

EFFECT EVALUATION OF PAIN RELIEF USING EXTERNAL RADIATION TECHNIQUE IN BONE METASTATIC CANCER PATIENTS AT MILITARY HOSPITAL 175

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ABSTRACT:

Objective: Evaluate the effectiveness of pain relief due to bone metastasis using external beam radiation therapy technique.

Subjects and Methods: Retrospective and prospective study describing 178 patients with stage IV cancer; bone metastases, treated for pain relief with external radiotherapy, at the Institute of Oncology and Nuclear Medicine, Hospital Military Medicine 175, from May 2021 to April 2022.

Results: Patients' mean age was 58.47 years old. The majority of patients were men (62.9%), primary lung cancer (54.5%), osteolytic lesions (80.3%), primary cancer with multifocal bone metastases (89, 9%). The proportion of patients responding to pain treatment after external radiotherapy at 1 week, 2 weeks, 4 weeks and 8 weeks was 40.4%, 76.4%, 88.8% and 85.9%, respectively. The pain relief response rate in the radiotherapy group combined with second- and third-line analgesics was highest at week 4 (56.2% and 32.6%). The average pain score of patients decreased significantly in both single-focal bone metastasis and multi-focal bone metastasis groups at 4 weeks and 8 weeks after radiotherapy treatment.

Keywords: Pain, radiation therapy, bone metastasis, spine.

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1. INTRODUCTION

Bone metastasis is a condition in which cancer cells metastasize from the original organ to the bone. Cancer cells can metastasize to many bones, such as the pelvis, femur, spine...; Among them, spinal bone metastases account for the majority [7], [4]. Pain is a very common symptom in patients with bone metastasis, significantly affecting the patient's quality of life and survival time [1]. External radiotherapy, is a common method used in many cancer centers, which is convenience, reasonable cost, and high pain relief [5]. Currently, in our country, there are few studies evaluating the effectiveness of pain relief due to bone metastases from cancer using external radiotherapy techniques, so there are not many summaries evaluating the pain relief effectiveness of external radiotherapy treatment.

We conducted this study to survey the clinical and paraclinical characteristics of patients with stage IV cancer with bone metastases; evaluating the pain relief effectiveness of external radiotherapy on patients with stage IV cancer with bone metastasis, at the Institute of Oncology and Nuclear Medicine, Military Hospital 175.

2. SUBJECTS AND METHODS

2.1. Subjects:

The patients were diagnosed with stage IV cancer with bone metastasis at

the Institute of Oncology and Nuclear Medicine, Military Hospital 175, from May 2021 to April 2022.

2.2 Inclusion criteria

- Patients with a confirmed diagnosis of cancer (pathological evidence)
- Imaging evidence of bone metastasis using CT-scan, MRI, PET-CT, and bone scan.
- Corresponding pain at the site of bone metastasis
- Failure to respond or intolerance to pain relief treatment after 48-72 hours of admission

2.3 Exclusion criteria

- Patients with paralysis due to spinal cord compression
- Severe comorbidity (pneumonia, liver failure, kidney failure...), with a prognosis of less than 1 month to live.
- Unstable lesions in 3 locations of the lumbar spine or high risk of pathologic fractures (Mirels score ≥ 8)
- History of trauma at the bone metastasis
- The patient does not agree to radiotherapy

2.4 Method

- Study design: retrospective, descriptive prospective.

- Research targets:

+ Clinical and paraclinical characteristics: age, gender, type of metastasis, number of bone metastases.

+ Characteristics of pain relief treatment using external radiotherapy technique (on Linac Precise radiotherapy machine): radiotherapy regimen, combined analgesics, pain relief rate. Assess pain relief response using the NRS scale (Numerical Pain Rating scale) with numbers from 0 to 10. Using the NRS scale, you can ask the patient to receive direct verbal answers to evaluate, there is no need for the patient to directly mark on the ruler like VAS, so the NRS scale is more widely applied in clinical practice.

