
Variation in Oncologic Opinion Regarding Management of Metastatic Bone Pain with Systemic Radionuclide Therapy

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The objective of this study was to determine whether there is consistency of opinion regarding the management of metastatic bone disease pain among medical oncologists who are given the option of using systemic radionuclide therapy (^{89}Sr , ^{153}Sm). **Methods:** One hundred board-certified medical oncologists were given a brief clinical summary of three patients with metastatic cancer. Management options included oral, parenteral and transdermal delivery forms of opioid analgesics; external beam irradiation; and systemic radionuclide therapy. The oncologists rated, in whole numbers from 1 (most appropriate) to 10 (least appropriate), their opinions on the appropriateness of each proposed intervention for each patient. **Results:** Systemic radionuclide therapy was perceived consistently as having low appropriateness for palliation of metastatic bony pain compared with opioid analgesics. A slight increase in appropriateness for systemic therapy was indicated for the patient with widespread metastatic disease, who, on the basis of literature reports, was unlikely to benefit from such therapy. The oncologists rated the appropriateness of systemic therapy as low in the patient with limited early disease, in which the literature indicates the greatest benefit will be derived from such intervention. **Conclusion:** Referring oncologists perceive the appropriateness of systemic radionuclide therapy as low. Their perception of its appropriateness increases with extent of disease. As a result, this palliative option is underutilized or used in less-than-optimal disease settings.

Key Words: cancer; oncology; ^{89}Sr

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The optimal management of metastatic bone pain remains complex and to be properly understood requires insights derived from multiple clinical perspectives (1). Both clinicians and patients view rapid resolution of bone pain as a sustainable goal in the management of metastatic disease. Rapid, supportable pain relief, however, comes at significant cost to the patient (e.g., mental status changes with opioid narcotics) and to the health-care system (e.g., inappropriate patient management).

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Attempts to formulate guidelines for the management of bone cancer pain are based almost exclusively on pharmacological and psychological modalities (2). This coincides with the relative under-representation of invasive therapies such as anesthetic and surgical techniques. Likewise, although external beam radiation therapy is a mainstay of cancer pain management, systemic radionuclide therapy remains severely underutilized, despite multiple studies defining its efficacy and cost-effectiveness (3-10).

This investigation was designed to achieve a better understanding of the basis for persistent underutilization of systemic radionuclide therapy for bone pain management. No data are available in the literature on the variation of medical oncologists' opinions regarding appropriate management of metastatic bone pain. The purpose of this study was to gain a perspective on the range of management techniques perceived to be appropriate by medical oncologists responsible for metastatic bone cancer pain management and to quantify the variation in these perceptions.

MATERIALS AND METHODS

One hundred board-certified medical oncologists were identified from the institutional membership of the University HealthSystem Consortium (UHC). They represented a broad range of ages, practice patterns and individual experience with bone cancer pain management. These oncologists volunteered to participate in the survey and each completed all components of the survey.

The oncologists were queried about their training, clinical experience, practice patterns and understanding of bone cancer pain management. Each participant was asked to rank a series of possible management options as to clinical appropriateness on a scale from 1 (most appropriate) to 10 (least appropriate). The cases and management options presented to the medical oncologists are as follows.

Case A. A 75-y-old man with metastatic adenocarcinoma of the prostate presents with a chief complaint of sharp, severe low back pain. This pain had become progressively more intense over the past 3 mo. It can be partially relieved with 600-mg ibuprofen every 4 h. Bone scintigraphy demonstrates three small foci of intense radionuclide uptake in the left sacroiliac joint. In addition, two small foci of radionuclide uptake are identified in the third and fourth right ribs in the midaxillary line. The abnormal increased uptake in the sacroiliac joint corresponds to the site of bony pain.

Case B. A 59-y-old woman with metastatic breast carcinoma presents with a chief complaint of right chest wall pain of 6-wk duration. The pain is intense but dull in character. She requires one or two acetaminophen with codeine tablets every 4–6 h to control the pain. She experiences moderate breakthrough pain every other day and takes additional acetaminophen with codeine for pain relief. A recent bone scan demonstrates multiple, small foci of radionuclide uptake throughout the right thoracic wall, which correspond to the site of her pain. Additional small foci of increased uptake are visualized in multiple left ribs and thoracic vertebral bodies.

Case C. A 62-y-old man presents with recent onset of left hip pain. He characterizes the pain as sharp and unremitting. He was diagnosed with metastatic adenocarcinoma of the prostate 14 mo ago. A recent bone scan demonstrates intense uptake in the left hip joint and additional intense uptake in the left intertrochanteric femoral region. There is widespread uptake of radionuclide throughout the skeleton, with no apparent sparing of any region. The patient requires a high-dose transdermal fentanyl (75 µg/h) patch and large doses of opioids to control his hip pain.

