# *Effect of metastatic site on emergency department disposition in men with metastatic prostate cancer*

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***Introduction:*** *Though the prevalence of metastatic prostate cancer is decreasing, the rate of admission from the emergency department (ED) is increasing. Little is known about the implications of metastatic site on a patient's ED course and admission.*

***Materials and methods:*** *A weighted estimate of 15,367 patients with metastatic prostate cancer who presented to the ED between January 1, 2006 and December 31, 2009 was abstracted from the United States Nationwide Emergency Department Sample (NEDS). Descriptive statistics were used to elaborate patient and hospital characteristics of the metastatic prostate cancer population and logistic regression models were fitted to identify predictors of admission.*

***Results:*** *The most common site of metastasis in patients with metastatic prostate cancer presenting to the ED was bone (80.6%), followed by liver (13.2%), lung (9.3) and other genitourinary sites (8.1%). Over the study period, there was an increase in prevalence of the four commonest metastatic sites, and admission rates varied between metastatic sites (83.2% for bone to 95.2% for nodal metastasis). Substantial variability in the rate of inpatient mortality was noted. Increasing age, Northeast region, increased comorbidity burden, and the presence of nodal metastases and other urinary metastases were shown to be independent predictors of hospital admission.*

***Conclusions:*** *The commonest metastatic site in patients presenting to United States EDs with metastatic prostate cancer between 2006 and 2009 was bone. Patients presenting with nodal metastases were most likely to be admitted. Independent predictors of hospitalization included age, Northeast region, increased comorbidities, nodal metastases and other urinary metastases.*

**Key Words:** prostate cancer, metastasis, emergency department, admission disposition

## Introduction

The incidence of prostate cancer in the United States (U.S.) increased significantly in the 1990s as a result of the advent of widespread prostate-specific antigen (PSA) screening, but has subsequently shown a persistent downward trend, with a consistent decrease over the past two decades.[1,2] There has also been a stage migration towards localized disease at presentation, occurring concomitantly with increased PSA screening.[3-6] Nonetheless, approximately 12% of new prostate cancer cases will present with lymph node metastases and 4% with distant metastases, which represents a substantial burden on the U.S. healthcare system.[7]

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The care of chronic medical conditions with an expected and protracted course, such as metastatic prostate cancer, could theoretically be organized in such a manner that minimizes the use of the ED as a point of care and as a pathway for hospital admission. Indeed, repeated ED visits for such conditions are often unnecessary and inefficient.[8,9] Nonetheless, an examination of U.S. hospitalization shows that patient admissions from the ED are rising in the U.S.[10] As such, recent efforts have sought to identify determinants of the need for acute care, in particular ED utilization. In this particular context, one may hypothesize that certain characteristics of patients with metastatic prostate cancer increase the odds of ED visits. For example, patients with brain metastases might be more prone to be hospitalization than patients with single bone metastases.

Based on these considerations, we sought to examine the effect of metastatic site on ED disposition (admission versus discharge), as well as mortality. Moreover, we looked to identify independent predictors of hospitalization following an ED visit for metastatic prostate cancer.

## Materials and methods

### *Data source*

Relying on the Nationwide Emergency Department Sample (NEDS), all patients with a diagnosis of metastatic prostate cancer, who presented to the ED between January 1, 2006 and December 30, 2009 were abstracted. The NEDS was constructed using records from State Emergency Department Databases (SEDD) and the State Inpatient Databases (SID), both of which are part of the Healthcare Cost and Utilization Project (HCUP) family of databases created by the Agency for Healthcare Research and Quality through a Federal-state partnership.[11] The NEDS is the largest all-payer ED database in the United States, containing between 25 and 30 million (un-weighted) records for ED visits per year for over 950 hospitals, providing an approximate 20-percent stratified sample of U.S. hospital-based EDs. The NEDS includes ED charge information regardless of payer, including patients covered by Medicare, Medicaid, private insurance, and the uninsured.

Each ED visit includes up to 15 diagnoses codes using the International Classification of Disease, 9th revision, Clinical Modification (ICD–9–CM) and 15 procedure codes using Current Procedural Terminology (CPT-4). The NEDS also includes information on ED disposition including admission, discharge, transfer and death in ED.

