The Health Care Burden of Skeletal Related Events in Patients with Renal Cell Carcinoma and Bone Metastasis

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Abbreviations and Acronyms

CCI = Charlson comorbidity index

EAPC = estimated annual percent change

NIS = Nationwide Inpatient Sample

RCC = renal cell carcinoma

SRE = skeletal related event

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Purpose: We examined temporal trends in skeletal related events and associated charges in patients with renal cell carcinoma metastatic to bone. We also identified patient and hospital characteristics associated with skeletal related events and related mortality.

Materials and Methods: Using the Nationwide Inpatient Sample we abstracted data on patients with renal cell carcinoma who were diagnosed with concomitant bone metastasis between 1998 and 2010. Patients who experienced a skeletal related event were identified and hospital charges were calculated. Multivariate regression models fitted with generalized estimating equations were used to examine predictors of skeletal related events and related in-hospital mortality.

Results: Between 1998 and 2010 a weighted estimate of 144,889 renal cell carcinoma hospital visits of patients with bone metastasis was identified in the Nationwide Inpatient Sample, of which 20.8% involved a skeletal related event. In these cases from 1998 to 2010 the inflation adjusted mean yearly costs associated with hospital admission increased by 207% in 2013 United States dollars (estimated annual percent change 8.94%, $p < 0.001$). Conversely, the rates of skeletal related events and skeletal related event associated mortality decreased significantly (estimated annual percent change −1.11% and −2.9%, respectively, each $p < 0.001$).

Conclusions: The prevalence and in-hospital mortality of skeletal related event associated hospitalization for metastatic renal cell carcinoma is decreasing but such charges to health care in the United States are increasing at an alarming rate. These findings highlight the need for cost-effective treatment strategies to prevent or treat these morbid complications.

Key Words: kidney; carcinoma, renal cell; bone and bones; neoplasm metastasis; hospital charges

THE incidence of RCC has been increasing by about 3% per year in North America with 65,000 newly diagnosed cases and almost 14,000 deaths estimated in 2013.[1] This increase is largely attributable to increased imaging with corresponding stage migration toward low stage

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disease. Nonetheless, more than 30% of newly diagnosed patients with RCC present with disseminated disease and even those treated with resection with curative intent are at 40% risk of distant recurrence.[2]

Bone represents a common site of metastasis in RCC with bony involvement in around 30% of patients at some stage of the disease.[3,4] Bone lesions in RCC tend to be osteolytic, predisposing patients to SREs, including bone pain, pathological fracture, spinal cord compression and radiotherapy or surgery to bone.[5] Recent data indicate that 85% of patients with RCC metastatic to bone experience SREs at some point in the disease course with a mean of more than 2 per patient.[4] Furthermore, SREs are associated with a significant economic burden. An American study showed that the average cost of a SRE in patients with metastatic prostate cancer ranged from $11,800 for radiotherapy to $88,000 for surgery.[6]

Antiresorptive agents, specifically bisphosphonates and denosumab, decrease the risk of SRE.[7,8] Contemporaneously, there have been similarly encouraging results using newer targeted therapies (tyrosine kinase inhibitors) to prolong time to progression of existing bone lesions in patients with metastatic RCC.[9] However, there is a paucity of data on costs associated with RCC SREs with only 1 European study estimating that mean discounted SRE related costs are between €4,500 and €6,500.[10]

We hypothesized that the changing treatment paradigms for metastatic RCC would positively influence the prevalence, morbidity and mortality associated with SREs. Based on these considerations we examined the prevalence, inpatient mortality and hospital charges associated with SREs in a contemporary, population based inpatient cohort with RCC and bone metastasis in the United States.

METHODS

Data Source

This study relied on the NIS database, which was developed as part of the Health Cost and Utilization Project. It comprises hospital discharge data compiled via federal-state partnerships. NIS data represent a 20% stratified sample of community hospitals in the United States and the NIS is the largest all-payer inpatient care database publicly available in this country. An institutional review board waiver was obtained in accordance with institutional policy when dealing with population based de-identified data.

Sample Population

Hospital visits from 1998 to 2010 associated with a diagnosis of RCC (ICD-9 code 189.0) and a concomitant diagnosis of bone metastasis (ICD-9 170.x or 1890x) were extracted from the NIS. Weighted population estimates were applied. Extraction resulted in the identification of 144,899 hospital visits.

Characteristics

Baseline patient. Patient characteristics included age, gender and race. Patients younger than 18 years were removed from analysis. Patient comorbidity was calculated using the validated algorithm reported by Deyo et al.[11] Insurance status was based on the expected primary payer, including for patients who were uninsured.

Hospital. Hospital characteristics included hospital volume, location and teaching status. Hospital volume was defined as the number of patients with RCC and bone metastasis treated annually, divided by the number of years that patients with RCC and bone metastasis had been treated at the hospital, for the entire study period and based on the current databases. Categories were based on volume quartiles, including very low—0 to 22 cases, low—23 to 46, high—47 to 86 and very high—87 or greater. Institutional teaching status was obtained from the American Hospital Association Survey of Hospitals. Teaching hospitals were identified as such if they had an American Medical Association approved residency program, were a member of the Council of Teaching Hospitals or had a ratio of full-time equivalent interns and residents to beds of at least 1:4.

Treatment, mortality, SRE and adverse effects. We evaluated SRE and adverse effects potentially associated with bone targeted therapy, such as osteonecrosis of the jaw, hypocalcemia and renal failure, using ICD-9 diagnostic codes according to a previous methodology.[6] Patients with bone metastasis were identified as having been diagnosed with bone lesions or experiencing hypercalcemia or bone marrow failure. Our definition of SRE included fracture, radiation at a bone metastasis site, surgery to treat or prevent pathological fracture, bone pain and spinal cord compression. Patients who underwent radiation or bone surgery were identified using ICD-9 procedure codes. Radiation to bone included prophylactic treatment as well as alleviation of bone pain. Surgery included procedures to stabilize bone, treat fracture, prevent impending fracture or decompress the spinal cord. In-hospital mortality information was coded from patient disposition.

Hospital Charges

The NIS provides information on hospital service charges. Zero charges as well as those less than $25 or greater than $1,000,000 between 1998 and 2006, and $100 and $1,500,000 were categorized as missing by the NIS, representing 2.5% of hospital visits. Consistent with previous studies, missing charge values were treated as missing at random and estimated based on a regression model using known variables. Specifically, hot deck imputation was done using patient age, insurance status and CCI as covariates. Total charges were adjusted for inflation relative to the value of the United States dollar in 2013.

Statistical Analysis

The median and IQR were generated for continuously coded variables, and the frequency and proportion were