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Research Article

Postoperative Radiation Referral Rates for Metastatic Bone Disease Within the Veteran's Health Administration and at an Academic Center

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ARTICLE INFO

Article history:

Received: 28 December, 2021

Accepted: 12 January, 2022

Published: 28 January, 2022

Keywords:

Neoplasm metastasis

femur

benchmarking

statistics

radiotherapy

spontaneous fracture

ABSTRACT

Background: External beam radiation therapy is an important aspect of multidisciplinary care for patients with metastatic bone disease. Referral to radiation oncology is within the control of the orthopaedic surgeon and has the potential to serve as a quality benchmark.

Methods: This is a retrospective cohort study. Patients with metastatic disease of the femur who underwent prophylactic femoral stabilization or fixation of a pathologic femur fracture from 2010-2015 at a single academic medical center or within the Veterans Health Administration (VHA) were included. A total of 950 VHA patients and 130 academic medical center patients were enrolled. The main outcome was the proportion of patients receiving a referral to radiation oncology by six weeks after the date of surgery. Results are presented for each institution and are stratified by type of procedure (prophylactic stabilization versus pathologic fixation). The study further evaluates regional differences within the VHA.

Results: The majority of patients received a referral for radiation after prophylactic stabilization (VHA: 290/361 patients [80% 95% CI: 76% - 84%]; academic medical center: 81/89 patients [91%, 95% CI: 85%, 97%]). The proportion referred was higher at the academic medical center (odds ratio [OR]: 2.5, 95% CI: [1.15, 5.36], $P=0.027$). After fracture fixation, 428/589 (73%, 95% CI: [69%, 77%]) of VHA patients and 30/41 (73%, 95% CI [59%, 87%]) of patients at the academic medical center received a referral to radiation. Receiving a referral was not associated with healthcare system (OR: 1.0; 95% CI: [0.50, 2.10]). Within the VHA, the proportion of patients referred varied by geographic location (Pearson's chi-squared test, $P=0.004$ for prophylactic stabilization and $P<0.001$ for pathologic fixation).

Conclusion: Referral rates at both institutions were moderate to high. The observed regional variation within the VHA highlights the importance of establishing quality benchmarks.

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Introduction

Metastatic bone disease is relatively prevalent and currently affects over 300,000 people in the United States [1, 2]. The management of the metastatic bone disease requires a multidisciplinary team of physicians, including medical oncologists, radiation oncologists, and orthopaedic surgeons, to create a treatment plan specific to each individual's needs.

External beam radiation therapy (EBRT) is an important component of multimodal treatment for patients who experience painful bone metastasis, improving a patient's functional status and reducing their risk of tumor recurrence. EBRT has been shown to relieve pain in 50-80% of patients, and surgical stabilization with EBRT has been shown to improve functional status relative to surgical stabilization alone [3-8].

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Existing literature suggests that patients with metastatic bone diseases are best served by a highly functioning, multidisciplinary team. Several national radiology and oncology societies conclude that patients presenting with metastatic bone disease and lesions concerning impending pathologic fracture should: i) be seen by an orthopaedic surgeon for possible stabilization and ii) receive palliative EBRT regardless of whether surgery occurred [9-14].

The proportion of patients receiving a referral to radiation oncology has the potential to serve as a quality metric for health systems that serve this vulnerable population. There is currently no accepted benchmark for the proportion of surgical patients receiving a referral. While variation in the patient populations amongst providers and institutions might appropriately affect radiation referral rates, the lack of benchmark makes it difficult for healthcare systems and individual providers to assess the quality and equity of care their patients receive. This study aimed to characterize appropriate benchmarks by quantifying and comparing the proportion of patients with metastatic disease of the femur referred to radiation oncology in two different healthcare settings and to examine whether the proportion of patients referred varied by region.

Methods

I Study Design and Setting

This was a retrospective cohort study. The study was designed and is reported using strengthening the reporting of observational studies in

epidemiology (STROBE) criteria. The cohorts were defined by healthcare setting - Veteran's Health Administration (VHA) versus an academic medical center. The cohorts in the VHA were further divided into subcohorts by region, defined as United States Census Bureau regions [15]. Quality benchmarks are likely to be most useful if based on metrics that are readily abstracted using existing structured electronic health record (EHR) data. Accordingly, variables obtained for VHA participants were abstracted without manual chart review using an existing radiation referral metric [16]. However, no structured variable for radiation referral existed within the EHR at the academic medical center. For these patients, referral to radiation was determined by manual chart review, and the diagnosis was verified during the review.

