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RESEARCH

Multidisciplinary approach to bone metastases: a single center experience in a tertiary cancer center

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Abstract

Purpose The increasing incidence of bone metastases frequently leads to skeletal-related events (SREs) and pain. While multidisciplinary management is recommended by scientific societies, a standardized model remains undefined. An example can be provided by the Osteoncology multidisciplinary outpatient clinic (OMC) of the Veneto Oncology Institute, created to offer support to patients with bone metastases.

Patients and methods Patients with bone metastases are evaluated by a multidisciplinary team since 2013. Access to the OMC is regulated by an internal protocol and a form filled out by the referring physicians, which establishes the priority of access and the specific query for the multidisciplinary team. We analyzed the characteristics and outcome of OMC visits of all patients who accessed between January 2018 and June 2023. All data were retrieved from a prospectively managed database.

Results 2,200 patients were evaluated at OMC, with a median age of 66 years. Breast (33.3%) and lung cancer (19.2%) were the most frequent primary sites. Most patients (85.1%) accessed the OMC in line with the priority indicated by their referral score, with a median waiting time of 6 days. Physicians most frequently asked the multidisciplinary team about the best treatment for bone metastases; 35% sent multiple requests. Following OMC visit, 31.5% of patients received two or more distinct indications. The most frequent were orthopedic corsets (28.3%) and radiotherapy (27.5%).

Conclusion This large series confirms the efficacy of a multidisciplinary approach for bone metastases. This method reduces patients' psychophysical stress through rapid and effective assessment and provide precise and tailored therapeutic indications.

Keywords Bone metastasis · Skeletal disease · Multidisciplinary · Osteoncology

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Introduction

Bones are one of the most common sites for metastasis, after lungs and liver [1]. Bone metastases are common with several cancers, but some malignancies have greater affinity for bones than others [2]; for instance, breast and prostate cancer have the highest incidence of bone metastases (around 70% of cases), whereas bone lesions are less common in thyroid (60%), lung (30–40%), bladder (40%) or kidney cancers (20–25%) and melanoma (14–45%) [3].

The epidemiology of metastatic bone disease is evolving. Cancer treatments have improved the overall survival of patients, leading to a higher number of patients with bone metastases, which is expected to grow further in the future [3, 4]. Moreover, patients with only bone metastasis have a better prognosis than patients with visceral disease [5–7]. Nevertheless, bone lesions are responsible for high morbidity in cancer patients, therefore causing pain and skeletal complications known as "skeletal related events" (SREs). SREs include pathologic fractures, spinal cord compression (SCC), hypercalcemia, need for radiation (RT) to bone or surgery to bone [8]. SREs are associated with lower mobility, reduced quality of life (QoL), worse patient survival and increased health care expenses [9].

For these reasons, bone management programs should start at the same time as cancer treatment to prevent bone metastasis complications. Moreover, an expert clinical exam joined with radiological charts review permits to focus undetected bone lesions manageable with radiotherapy or surgery. The most prominent international scientific societies recommend multidisciplinary management [9–12], but there are no shared or optimal models.

Currently available options are often unsatisfactory for patients, who have to queue on long waiting lists for multiple different specialists, increasing distress and leading to poor healthcare continuity. At the same time, the care of patients suffering from bone metastases is of paramount importance for improving their quality of life and their prognosis.

Therefore, in the 2000 s a new discipline in Oncology, called Osteoncology, dedicated to primary and metastatic bone tumors, was created in Italy. A strong focus of Osteoncology is to foster the development of multidisciplinary centers for diagnosis, treatment and rehabilitation of cancer-related bone diseases [13].

The distinguishing factor of Osteoncology is the creation of a dedicated team of specialists comprising medical oncologists, radiation oncologists, orthopedic surgeons, (interventional) radiologists, nuclear medicine physicians and pain specialists with expertise in bone complications from cancer. The treatment strategy is developed with an integrated approach, considering the patient's prognosis, the condition of the primary cancer and social background**.** The aim is to prevent skeletal related events and decrease the significant morbidity, hospitalization frequency and economic impact related to the treatment of advanced stage cancers [14, 15].