### *Patient and hospital characteristics*

Available patient variables included age, gender, date of visit/date of admission (if applicable), Charlson Comorbidity Index (CCI) and insurance status. Baseline comorbidities were determined using the CCI, as adapted by Deyo and colleagues for use in administrative datasets;[12] CCI was stratified by 0-2 versus >/=3. Insurance status was combined into general groups, namely private insurance, Medicare, Medicaid, and other (self-pay). Hospital characteristics include hospital region (Northeast, Midwest, South, West) as defined by the United States Census Bureau and academic status, which were obtained from the American Hospital Association (AHA) Annual Survey of Hospitals. A hospital is considered to be a teaching hospital if it has an American Medical Association (AMA)-approved residency program, is a member of the Council of Teaching Hospitals or has a ratio of full-time equivalent interns and residents to beds of 0.25 or higher. The NEDS also contains information on annual ED volume and detailed designation of metropolitan area.

### *Sample population*

Relying on ED records, all patients with a primary diagnosis of prostate cancer (ICD-9-CM code 185.0) and concomitant diagnostic code for metastatic sites were abstracted and considered for the study. Weighted population estimates were projected to national levels using discharge weight variables from NEDS. This resulted in the identification of 15,367 ED visits for metastatic prostate cancer between 2006 and 2009. Incidences were normalized to population estimates from U.S. census data and inter-census population estimates.[13]

### *Outcomes*

The primary outcome was ED discharge disposition and mortality following a visit to the ED for metastatic prostate cancer. Categories of discharge disposition examined were: admitted to the hospital, discharged from ED and died in ED.

### *Statistical analysis*

Medians and interquartile ranges (IQRs) were generated for continuously coded variables; frequencies and proportions were generated for categorical variables. Temporal trends in rates were assessed with chi-square for trends.

The Mann-Whitney test and chi-square test were used to assess the statistical significance of differences in medians and proportions, respectively. All tests were two sided with a statistical significance set at p <

TABLE 1. **Weighted distribution of demographic characteristics of patients presenting to the emergency department with metastatic prostate cancer, Nationwide Emergency Department Sample, 2006-2009**

| | Total | Discharged | Admitted | p value |
|---|---|---|---|---|
| **Patients** | n (%) 15291 | n (%) 2583 | n (%) 12708 | |
| **Median age (IQR)** | 76 (67-83) | 73 (64, 81) | 77 (67, 83) | < 0.001 |
| **Year** | | | | < 0.001 |
| 2006 | 24.5 | 22.9 | 24.9 | |
| 2007 | 26.7 | 30.1 | 26.0 | |
| 2008 | 23.9 | 23.6 | 24.0 | |
| 2009 | 24.9 | 23.4 | 25.2 | |
| **Charlson Comorbidity Index†** | | | | < 0.001 |
| 0-2 | 93.2 | 97.5 | 92.3 | |
| ≥ 3 | 6.8 | 2.5 | 7.7 | |
| **Insurance status** | | | | < 0.001 |
| Medicare | 71.5 | 67.1 | 72.4 | |
| Medicaid | 7.8 | 7.8 | 7.8 | |
| Private insurance | 14.3 | 16.2 | 13.9 | |
| Other | 6.4 | 8.9 | 5.9 | |
| **Hospital region‡** | | | | < 0.001 |
| Northeast | 22.9 | 14.8 | 24.6 | |
| Midwest | 20.3 | 25.0 | 19.3 | |
| South | 37.4 | 36.9 | 37.5 | |
| West | 19.4 | 23.3 | 18.6 | |
| **Emergency department visits tertile** | | | | < 0.001 |
| Low (=< 33978) | 33.1 | 42.5 | 31.2 | |
| Medium (33979-53428) | 33.2 | 33.6 | 33.1 | |
| High (=> 53429) | 33.7 | 23.8 | 35.7 | |
| **Bone metastases** | | | | 0.002 |
| Absent | 19.4 | 21.6 | 19.0 | |
| Present | 80.6 | 78.4 | 81.0 | |
| **Liver metastases** | | | | 0.069 |
| Absent | 86.8 | 87.9 | 86.6 | |
| Present | 13.2 | 12.1 | 13.4 | |
| **Lung metastases** | | | | < 0.001 |
| Absent | 90.7 | 92.7 | 90.3 | |
| Present | 9.3 | 7.3 | 9.7 | |
| **Nodal metastases** | | | | < 0.001 |
| Absent | 92.4 | 98.0 | 91.2 | |
| Present | 7.6 | 2.0 | 8.8 | |
| **Other urinary metastases** | | | | < 0.001 |
| Absent | 91.9 | 95.7 | 91.1 | |
| Present | 8.1 | 4.3 | 8.9 | |
| **Brain and nervous system metastases** | | | | 0.291 |
| Absent | 95.6 | 96.0 | 95.5 | |
| Present | 4.4 | 4.0 | 4.5 | |
| **Other metastases** | | | | < 0.001 |
| Absent | 89.1 | 91.1 | 88.7 | |
| Present | 10.9 | 8.9 | 11.3 | |

