B during the 13 months prior to and including the month of diagnosis
- Diagnosis of distant metastasis (i.e., M1 PCa)
- Health maintenance organization (HMO) enrollment during the 12 months prior to and including the month of diagnosis
- History of other cancers within 5 years prior to PCa diagnosis
- PCa diagnosis occurred at the autopsy

Measures:

- Occurrence of PF, SCC, and BS following PCa diagnosis was identified using Medicare claims and utilized in defining an SRE using three approaches.
- Measure 1: SRE concurrent with or following a claim with a BM ICD 9 diagnosis code
- Measure 2: SRE claim includes BM ICD 9 coding directly on the SRE claim
- Measure 3: SRE is not anchored to a claim with a BM ICD 9 code.

Statistical analysis:

- Statistical analyses examined the association between SREs and PCa-specific mortality using the Cox proportional hazards regression model in the original sample and in a propensity score-matched sample (PSMS).
- Stratified direct-adjusted survival curves were produced in the case of statistically significant non proportional hazards associated with an SRE.

Results

- Application of inclusion criteria resulted in 7,181 patients (1,776 in PSMS).
- PCa-specific and all-cause mortality were 54% and 80% at a median follow-up of 60 months (mean, min, max) follow-up of (60, 0.5–131, 3,653).
- The average age for the sample was 78 years and 14% were non-Hispanic African American.
- The proportion with any event, SCC, PF, and BS differed according to the measure utilized (Table 1).

Table 1: Descriptive statistics for individuals diagnosed with stage IV PCa prostate cancer, stratified by measure-specific mortality (N=7,181).

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Follow-up</th>
<th>SCC-specific Mortality</th>
<th>PF-specific Mortality</th>
<th>BS-specific Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Full sample</td>
<td>N=1,729</td>
<td>N=1,729</td>
<td>N=1,729</td>
</tr>
<tr>
<td></td>
<td>% (N)</td>
<td>% (N)</td>
<td>% (N)</td>
<td>% (N)</td>
</tr>
<tr>
<td>SRE concurrent with or following a claim with a BM ICD 9 diagnosis code</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skeletal related event (SRE)</td>
<td>51.6% (3,705)</td>
<td>51.6% (3,705)</td>
<td>51.6% (3,705)</td>
<td>51.6% (3,705)</td>
</tr>
<tr>
<td>Spinal cord compression (SCC)</td>
<td>7.4% (125)</td>
<td>7.4% (125)</td>
<td>7.4% (125)</td>
<td>7.4% (125)</td>
</tr>
<tr>
<td>Pathological fracture (PF)</td>
<td>8.3% (195)</td>
<td>8.3% (195)</td>
<td>8.3% (195)</td>
<td>8.3% (195)</td>
</tr>
<tr>
<td>Bone surgery (BS)</td>
<td>4.0% (153)</td>
<td>4.0% (153)</td>
<td>4.0% (153)</td>
<td>4.0% (153)</td>
</tr>
<tr>
<td>Bone metastasis ICD 9 code on SRE claim</td>
<td>3.2% (93)</td>
<td>3.2% (93)</td>
<td>3.2% (93)</td>
<td>3.2% (93)</td>
</tr>
<tr>
<td>Any SRE post diagnosis of M1 prostate cancer</td>
<td>13.8% (932)</td>
<td>13.8% (932)</td>
<td>13.8% (932)</td>
<td>13.8% (932)</td>
</tr>
<tr>
<td>Skeleton-related event (with BM code)</td>
<td>3.2% (93)</td>
<td>3.2% (93)</td>
<td>3.2% (93)</td>
<td>3.2% (93)</td>
</tr>
<tr>
<td>Spinal cord compression (with BM code)</td>
<td>5.5% (158)</td>
<td>5.5% (158)</td>
<td>5.5% (158)</td>
<td>5.5% (158)</td>
</tr>
<tr>
<td>Pathological fracture (with BM code)</td>
<td>9.0% (268)</td>
<td>9.0% (268)</td>
<td>9.0% (268)</td>
<td>9.0% (268)</td>
</tr>
<tr>
<td>Bone surgery (with BM code)</td>
<td>1.9% (58)</td>
<td>1.9% (58)</td>
<td>1.9% (58)</td>
<td>1.9% (58)</td>
</tr>
</tbody>
</table>

- The hazard of PCa-specific mortality associated with an SRE varied according to the measure utilized (Table 2).
- The hazard of all-cause mortality also varied with the measure utilized and results were similar to results from the PCa-specific mortality model (Table 3).
- Using Measures 1 and 2 there was a statistically significant interaction with time, indicating that the mortality hazard associated with an SRE increased over time (Figure 1).
- Regarding the SRE components, the HRs on SCC and PF were statistically significantly associated with PCa-specific mortality across the three measures. The results for BS were sensitive to the approach used in defining the event.
- Results for SCC and BS were unchanged from Measure 1 when using a propensity score matched sample.

Conclusion

Compared to fractures and spinal cord compression, the relationship between bone surgery and PCa-specific mortality is more favorable.

Acknowledgements

Funding for the study was provided by Bayer Healthcare Pharmaceuticals. The authors wish to thank Corinne Woods and Lori Walker from the University of Maryland School of Pharmacy’s Pharmaceutical Research Computing for programming assistance on the primary datasets.

Contact Information

Eberechukwu Onukwugha, PhD
Department of Pharmaceutical Health Services Research
University of Maryland School of Pharmacy
onukwugha@rsv.umd.edu

Predictors and prognostic implication of pathologic fracture, spinal cord compression and bone surgery following diagnosis of metastatic prostate cancer

E Onukwugha1, C Yong1, CD Mullins1, B Seal2, A Hussain1

1 University of Maryland School of Pharmacy, Baltimore, MD
2 Bayer HealthCare Pharmaceuticals, Inc.
3 University of Maryland School of Medicine, Baltimore, MD