The Veneto Institute of Oncology (IOV) is an Italian national comprehensive cancer center that takes care of more than 8,000 new cancer patients per year, offering preventive, curative and palliative care services. In 2013 an osteoncology multidisciplinary outpatient clinic (OMC) was launched in the attempt to offer patients the best management of metastatic skeletal disease with a multidisciplinary approach.

Patients and methods

OMC is available to cancer patients with metastatic bone disease, whether symptomatic or non-symptomatic, while they are on an active cancer treatment. The referral is possible for patients treated in the Clinical Unit of IOV (Medical Oncology, Radiotherapy, Hereditary Tumors and Pain Therapy and Palliative Care), as well as to external oncology patients referred by other specialists or general practitioners.

Patients are assessed by a team of specialists composed of a medical oncologist, a radio-oncologist, a pain specialist, an orthopedic, an endocrinologist, a radiologist and a case manager nurse. Visits are scheduled weekly to allow for rapid patient care and early coordination between specialists.

The physician referring the patient decides on one of two ways to examine the case: (a) a clinical assessment of the patient and radiological images or (b) discussion of the radiological images alone (radiological or nuclear medicine images), without the need for the patient's presence. For all the symptomatic patients the clinical assessment is required; for other situations, the decision between clinical assessment and images discussion is left to the referring physician.

Symptom burden and the status of oncological disease are defined during the visit, along with the patient's need for locoregional or medical treatments and the most appropriate care pathway.

The multidisciplinary team decides on a customized treatment for each patient: continuation of active oncological treatment, indication to radiotherapy, referral to the orthopedic surgeon, prescription of orthopedic corset, referral to the pain therapy and palliative care unit, loco-regional treatments or osteo-metabolic treatments.

In 2017, the multidisciplinary team also defined a referral form and procedure to establish priority access. The referring doctors fill in a specific form (Fig. 1) and clearly express the query for the multidisciplinary team. The items included in this form are: Karnofsky Performance Status, symptoms, tumor site and presence of visceral metastasis, estimated

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Update 10-7-17	**OSTEONCOLOGY OUTPATIENT MULTIDISCIPLINARY CLINIC REQUEST FORM**	Mod1-P_AMO

Surname & Name _____ DOB _____ Phone _____

Referral Unit _____ Ref. Physician _____

Cancer and stage _____

Expected survival ○ ≥ 12 months ○ 6 - 12 months ○ < 6 months

Oncological treatments with impact on survival? ○ Yes ○ No

Specific request for OMC _____

_____

PS (Karnofsky)	0-1	2	≥ 3	**SCORE**
	☐ 2 points	☐ 1 punto	☐ 0 points	_____
Signs and Symptom	None	Bone pain	Compression symptoms	+
	☐ 0 points	☐ 2 points	☐ 3 points	_____
Visceral disease	Multiple visceral disease	Oligometastatic visceral disease (1 to 3 lesions)	None (only bone disease)	+
	☐ 2 points	☐ 1 punto	☐ 0 punto	_____
No. of vertebral metastasese	0-1	2	≥ 3	+
	☐ 2 points	☐ 1 punto	☐ 0 points	_____

Site of primary cancer	Prostate, breast, thyroid, haematological neoplasm	Kidney, colon, rectum, gynae	Others	Biliary tract, liver, lung, stomach, oesophagus, CUP	+
	☐ 1 points	☐ 2 points	☐ 3 punto	☐ 4 points	_____

TOTAL SCORE _____

Urgent cases (with confirmatory imaging)	☐ Spinal cord compression	☐ Pathological fracture	URG

SCORE 1-5 OMC within 30 days
6-9 OMC within 20 days
≥ 10 OMC within 10 days

Fig. 1 Osteoncology Outpatient Multidisciplinary Clinic Request Form

survival, availability of cancer treatment with possible survival impact, number of bone lesions, and stage of disease.