†Based on Comorbidity developed by Charlson et al and adapted by Deyo et al; IQR = interquartile range
‡Hospital region is defined by the United States Census Bureau

0.05. Analyses were conducted using the R statistical package (R Foundation for Statistical Computing, v.2.15.2). This study was exempt from institutional review board approval in accordance with provincial and federal legislation when dealing with population-based publicly available data.

## Results

Between 2006 and 2009, an estimated 15,291 ED visits from prostate cancer were recorded in NEDS, after excluding 75 patients who died in the ED. Baseline demographic characteristics of metastatic prostate cancer patients are listed in Table 1. Patients with metastatic prostate cancer admitted via the ED were, on average, older (median: 77, IQR: 67-83) than those who were discharged (73, IQR 64-81), had more comorbidities (CCI ≥ 3 in 7.7 versus 2.5%, $p < 0.001$), were less likely to hold private insurance (13.9 versus 16.2%,$p < 0.001$) and more likely to hold Medicare insurance (72.4 versus 67.1%,$p < 0.001$). Compared to those patients who were treated and discharged from the ED, metastatic prostate cancer patients who were admitted were more likely to be seen in the Northeastern region (24.6 versus 14.8%, $p < 0.001$) and in higher volume EDs (35.7 versus 23.8%, $p < 0.001$). They were also more likely to have bone (81.0 versus 78.4%, $p = 0.002$), lung (9.7 versus 7.3%, $p < 0.001$), nodal (8.8 versus 2.0%, $p < 0.001$) and other urinary metastases (11.3 versus 8.9%, $p < 0.001$).

The most common site of metastasis in patients with metastatic prostate cancer presenting to the ED was bone (80.6%), followed by liver (13.2%), lung (9.3) and other GU sites (8.1%). An increase in the prevalence of bone and lung metastases was recorded between 2006 and 2009. There was significant variability in the odds of admission according to metastatic site (range: 83.2% for bone versus 95.2% for nodal metastasis) as well as substantial variability in the odds of inpatient mortality (range: 5.1% for other GU sites versus 13.3% for liver).

In univariable analyses, patient and hospital characteristics associated with admission included age (OR = 1.02, $p < 0.001$), Medicare insurance status versus Medicaid (HR = 0.87, $p = 0.03$), Northeast location in comparison to Midwest (OR = 0.47, $p < 0.001$), South (OR = 0.62, $p < 0.001$) and West (OR = 0.52, $p = 0.001$), increased comorbidity burden (OR = 3.11, $p < 0.001$), lung metastases (OR = 1.58, $p = 0.014$), nodal metastases (OR = 4.19, $p < 0.001$) and other urinary metastases (OR = 2.09, $p < 0.001$). In multivariable analyses, the only independent predictors of hospitalization were age (OR = 1.03, $p < 0.001$), Northeast ED institution location in comparison to location in the Midwest (OR = 0.51,$p < 0.001$), South (OR = 0.67, $p = 0.005$) and West (OR = 0.55, $p < 0.001$), increased comorbidity burden (CCI >= 3, OR = 3.21, $p < 0.001$), and the presence of nodal (OR = 1.47, $p = 0.043$), and other urinary metastases (OR = 1.89, $p = 0.004$), Table 2.