II Participants

Eligible participants underwent prophylactic femoral stabilization or operative intramedullary nailing of a realized pathologic fracture between September 30, 2010, and October 1, 2015, at the VHA or a single academic medical center. After obtaining Institutional Review Board approval, eligible participants in each healthcare setting were identified using a combination of Current Procedural Terminology (CPT) and International Classification of Disease (ICD) codes (Table 1).

Table 1: CPT and ICD codes used to query patients from the databases.

For Prophylactic Stabilization Cases – Any of the CPT codes below	For Pathologic Fixation Cases – Any of the CPT codes below combined with any of the ICD codes below	
<i>CPT codes</i>	<i>CPT codes</i>	<i>ICD codes</i>
27495 - prophylactic treatment (nailing, pinning, plating, or wiring) with or without methyl methacrylate, femur	27236 - Open treatment of femoral fracture, proximal end, neck, internal fixation or prosthetic replacement	733.14 - Pathologic fracture neck of femur
27187 - prophylactic treatment (nailing, pinning, plating or wiring) with or without methyl methacrylate, femoral neck and proximal femur	27244 - Treatment of intertrochanteric, peritrochanteric, or subtrochanteric femoral fracture; with plate/screw-type implant, with or without cerclage	733.15 - Pathologic fracture of other part of femur
	27245 - Treatment of intertrochanteric, peritrochanteric, or subtrochanteric femoral fracture; with intramedullary implant, with or without interlocking screws and/or cerclage	733.10 - Pathologic fracture unspecified site
	27269 - Open treatment of femoral fracture, proximal end, head, includes internal fixation, when performed	
	27506 - Open treatment of femoral shaft fracture, with or without external fixation, with insertion of the intramedullary implant, with or without cerclage and/or locking screws	
	27511 - Open treatment of femoral supracondylar or transcondylar fracture without intercondylar extension, includes internal fixation, when performed	

At the academic medical center, cases were removed if the primary provider listed was a physician assistant, as these cases were duplicates of cases performed by physicians. This resulted in 171 patients who received prophylactic stabilization and 71 who received fixation of a pathologic fracture. Because the academic medical center cohorts were found to have a moderate proportion of patients without metastatic disease, patients without confirmed metastatic disease were excluded. Excluded patients had a variety of surgical indications, including but not limited to large benign cysts, congenital dysplasias, and severe osteoporosis. In the final analysed cohort, there were 87 patients who received prophylactic fixation for metastatic disease and 41 patients who received fixation of a pathologic fracture for metastatic disease at the academic medical center. At the VHA, cases were included based on CPT and ICD codes only. No further exclusion criteria were applied.

III Demographic Variables

For VHA patients, demographic variables including age, sex, and operation type were abstracted from the Veterans Affairs Informatics and Computing Infrastructure (VINCI) Corporate Data Warehouse (CDW). Within VHA, individual centers were categorized into four geographic areas as determined by the US Census Bureau.

For the academic medical center data, age, sex, and operation were abstracted. Chart review was conducted to confirm the operation as documented in the operative report. Cancer diagnosis was determined through a review of the surgical pathology report, operative report, and/or office visit note.

IV Covariates

Whether the patient received prophylactic stabilization or fixation was considered to be a likely confounder. We hypothesized that patients with completed fractures would be more likely to receive a radiation referral due to the perceived severity of the disease. Preliminary analysis of our samples revealed that the VHA saw a greater proportion of patients with complete fractures, which underscored the potential confounding effect.

V Outcome Variable

The outcome of interest was whether the patient was referred for radiation. The rationale is that a referral to radiation can be placed by any member of the multidisciplinary team, and this outcome can therefore be directly influenced by the orthopaedic surgeon. In contrast, actually being seen for radiation therapy within a set time period may be influenced by a variety of external factors, including insurance issues, radiation oncology scheduling, and patient availability. In the VINCI CDW database for VHA patients, radiation referral status was abstracted from the chart as part of the database query. In this system, patients were considered to have received a radiation referral if a referral to radiation oncology for treatment to any site had been placed within six weeks after the operation.