Participating medical oncologists were asked to rate from 1 to 10 the clinical appropriateness of each proposed intervention in whole numbers, with 1 representing the most appropriate and 10 the least. Their choices of management procedures are summarized in Table 1.

The mean, SD and range of answers for each case were calculated. Disagreement among oncologists was determined by calculating the mean absolute difference of individual and average scores, the coefficient of prediction and the unweighted κ statistic for interobserver variability across grouped responses. The κ statistic is used to measure inter-rater or intrarater agreement for nominal measures and demonstrates the degree of agreement exceeding that anticipated by chance agreement. Chance agreement corresponds to a κ of nearly zero, whereas nearly perfect agreement corresponds to a $\kappa > 0.90$. Responses of 1, 2 and 3 were classified as the “most appropriate” group; responses of 4, 5, 6 and 7 were classified as the “middle” group; and responses of 8, 9 and 10 were categorized as the “less appropriate” group. Multivariate analysis of variance was performed to assess how much variation could be attributed to such characteristics as oncologist age, geographic location and practice type.

RESULTS

The characteristics of the 100 medical oncologists who completed this study are detailed in Table 2. The majority of oncologists practiced in urban regions and each year treated between 10 and 50 patients who had severe bone cancer pain.

The responses regarding appropriateness of patient man-

TABLE 1
Selected Pain Management Options

Oral morphine
Parenteral morphine
Oral meperidine
Oral codeine
Oral hydrocodone
Transdermal fentanyl
External beam irradiation
Systemic radionuclide therapy (⁸⁹ Sr, ¹⁵³ Sm)

TABLE 2
Summary of Survey Results

Category	Percentage of respondents (%)
Gender	
Male	79
Female	21
Practice type	
Single-specialty group	38
Multispecialty group	36
Full-time academic	16
Clinical faculty	10
State	
CA	22
NY	10
IL	9
FL	9
MN	8
TN	8
NC	7
GA	6
MA	6
OR	5
TX	5
LA	5
Population base	
<100,000	5
100,000–1 million	37
1–5 million	50
>5 million	8
Patients with severe bone cancer pain per year	
<10	2
10–50	56
50–100	30
>100	12

agement are detailed for each case in Tables 3–5. Mean and SD values for each response are indicated along with the range of responses. The number of responses indicating the “most appropriate” and “least appropriate” options are also detailed in the tables.

The κ statistic for agreement response rates among

TABLE 3
Appropriateness Rankings for Case A

Response	Mean	SD	Range	Most appropriate (scores 1–3)	Least appropriate (scores 8–10)
Oral morphine	8.7	3.4	2–9	5	78
Parenteral morphine	9.5	0.7	1–10	1	97
Oral meperidine	4.6	2.8	2–8	32	17
Oral codeine	2.1	0.7	1–6	91	0
Oral hydrocodone	2.0	0.7	1–6	90	0
Transdermal fentanyl	3.2	2.1	1–9	57	12
External beam irradiation	8.8	3.4	2–8	3	88
Systemic radionuclide therapy	7.6	1.8	1–10	5	68

TABLE 4
Appropriateness Rankings for Case B

Response	Mean	SD	Range	Most appropriate (scores 1-3)	Least appropriate (scores 8-10)
Oral morphine	7.4	1.8	1-9	7	74
Parenteral morphine	9.2	0.9	1-10	0	93
Oral meperidine	4.1	2.3	1-8	45	4
Oral codeine	2.1	0.9	1-6	94	0
Oral hydrocodone	1.9	0.7	1-6	89	0
Transdermal fentanyl	2.6	1.1	1-9	68	4
External beam irradiation	8.1	3.7	2-10	20	56
Systemic radionuclide therapy	6.7	2.2	1-10	18	44

appropriateness categories for the management of procedures in the three cases ranged from 0.11 to 0.62, with a grand mean of 0.36. The grand mean of 0.36 represents fair interobserver agreement. The mean average deviation, which is calculated to assess the average of the deviations from the median answer, is 1.32. This represents moderate disagreement, with a score of 1 representing agreement and a score of 2 representing disagreement.

Despite uniform differences in agreement, certain trends emerge on examination of cancer pain management options. The use of opioid analgesics is accepted commonly as an appropriate tool, even in early stages of skeletal involvement (case A). The frequency of identifying opioids as appropriate interventions increases significantly with evidence of more progressive disease (from case A [least severe skeletal metastatic disease] to case C [most severe skeletal metastatic disease]; $P < 0.01$, t test). Acetaminophen appears to be considered widely as an appropriate agent for pain management. Oral hydrocodone is also perceived as an appropriate choice by most oncologists.