## Discussion

The ED is the route of entry for most patients admitted to hospital and, given rapidly rising healthcare costs, represents an important target for efficiency savings. Prostate cancer is the commonest cancer in men in the U.S.,[14] and carried an estimated healthcare cost in excess of $35,000 (in year 2000 terms) for each person diagnosed with the disease over the duration of their illness, with the majority of these costs accruing at the latter months of care (i.e. principally for those with metastatic disease).[15] Therefore, any reduction in treatment costs, particularly at this stage of disease and particularly in those presenting via the ED, is likely to have a significant positive economic impact.

Rising utilization of the ED for the admission of patients with metastatic prostate cancer has been seen in recent years, highlighting the important role of the ED in the care of patients with metastatic prostate cancer. In this manuscript, we therefore sought to characterize the patient and hospital characteristics that were associated with inpatient admission through the ED. To the best of our knowledge, this study represents the first attempt to examine ED admissions for patients with metastatic prostate cancer.

Several of our findings are noteworthy. First, we demonstrated that the three most common sites of metastases in prostate cancer patients presenting to the ED were bone (80.6%), liver (13.2%) and lung (9.3%). Our results corroborate previous findings that bone is by far the commonest metastatic deposit in prostate cancer.[16] In a series of routine autopsies, solid metastases were present in 35% of patients with prostate cancer on post-mortem examination, with he most frequent metastatic site being bone (90%), followed by lung (46%) and liver (25%).[17] The high prevalence of bone metastases, as well as the associated risk of skeletal related events (SREs), likely has a synergistic effect on increasing ED visits, with prior reports showing that the rate of skeletal related events may be as high as 44% in men with hormone refractory disease.[18,19]

We also recorded noteworthy associations between metastatic sites and the likelihood of hospital admission and in-hospital mortality. For example, nodal metastases were associated with the highest odds of

TABLE 2. **Univariable and multivariable predictors of admission for metastatic prostate cancer**

| Variable | Univariable predictors of admission | | Multivariable predictors of admission | |
|---|---|---|---|---|
| | Hazard ratio | p value | Hazard ratio | p value |
| **Age (continuous)** | 1.02 (1.02-1.03) | < 0.001 | 1.03 (1.02-1.04) | < 0.001 |
| **Year** | | | | |
| 2006 | 1.00 (Ref.) | --- | | |
| 2007 | 0.8 (0.62-1.04) | 0.289 | | |
| 2008 | 0.97 (0.74-1.27) | 0.093 | | |
| 2009 | 0.96 (0.73-1.26) | 0.844 | | |
| **Insurance** | | | | |
| Medicare | 1.00 (Ref.) | --- | 1.00 (Ref.) | --- |
| Medicaid | 0.87 (0.62-1.22) | 0.03 | 1.29 (0.88-1.9) | 0.191 |
| Private | 0.81 (0.63-1.05) | 0.408 | 1.08 (0.81-1.45) | 0.601 |
| Other | 0.63 (0.45-0.88) | 0.12 | 0.91 (0.63-1.33) | 0.635 |
| **Region** | | | | |
| Northeast | 1.00 (Ref.) | --- | 1.00 (Ref.) | --- |
| Midwest | 0.47 (0.35-0.64) | < 0.001 | 0.51 (0.37-0.69) | < 0.001 |
| South | 0.62 (0.47-0.81) | < 0.001 | 0.67 (0.51-0.89) | 0.005 |
| West | 0.52 (0.38-0.7) | 0.001 | 0.55 (0.4-0.74) | < 0.001 |
| **Charlson Comorbidity Index** | | | | |
| 0-2 | 1.00 (Ref.) | --- | 1.00 (Ref.) | --- |
| >= 3 | 3.11 (1.8-5.39) | < 0.001 | 3.21 (1.84-5.58) | < 0.001 |
| **Bone metastases** | | | | |
| Absent | 1.00 (Ref.) | --- | | |
| Present | 1.17 (0.94-1.47) | 0.161 | | |
| **Liver metastases** | | | | |
| Absent | 1.00 (Ref.) | --- | | |
| Present | 1.2 (0.9-1.59) | 0.218 | | |
| **Lung metastases** | | | | |
| Absent | 1.00 (Ref.) | --- | 1.00 (Ref.) | --- |
| Present | 1.58 (1.1-2.27) | 0.014 | 1.47 (1.01-2.13) | 0.043 |
| **Nodal metastases** | | | | |
| Absent | 1.00 (Ref.) | --- | 1.00 (Ref.) | --- |
| Present | 4.19 (2.33-7.55) | < 0.001 | 4.25 (2.35-7.68) | < 0.001 |
| **Other urinary metastases** | | | | |
| Absent | 1.00 (Ref.) | --- | 1.00 (Ref.) | --- |
| Present | 2.09 (1.37-3.19) | 0.001 | 1.89 (1.23-2.9) | 0.004 |
| **Brain and nervous system metastases** | | | | |
| Absent | 1.00 (Ref.) | --- | 1.00 (Ref.) | --- |
| Present | 1.15 (0.72-1.85) | 0.552 | 1.28 (0.79-2.06) | 0.316 |
| **Other metastases** | | | | |
| Absent | 1.00 (Ref.) | --- | | |
| Present | 1.28 (0.94-1.75) | 0.12 | | |