- Ethical approval: this study was approved by the Ethics Council of Military Hospital 175. All patient information was kept confidential and used only for scientific research purposes.

- Procedure:

Step 1: Choose patients with pain due to bone metastases who were indicated for external radiotherapy; radiotherapy planning.

Step 2: Assess pain score according to NRS at the time of admission, 1 week, 2 weeks, 4 weeks, 8 weeks after radiotherapy.

Step 3: Data collection and statistical analysis

- Statistical analysis: using SPSS 20.0 software. Use non-parametric tests for non-normal distributions, Chi-square tests and t-tests for normal distributions. The difference is statistically significant when $p < 0.05$.

3. RESULTS.

3.1. Clinical and paraclinical features:

- **Age:** Patients were distributed from 33-82 years old; Average age was 58.47 years old.

- **Gender:** 112 patients (62.9%) were men; 66 patients (37.1%) were female.

- Primary cancer

+ Lung cancer: 97 patients (54.5%).

+ Breast cancer: 19 patients (10.7%).

+ Prostate cancer: 16 patients (9.0%).

+ Colorectal cancer: 17 patients (9.6%).

+ Unknown primary tumor: 12 patients (6.7%).

- Metastatic bone location

+ Spinal Bones: 158 (88.76%)

+ Pelvis: 33 (22.19%)

+ Shoulder bones: 07 (3.93%)

+ Femur: 8 (4.49%)

+ Ribs: 07 (3.93%)

- Bone metastase types

+ Osteolytic: 143 patients (80.3%).

+ Osteoblastic: 06 patients (3.4%).

+ Mixed form: 29 patients (16.3%).

+ Invasion of surrounding soft tissue: 13 patients (7.3%)

The majority of primary cancer cases with bone metastases were osteolytic (80.3%)

- Number of metastatic foci:

+ Multifocal: 160 patients (89.9%).

+ Single focus: 18 patients (10.1%).

- Radiotherapy regimen:

+ 30Gy/10Fx regimen: 155 patients (87.1%).

+ 20Gy/5Fx regimen: 20 patients (11.2%).

+ 8Gy/1Fx regimen: 03 patients (1.7%).

- Using combined pain relievers:

+ Using level 2 painkillers (according to WHO): 64 patients (35.95%).

+ Using level 3 narcotic pain relievers: 114 patients (64.05%).

3.2. Treatment features:

- Pain treatment response rate:

Table 1. Response rate to analgesic treatment after external radiotherapy (n = 178).

Response after treatment		Time after treatment			
		1 week	2 weeks	4 weeks	8 weeks
Response	Complete	18.5%	38.2%	69.7%	59.5%
	Partial	21.9%	38.2%	19.1%	26.4%
None response	Stable	42.1%	14.6%	5.6%	9.6%
	Progress	17.5%	9.0%	5.6%	4.5%

The rate of patients responding to pain relief treatment after radiotherapy at 1 week, 2 weeks, 4 weeks and 8 weeks was 40.4% and 76.4%, 88.8% and 85.9%, respectively. Meanwhile, the rate of patients with increased pain after radiotherapy at 1 week, 2 weeks, 4 weeks, and 8 weeks was 17.5%, 9.0%, 5.6%, and 4.5%, respectively.

Table 2. Evaluation of analgesic response and combined drug treatment (n = 178).

Combine drugs and response		Time after treatment		
		2 weeks	4 weeks	8 weeks
Level 2 painkillers (n=64)	Response	49.4%	56.2%	53.4%
	None response	14.6%	7.9%	10.7%
Level 3 painkillers (n=114)	Response	27.0%	32.6%	32.6%
	None response	9.0%	3.3%	3.3%
p		0.891	0.942	0.594

The pain relief response rate in the radiotherapy group combined with second- and third-line analgesics was highest at week 4 (56.2% and 32.6%). The non-response rate after radiotherapy in both groups was highest at week 2 (14.6% and 9.0%).