All these items do have a score and the priority of patients' access to OMC is based on the final score. Patients are informed by their doctors about the benefits of this OMC visit and are strongly recommended to attend it.

The scored used in OMC to determinate the priority in the access to the clinic has been specifically adapted for our Institution based on the 2005 revised Tokuhashi score [16].

Patients with a final score equal or greater than 10 have priority access within 10 days from referral; patients with a score between 6 to 9 have priority access within 20 days from referral; and patients with a score from 0 to 5 should be assessed within 30 days.

Emergencies (e.g., spinal cord compression with neurological symptoms or signs of a pathological fracture of limb or pelvis) must be assessed urgently, without referring to the OMC visit. The OMC will evaluate the situation by access or discussion, after sending the request form specifying the urgency character.

All consecutive patients assessed in the OMC between January 2018 and December 2023 were included in this analysis. Data were retrieved from the OMC prospectively maintained database. The following data have been collected: demographic information (age, sex), tumor site and extension, referral form scores, time to access to the OMC, multidisciplinary decision, and outcome. All the patients gave their consent to data collection and reporting.

Results

Over a six years period, 1,500 patients had access to OMC, whereas 720 patients were discussed. Out of 2,220 patients, 1384 were female (62.3%); most of them (2,070, 93%) have been presented by medical oncologists, while external referrals were marginal among the clinic activity. Median age at referral was 66 years old (range: 18–94 years). Most of the patients were affected by breast cancer (740, 33.3%), followed by lung (426, 19.2%), colorectal (257, 11.6%) and prostate cancers (113, 5.1%). All the patients eligible for bone modifying agents according to national guidelines were receiving bone modifying agents. In our series, 1618 patients (73,5%) where on treatment with specific drugs, mainly zolendronate, or denosumab.

According to the urgency referral score, 503 patients (22.7%) needed assessment within 10 days, 1,202 (54.1%) within 20 days and 515 (23.2%) within 30 days from referral. Median waiting time to access OMC was 6 days (range: 1–75); mean waiting time was 8.6 days.

Most of the patients (1890, 85.1%) had access to the OMC in line with the urgency based on the referral score. A minority of them (330, 14.9%) had a longer waiting time, with a median delay time of 5 days (range: 1–60). The main reasons for this late access were: patients' request to reschedule the appointment (196, 8.8%), radiological imaging not yet ready (74, 3.3%), hospitalization in another hospital (36, 1.6%), other reasons (24, 1.1%).

Apart from late referral due to patients' preference, the rate of adherence to the urgency score was 93.9%.

A post-hoc evaluation of the referrals has been conducted. According to the referral form, the most frequent query to the multidisciplinary team was about the choice and indication of the treatments for bone metastases: prescription of an orthopedic corset (1087, 34.7%), radiotherapy (488, 15.6%), space for locoregional treatments (421, 13.4%), surgery (86, 2.7%) or percutaneous vertebroplasty (52, 1.6%).

The referring physicians also asked to examine diagnostic images to confirm the presence of bone lesions at risk of fracture in 342 (10.9%) cases or to perform a pain assessment in 270 (8.6%) cases.

Additional queries related to the indication were: osteometabolic visit (166, 5.2%), weight-bearing activity (134, 4.3%), weaning from the orthopedic corset (33, 1.1%), bone biopsy (25, 0.8%) or other (33, 1.1%). The multidisciplinary team can assess multiple indications or choices at the same time; indeed, 35% of referring physicians asked more than one query.

The sites of bone metastases involved were vertebrae in most patients (1282, 58.3%), followed by vertebrae and pelvis (172, 7.8%), pelvis (138, 6.3%), vertebrae and rib cage (80, 3.63%), limbs (57, 2.3%), femur and vertebrae (44, 2%), femur and pelvis (34, 1.5%), ribs (30, 1.3%) and other multiple bone sites (362, 16.5%).