hospital admission. It is likely that patients with a substantial burden of nodal metastases have more advanced disease, in addition to multiple coexisting metastatic locations.[20] The finding that liver metastases most commonly predisposes to in-hospital mortality corroborates a previous report by Hemminki and colleagues, who used registry data to show that median survival in patients with carcinomas of unknown primary was shortest in those who had metastatic disease to the liver.[21]

Finally, we identified independent predictors of hospital admission in patients with metastatic prostate cancer presenting to the ED. Age and increased comorbid status were unsurprisingly predictive for hospital admission, given that elderly patients tend to present with more advanced disease[22] and the likelihood of more conservative decision-making by physicians when dealing with older patients or those with multiple other medical issues. While the association between hospital admission and the Northeastern region is unclear, our data confirmed that higher volume centers were more likely to admit patients with metastatic prostate cancer. This concurs with a recent study, which demonstrated that low volume institutions were more likely to transfer patients to another type of facility.[23]

Our finding that the presence of nodal and other urinary metastases were independently predictive for hospital admission (whilst the presence of bone metastases were not) is also surprising, given that one may think the latter would predispose to SREs and therefore provoke admission. Interestingly, while the presence of liver metastases was not predictive of admission, men with such disease were the most likely to die if they were admitted, data not shown. This may be due to solitary liver deposits (as is likely in the majority of such disease) not causing significant medical problems to patients; however, those with liver metastases who were admitted are likely to have several deposits, deeply compromising liver function, and are thereby most vulnerable to suffer in-hospital mortality. From a practical perspective, an awareness of such predictors of admission may contribute to better counseling of patients, especially in those with nodal and genitourinary disease. Furthermore, patients with a high probability of hospital admission and in-hospital mortality may benefit from a more robust outpatient social and medical support system as well improved access to hospice services.

Our analysis has many of the limitations that should be accounted for when considering our findings. Although the NEDS is the largest all-payer ED database in the U.S., some degree of bias related to sampling error may be present. Additionally, the sample is representative of the U.S. population only and therefore, our findings are not necessarily generalizable beyond North America. Moreover, the NEDS does not provide specific cause of death for the metastatic prostate cancer patients visiting the ED, thereby limiting the attribution of in-hospital mortality.

## Conclusion

In patients presenting to the ED with metastatic prostate cancer between 2006 and 2009, the most common site of metastasis was, overwhelmingly, to bone. However, patients presenting with nodal metastasis were the most likely to be admitted. Increasing age, Northeast ED institution location, increased comorbidity burden, nodal metastases as well as other urinary metastases were found to be independent predictors of hospital admission. Knowledge of these factors can help healthcare providers better identify areas for further resource allocation and increase the efficiency of the care provided to men with metastatic prostate cancer. □

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