Table 3. Average pain score with number of bone metastases after radiotherapy treatment.

Time of evaluate	Number of metastatic foci		p
	Single focus	Multifocal	
NRS at admission	6.94	6.36	0.122
NRS 1 week	5.83	5.31	0.242
NRS 2 weeks	5.17	4.66	0.283
NRS 4 weeks	4.28	3.68	0.208
NRS 8 weeks	4.39	4.17	0.655

The average pain score at admission in the group of patients with single-focal bone metastases was higher than the group of patients with multi-focal bone metastases, the difference was not statistically significant at all time points. The average pain score decreased significantly in both the group of patients with single and multifocal bone metastases at 4 weeks and 8 weeks after radiotherapy treatment.

4. DISCUSSION.

Clinical features

Table 4. Primary tumors in some studies around the world

Primary tumors	Velden (2008) n=432	Van Liden (2004) n=1157	Steenland (1999) n=1157	Franco (2014) n=130
Breast	97 (23)	451 (39)	451 (39)	24 (18)
Prostate	127 (29)	267 (23)	266 (23)	24 (18)
Lung	97 (23)	287 (25)	289 (25)	35(27)
Other	111 (25)	152 (13)	150 (13)	47 (37)

The rate of primary cancer in patients in our study is similar to some studies in the world, in which lung cancer, breast cancer, and prostate cancer account for the highest rates. However, our study and some domestic studies show that the rate of lung cancer is the highest compared to studies in the world.

Table 5. Location of bone metastases in some studies

Location	Velden (2008) (n=432)	Van Liden (2004) (n=1157)	Steenland (1999) (n=1157)	Franco (2014) N=130
Spinal Bones	302 (63)	342 (29.6)	347 (30)	80 (67.7)
Pelvis	98 (20)	432 (37.3)	422 (36.5)	50 (38.4)
Femur	33 (7)	170 (14.7)	179 (15.5)	33 (25.3)
Ribs	12 (3)	97 (8.4)	98 (8.5)	14 (10.7)
Other	35 (7)	123 (10.6)	111 (9.6)	

The most common bone locations for metastasis were the spine and pelvis. This result is similar to many studies around the world. The mechanism of bone metastasis of some types of “osteophilic” cancers such as lung cancer and breast cancer favors metastasis to the thoracic spine because breast and lung cancer cells often pass through the drainage of the Azygos venous

system with the plexus Baston vein while lung cancer cells follow the pulmonary vein to the left heart and then to bone tissue. Prostate cancer often metastasizes along the lumbar iliac venous plexus to the pelvis, lumbar spine, and sacrum. Colorectal cancer cells metastasize mainly through the portal vein system to the liver and lungs and finally metastasize to the spine.

Assessment of treatment response

With external radiotherapy, the rate of patients with bone metastases responding to pain relief in this study is similar to a number of other studies in the world [2], [8], [9]. Specifically: the complete pain relief response rate after 8 weeks of radiotherapy reached 73.6%; The rate of increased pain and non-

response to radiotherapy after 8 weeks was 6.5%. However, this result is lower than the study by Yoshida (2006) on the Asian patient group (complete response rate reached 80% [10]), but higher than the results of some other studies (table 4). This difference may be due to the fact that our study did not consistently reduce the dose of painkillers.