At the academic medical center, patients were determined to have a completed radiation referral if radiation to the femur occurred prior to surgery or any of the following were seen in the chart within six weeks of the operation:

- i. there was a formal referral order from any provider.
- ii. radiation was explicitly recommended in the orthopaedic surgeon's notes in the chart.
- iii. the patient had a documented visit or contact with radiation therapy within or outside the academic medical center.

We note that the outcome variable is defined differently at each institution, which mirrors that institutions are likely to have various ways of calculating quality benchmarks based on the types of data available to them.

VI Statistical Analysis, Study Size

The primary outcome of this study was a referral to radiation oncology within six weeks of surgery. Logistic regression was planned to obtain crude and adjusted odds ratios for the association between healthcare setting and whether or not the patient was referred to radiation. However, given the small sample size and rare occurrence of non-referral at the academic medical center, logistic regression was expected to produce biased results. Accordingly, the association between the healthcare system and receiving a referral was analysed using a Pearson's chi-square test with an alpha of 0.05. The association of healthcare system with demographic variables is reported using a Person's chi-square test with an alpha of 0.05 except when expected cell counts were less than five, in which case a Fisher's exact test is reported. Because completed versus impending fracture was hypothesized to be an important confounder, results were stratified by type of fixation (prophylactic for impending fracture or fixation for completed fracture). In the prophylactic group, our study was powered to detect a difference in proportions of 0.1125 with 80% power, assuming the lower proportion was 0.7. In the pathologic group, our study was powered to detect a difference in proportions of 0.1726 with 80% power, assuming the lower proportion was 0.7. Odds ratios and their corresponding 95% confidence intervals (CI) are reported. All analyses were preplanned. Initial queries to the CDW were performed in SQL, with statistical analysis performed in R version 3.4.3 [17].

Results

I Demographics

The VHA cohorts from the national database included 361 patients who received prophylactic stabilization and 589 patients who had a completed pathologic fracture that was operatively treated (Table 2). The academic medical center database included 89 patients who received prophylactic stabilization and 41 patients who had a completed pathologic fracture that was operatively treated. In the prophylactic stabilization cohorts, patients at the academic medical center had an average age of 64 years compared to an average age within the VHA of 67 years (t -test, $P=0.045$). In the pathologic fixation groups, the average age at the academic medical center was 63 years compared to an average age of 69 years within the VHA (t -test, $P=0.009$). Within the prophylactic group, the academic medical center had a higher proportion of female patients (40%) compared to the VHA (6%; Pearson's chi-squared test, $P<0.001$). In the pathologic fixation group, the academic medical center again had a higher proportion of female patients (46%) compared to the VHA (5%; Fisher's exact test, $P<0.001$). There were no patients with missing data for any of the variables of interest.

Table 2: Patient characteristics by healthcare setting. Results are stratified by operation type.

Characteristic	Prophylactic Stabilization		Pathologic Fixation	
	Academic Medical Center ¹	VHA	Academic Medical Center*	VHA
Total Number	89	361	41	589
Age in years, mean (SD)	64 (11)	67 (11)	63 (13)	69 (11)
Sex n (%)				
Females	36 (40)	20 (6)	19 (46)	31 (5)
Males	53 (60)	341 (94)	22 (54)	558 (95)

VHA: Veteran's Health Administration; SD: Standard Deviation.

¹Patients with confirmed metastatic disease by manual chart review.

II Prophylactic Stabilization

Of the 89 patients with confirmed metastatic disease, 81 patients (91%) received a referral to radiation. Within the VHA, radiation oncology referrals were placed for 290 of the 361 patients (80%) that received prophylactic stabilization of the femur for metastatic disease. The odds of a patient with metastatic disease at the academic medical center receiving a radiation referral were 2.48 times the odds of being referred at the VHA (95% CI: [1.15, 5.36]) and the association of radiation referral with the healthcare system was statistically significant (Pearson's chi-squared test, $P=0.027$).