As evidence of metastatic extent of disease increased

TABLE 5
Appropriateness Rankings for Case C

Response	Mean	SD	Range	Most appropriate (scores 1-3)	Least appropriate (scores 8-10)
Oral morphine	4.7	3.8	1-8	32	14
Parenteral morphine	8.6	1.9	1-10	7	72
Oral meperidine	3.3	1.4	1-8	47	6
Oral codeine	1.9	1.2	1-7	96	0
Oral hydrocodone	2.0	1.1	1-7	94	0
Transdermal fentanyl	2.5	3.6	1-9	68	5
External beam irradiation	2.1	1.4	1-7	83	4
Systemic radionuclide therapy	5.9	3.0	1-8	53	10

(case C versus case A), however, oncologists increasingly identified systemic radionuclide therapy as an appropriate management choice. This trend was also evident with external beam irradiation, although this form of intervention appeared to be reserved for established indications (e.g., prevention of hip fracture).

There was no significant correlation between gender or geographic location and the use of systemic radionuclide therapy. Multivariate analysis did not demonstrate a statistically significant difference ($P = 0.328$) to exclude the possibility that random sampling variability could account for any apparent correlation. However, the ranking of systemic radionuclide therapy as a more appropriate intervention in earlier stages of disease (case A versus case C) did correlate significantly to practice type (multivariate result of $P = 0.012$ with the power of the performed test being 0.88 at that α). Specifically, oncologists who were part of single-specialty groups were approximately three times ($r^2 = 0.77$, $P < 0.01$) more likely than those in any other practice type to include systemic radionuclide therapy as "most appropriate" for palliation during early stages of metastatic disease. No other significant correlation was identified.

DISCUSSION

Appropriateness of care is difficult to define and achieve in the setting of palliative cancer pain management with radiation therapy (11-12). It also appears difficult to define clearly the role of systemic radionuclide therapy in this setting. The results of this investigation demonstrate a wide range of oncologic opinion regarding the appropriate management of metastatic bone pain. The results demonstrate that systemic radionuclide therapy is not considered as a highly appropriate choice during initial stages of bony disease, a time that the literature has established as optimal for this purpose.

Medical oncologists continue to manage bony pain with a spectrum of options. However, their choices favor opioid analgesics over systemic radionuclide therapy, despite evidence that the latter is more cost beneficial (10). The net 12-mo cost minimization after systemic radionuclide therapy for palliation of pain from prostate cancer is approximately \$6725 at 1997 pricing and costing levels. This reduction in cost is accompanied by pain diminution as measured by the McGill Pain Questionnaire, a validated survey. Systemic radionuclide therapy significantly minimized the direct costs associated with palliation by diminishing the use of narcotic opioids, therein altering provider behavior. External beam irradiation is not considered until very advanced disease is present and often only because of a threat of pathological fracture or other clinical catastrophe.

The methods used in this study contain several potential limitations. Unfortunately, there are few alternative methods available for gathering opinions about management options. The case-simulation method used here permits respondents to consider the full range of options before making decisions. Although the options were inclusive in considering

different forms of management, they were not comprehensive, and several common options within these types of therapy likely were excluded. Likewise, combinations of medical and nonmedical management were excluded, as were psychological interventions. These latter options were omitted because of the significant added complexity associated with their analysis. Surveying a large group that permitted the analysis to be powered above the generally accepted cutoff of 0.85 reduced the likelihood of sampling error.

The results of this study demonstrate a persistent, surprisingly poor consideration of systemic radionuclide therapy as an appropriate choice for cancer bone pain management by medical oncologists across a broad spectrum of demographics. Although the literature supports the use of radionuclide therapy as an effective form of palliation, there remains an underutilization of these agents because of poor understanding of their appropriateness. Further investigation is aimed at delineating the level of understanding and identification of limiting factors that prevent wider utilization of systemic radionuclide therapy.

CONCLUSION

This study demonstrates that systemic radionuclide therapy is perceived by referring medical oncologists as holding an overall low appropriateness rating among options for palliative intervention for metastatic bony pain. Oncologists prefer to use systemic opioids instead of radionuclides, even in cases for which the literature supports the effectiveness and cost efficiency of radionuclides. The underutilization of radionuclide therapy is associated with perceptions of its appropriateness in various stages of progressive disease involvement. Oncologists incorrectly believe that radionuclide therapy is more appropriate with widespread disease than for the palliation of limited index pain sites. These

practice patterns contradict the literature reporting on the efficacious use of palliative radionuclide therapy.

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