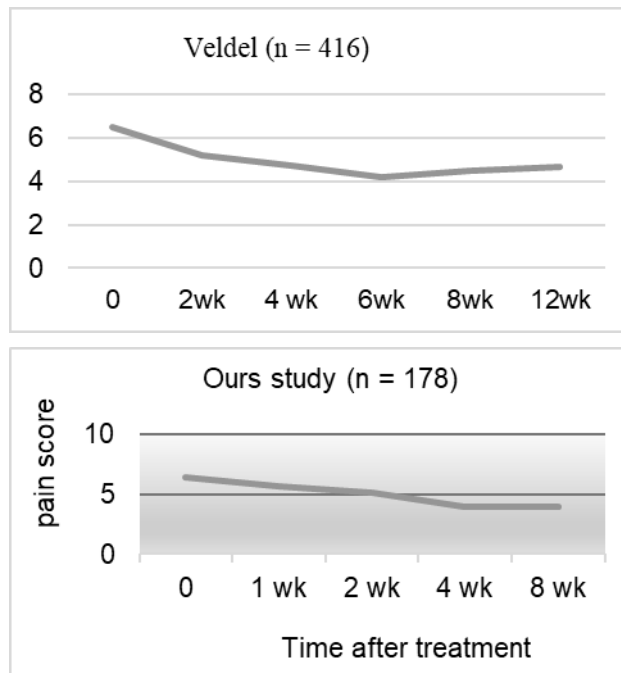
Table 6. Percentage of cancer patients responding to analgesic radiotherapy according to some studies [2], [8], [9].

Response	Harstsell (2005) (n = 573)	Steenland (1999) (n = 528)	Veldel (2018) (n = 416)
Complete	16.5%	33.0%	26.0%
Partial	49.0%	36.0%	36.0%
Stable	25.0%	15.0%	16.0%
Progress	9.5%	16.0%	10.0%
Unidentified			12.0%

The rate of patients responding to pain relief after radiotherapy in the group of patients using a second-line analgesic (tramadol) was higher than the group using a third-line analgesic (morphine) at all assessment times, but there was no difference statistical significance. Our results are different from Hartsell’s (2005) study, possibly because in our study, 26 patients died, while in Hartsell’s study, 70 patients died after 2 months end of radiotherapy. On the other hand, the step-down of narcotic analgesics was not carried out synchronously in our study, so we did not compare the effectiveness of combined analgesics in groups of patients

who did/did not use narcotic analgesics with other studies. According to some authors, narcotic analgesics are not considered the optimal treatment method for local pain control in patients with bone metastases [3], [6].

Evaluation of pain after radiotherapy: we found that the average pain score of patients decreased significantly in both groups of patients with single and multifocal bone metastases at 4 weeks and 8 weeks after radiotherapy; equivalent to Veldel’s (2018) study on 416 patients (lowest average pain score at 4 to 6 weeks after radiotherapy) [9] (Picture 1).

Picture 1. Average pain scores after radiotherapy

The average pain score in the group of patients with single-focal bone metastases at admission was greater than in the group of patients with multifocal bone metastases, the difference was not statistically significant ($p = 0.122$). However, the average pain score at the time points 1 week, 2 weeks, 4 weeks, and 8 weeks after radiotherapy in the group of patients with multifocal bone metastases was lower than in the group of patients with single focal bone metastases, but there was no difference statistical significance ($p > 0.05$). We think that this result can be explained because patients with single-focal bone metastases often tend to pay attention to only one pain location, cause increasing subjective assessment of pain. With the results of this study and reference to similar studies, we believe that external radiotherapy is an effective method to

control pain in patients with stage IV cancer with bone metastases.

5. CONCLUSION.

Research on 178 patients with stage 4 cancer, bone metastases, pain relief treatment with external radiotherapy, at the Institute of Oncology and Nuclear Medicine, Military Hospital 175, from May 2021 to April 2022, conclusion:

Average patient age was 58 years old. The majority of patients were men (62.9%), primary lung cancer (54.5%), osteolytic bone metastases (80.3%), and multifocal bone metastases (89.9%).

The average pain score of patients decreased significantly in both groups of patients with single and multifocal bone metastases at 4 weeks and 8 weeks after radiotherapy treatment.

External radiotherapy technique was highly effective in reducing bone pain caused by metastases (at 4 weeks and 8 weeks after radiotherapy, response rates were 88.8% and 85.9%). The rate of patients responding to pain relief in the radiotherapy group combined with second- and third-line analgesics was highest at week 4 (56.2% and 32.6%), however this difference was not statistically significant.

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