III Pathologic Fracture Fixation

Of the 41 patients with confirmed metastatic disease and pathologic fracture fixation at the academic medical center, 30 (73%) received a radiation referral (Table 3). Within the VHA, 428 of the 589 pathologic femur fracture patients (73%) received a referral to radiation oncology. Comparing the cohort of patients with verified metastatic disease at the academic medical center to those at the VHA, the odds of referral were the same (OR: 1.0; 95% CI: [0.50, 2.10]). Radiation referral status was not correlated with healthcare system (Pearson's chi-squared test, $P=1$).

Table 3: Proportion of patients referred to radiation oncology by healthcare setting. Results are stratified by operation type.

	Prophylactic Stabilization				Pathologic Fixation			
	Referred	Not referred	Total	Proportion referred	Referred	Not referred	Total	Proportion referred
VHA	290	71	361	0.80	428	161	589	0.73
Academic Medical Center ¹	81	8	89	0.91	30	11	41	0.73

VHA: Veteran's Health Administration.

¹Patients with confirmed metastatic disease by manual chart review.

IV Geographic Variation

Within the prophylactic stabilization cohort at the VHA, the proportion of patients referred was associated with geographic location (Pearson's chi-squared test, $P=0.004$). The proportion referred ranged from 64% in

the West to 87% in the Northeast (Table 4). The proportion of patients referred for radiation was also associated with geographic location in the pathologic fixation group at the VHA (Pearson's chi-squared test, $P<0.001$). The proportion referred ranged from 65% in the South to 91% in the Northeast (Table 4).

Table 4: Proportion of VHA patients referred to radiation oncology by geographic region.

	Prophylactic Stabilization				Pathologic Fixation			
	Referred	Not referred	Total	Proportion referred	Referred	Not referred	Total	Proportion referred
Midwest	115	21	136	0.85	101	27	128	0.79
Northeast	47	7	54	0.87	74	7	81	0.91
South	89	21	110	0.81	166	90	256	0.65
West	39	22	61	0.64	61	31	92	0.66

Discussion

The high proportion of patients was referred to the VHA group and at the academic medical center, which is consistent with recommendations. Our findings suggest that a quality benchmark for referral to radiation might reasonably fall between 80% and 91%, depending on how the patient population is defined. We found that the proportion of prophylactic stabilization patients receiving a radiation referral was higher at the academic medical center compared to the VHA. This could

be due to the difference in the determination of outcome, variability in underlying diagnoses or patient population, or better adherence to the guidelines. Benchmarks might be expected to vary by healthcare system as different charting systems and databases will affect what data can reasonably and reliably be obtained. The proportions of patients referred for radiation were relatively high for pathologic fracture fixation at the VHA (73%) and at the academic medical center (73%). The rates of referrals were the same in both healthcare settings.

I Analysis by Region

Analysis of the proportion of VHA patients referred for treatment after prophylactic stabilization and pathologic fixation by region demonstrate regional heterogeneity in referral prevalence. Patients receiving care in the Northeast had greater odds of being referred to radiation in both the pathologic and prophylactic groups, while those in the South and West had lower odds. It is possible that surgeon fellowship training, local variability in diagnoses, or healthcare system resources explain part of this difference. Such regional heterogeneity highlights the importance of setting appropriate quality benchmarks to guide efforts to provide high reliability care.

Considering the consistent recommendations regarding the importance of radiation referral when treating metastatic bone disease, our results suggest that establishing quality benchmarks for radiation referral is important to ensuring high quality and equitable care [9-14]. We note that a target benchmark of 100% would not be appropriate, as there are valid reasons some patients may not receive a referral; analysis of the academic medical center suggests several situations, including incompatibility with patient goals of care. In addition, in cohorts defined without manual verification of diagnosis, we expect at least a small proportion of patients to be included who do not have metastatic disease. As above, our analysis suggests these patients may include patients with metabolic disorders, congenital disorders, and radiation-induced fractures.

Patients with the metastatic bone disease require a multidisciplinary team to ensure quality care, and evaluation of such patients by a radiation oncologist for possible EBRT is widely recommended. However, there is a paucity of data characterizing appropriate radiation referral benchmarks for patients receiving surgical care for cancer that has metastasized to the femur. These data are from a large cohort and represent an early attempt to estimate appropriate benchmarks. Furthermore, the EHR data from the academic medical center are representative of the data that are likely to be available to institutions to assess their performance in a timely fashion. Large multi-institution databases are unlikely to provide timely and actionable feedback.