The specialists composing the OMC team were all present in 97.7% of the clinics (the orthopedic surgeon was absent because of operating room urgencies in 6 times). The table shows the decisions at the end of the OMC visit or discussion. Orthopedic corsets were prescribed in 771 (28.3%) patients to prevent pathological fractures and weaning from the use of the brace was indicated in 33 cases (1.2%). Radiotherapy was indicated in 748 patients (27.5%) for pain or skeletal related events. Further diagnostic imaging was required on 343 patients (13.7%), additional pain management was required for 255 patients (9.4%), and orthopedic surgery was indicated for a limited number of patients (110, 4.1%). For a number of patients (166, 5.2%), a specific osteometabolic assessment has been required, while follow up visit in the OMC was indicated for 99 patients (3.6%). Locoregional approaches were prescribed to 131 patients (4.9%), either bone biopsy (59 patients), percutaneous vertebroplasty (42 patients) or other locoregional treatments (34 patients).

The OMC examination provides a multidisciplinary approach to the patient: 1,170 patients (53.5%) received a single therapeutic indication, 546 patients (24.8%) two

different therapeutic decisions, three indications in 134 cases (6.1%) and 13 patients (0.6%) had four different prescriptions. Moreover, 85 patients referred to OMC did not show up for the examination because of different reasons, whereas 245 patients (11%) were deemed not needing specific osteoncology indications.

The average calculated time for decision delivery was 19 days for pain specialist examinations, 27 days for radiotherapy, 37 days for both bone biopsy and surgical take-in-charge, 45 days for osteometabolic examinations and 84 days for vertebroplasty.

Patients' characteristics and referral and decisions data are globally summarized in Table 1.

Table 1 Patients' characteristics and OMC decisions

Characteristics	N	%
Referral	2090	94.1
- Oncology Units	37	1.7
- Radiotherapy Unit	6	0.3
- Pain Clinic	35	1.6
- Ereditary Tumour Unit	53	2.3
- Other		
urgency for assessment	503	22.7
- within 10 days	1202	54.1
- within 11 to 20 days	515	23.2
- within 21 to 30 days		
primary cancer	740	33.3
- breast	426	19.2
- lung	257	11.6
- colorectal	113	5.1
- prostate	88	3.9
- pancreas	78	3.5
- myeloma	83	3.7
- upper GI tract	69	3.1
- kidney	369	16.6
- other		
referral query	1087	34.7
- orthopedic corset	488	15.6
- radiotherapy	421	13.4
- locoregional treatment	342	10.9
- imaging review	270	8.6
- pain therapy	166	5.2
- osteometabolism	134	4.3
- weight-bearing activity	86	2.7
- surgery	52	1.6
- vertebroplasty	33	1.1
- weaning orthopedic corset	25	0.8
- biopsy	33	1.1
- other		
type of intervention	771	28.3
- orthopedic corset	748	27.5
- radiotherapy	373	13.7
- imaging	255	9.4
- pain therapy	110	4.0
- surgery	99	3.6
- follow-up in OMC	164	6.0
- osteometabolic assessment	59	2.2
- bone biopsy	42	1.5
- vertebroplasty	34	1.3
- locoregional treatments	33	1.2
- weaning orthopedic corset	34	1.3
- other		

Discussion

Skeletal cancer lesions are an important issue in oncology, due to morbidity and mortality. The management of patients requires the involvement of and discussion among different physicians. Therefore, a multidisciplinary approach is an attempt to provide quick and appropriate answers to this issue. Indeed, the core function of a multidisciplinary team is to bring together a group of healthcare professionals from different fields in order to determine the treatment plan that is more suitable for a patient, in a safe and time-effective way. At the same time, a multidisciplinary approach significantly improves the quality of cancer care [17–19]. Reports actually prove that multidisciplinary discussion leads to substantial improvements in therapy and adherence to guidelines, positively impacting the oncological outcome [20–22].