II Limitations

We recognize multiple limitations in this retrospective cohort study. We note that the comparison between radiation referral rates at the VHA and the academic medical center is very likely impacted by biases introduced by cohort definition, cohort composition, and determination of outcome.

First, the referral rates at the academic medical center were from a cohort with confirmed metastatic disease. Within the VHA cohort, the diagnosis was not confirmed by a manual chart or pathology review. We hypothesized that the academic medical center cohort was more likely to overrepresent patients with unusual indications, including metabolic diseases and congenital defects. Therefore, there was a large difference in referral rates that were observed between patients identified by CPT and ICD codes and those with confirmed metastatic disease at the academic medical center. Within the VHA system, the large number of patients and the large geographic area would, on average result in a lower proportion of patients with rare conditions. We felt it was important to

report the VHA statistics without manual review, as benchmarks that are easily abstracted from structured data are easier to implement and track. However, within the academic medical center, chart review was already required to determine the outcome of interest, and we felt the number of patients with non-metastatic surgical indications was likely to have a greater impact on our results. The overall effect of this difference would be to bias the results such that those seen at the VHA would be lower than expected if similar exclusion criteria were applied.

Furthermore, radiation referral at the academic medical center was site-specific, such that previous radiation to a different site (i.e., the spine) was not considered a successful referral to radiation oncology. This was not the case at the VHA, where referral to radiation oncology was not site specific. This differential determination of outcomes is due in part to differences in the electronic health record in each system. We expect the site-specificity to decrease the proportion of patients considered to have a referral at the academic medical center. However, as radiation referrals were only counted if they occurred within six weeks of the surgery within both systems, we expect this differential determination of outcome is unlikely to have significantly impacted our results.

By design, our study did not include arthroplasty operations. Whether for impending or completed pathologic fractures, arthroplasty is a well-recognized treatment option [18]. However, we excluded arthroplasty codes in order to delineate prophylactic stabilization and improve the internal validity of a CPT-driven cohort creation. We included CPT code 27236 at the VHA, which could represent arthroplasty. We then did a sensitivity analysis excluding these patients, which did not significantly affect our results. This may limit the external generalizability of the study; however, for the purpose of validation in other cohorts or use as a quality metric, it is advantageous to not rely on manual chart review in large datasets.

We note that there are many potential confounding variables, including sex, age, the proportion of patients with non-metastatic indications for surgery, and whether the operating surgeon was oncology-trained, that are not controlled for when comparing referral rates geographically and between healthcare settings. However, we feel an inclusive analysis of the rates presented here provides a useful starting point for considering possible quality metrics.

Conclusion

A large majority of patients undergoing surgery for metastatic bone disease in the femur were referred to radiation oncology within VHA and at an academic medical center. The nationwide variation in referral rate within VHA suggests that establishing radiation referral benchmarks may help in promoting high-reliability care. The overall high rates of referral in both cohorts in both settings suggest that appropriate benchmarks are likely high. While the specific target may vary by healthcare setting and patient cohort, based on our results, appropriate benchmarks should fall between 80% and 91% for patients receiving prophylactic stabilization, and around 73% for patients undergoing fixation for pathologic fracture of the femur. Underperforming locations may be appropriate targets for interventions to improve the multidisciplinary care of metastatic bone disease.

Ethical Statement

The Institutional Review Boards of the local VA Medical Center and the academic center approved this study prior to its initiation and have ongoing continuing reviews approved. It was determined exempt from informed consent. Study completed in compliance with the Helsinki Declaration.

Conflicts of Interest

None.

Funding

None.

Acknowledgment

This material is the result of work supported with resources and the use of facilities at the Portland VA Medical Center.

Disclaimer

The contents do not represent the views of the U.S. Department of Veterans Affairs or the United States Government.

STROBE Statement

The study was designed and is reported using strengthening the reporting of observational studies in epidemiology (STROBE) criteria and checklist.

Abbreviation

VHA: Veterans Health Administration

OR: Odds Ratio

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