In our experience, the introduction of the OMC has proven to favor the cultural and scientific growth of health professionals in this field and improve the appropriate care for patients with bone metastases. Our OMC mainly aims to decrease the high morbidity of bone disease, reduce complications, minimize psychophysical distress, and improve quality of care.

Few data and experiences regarding the osteoncology multidisciplinary approach have been reported so far. Ibrahim et al. have initially reported on their experience in OMC [23] and then they updated their data with a longer observational period [15]. Over a 10-year period, they performed 2,194 osteoncology assessments with a significative prevalence of breast cancer diagnosis. In our Institution, in a period of six years, 2,220 patients have been referred to the OMC, with 1,500 clinical examinations carried out, and 720 multidisciplinary team-only meetings held to discuss cases. The number of clinical activities carried out in our OMC is higher compared to the time period. This is probably due to both a wider diffusion of the multidisciplinary approach and the increasing number of prevalent cancer patients, which is a well-established consequence of cancer care improvements.

The vast majority of the patients in our cohort were female affected by breast cancer, which is consistent with the literature information [15] and the epidemiology of neoplasm in our area, according to the regional tumor registry [24]. In our population, as well as in the cited cohort reported by Bongiovanni and colleagues, lung cancer was the second most frequent tumor. This may be due to the increased incidence of this neoplasm in which bone lesions are usually lytic, causing

more complications, along with the increased survival of lung cancer patients thanks to an improving therapeutic management of these patients. Colorectal cancer is the third histology in our cohort, reflecting the changes in the natural history of this neoplasm, with improved survival and increased number of bone metastases. Interestingly, a lower-than-expected number of patients with prostate cancer were referred to the OMC. The reason can be found in the fact that prostate cancer usually causes blastic metastases [25], which are easier to manage compared to lytic lesions and determine less complications. It is also known that prostate cancer cells undergo epithelial-mesenchymal-transition to disseminate and acquire a bone-like phenotype to metastasize in bone tissue, and their crosstalk with the bone microenvironment defines their osteoblastic pattern, which is unique in the contest of cancer and could conferrer a complex situation from a therapeutical and biological perspective. Moreover, the wide diffusion of Prostate Cancer Multidisciplinary Units in our region allows for better global management of these patients.

Overall, 2,722 interventions were recommended, with only 11% of patients deemed not in need of a specific osteoncology indication, mainly because they were still well managed in their clinic. Globally, interventions varied among surgical indications: orthopedic corset prescription, radiation therapy courses, pain therapy, imaging assessment, and biopsy procedures. As a consequence, each patient received an average number of 1.4 indications and a median number of 2 indications in a single examination or discussion. Moreover, for each patient only the recommended osteoncological indications were considered: thus, when advising for a radiation therapy course, the need or space for surgery was excluded. This is of paramount importance for cancer patients, who benefit from single access to all the appropriate clinical indications, and data are in line with published literature [15].

We also analyzed the referral time of the OMC clinic to other indicated activities, which appears to be satisfactory, even though no other data in this setting was ever reported, thus not providing any sort of benchmark.

Finally, we have reported here about the referral form adopted in our Institution to define the priority for each patient to access the OMC. To the best of our knowledge, this is the first time such a score has ever been reported. The referral procedure takes into account different clinical features related to the disease and the patient's status, and is an effective way to properly establish priority access.

Conclusion

In conclusion, we believe a multidisciplinary approach can become the standard of care for bone metastases management in a major tertiary healthcare center. Considering the documented evidence of improvements in the use of these approaches, reduced time-to-treatments, and patient outcomes resulting from interventions, the implementation of such an approach has the capacity to positively impact the quality of life and the oncological outcome of patients. Prospective studies are needed to validate these findings and to better evaluate patient outcomes and cost savings in relation to the use of a multidisciplinary strategy in a clinical setting.

Authors contributions All authors contributed to the study conception and design. Material preparation and data collection were performed by Marco Maruzzo, Chiara Pittarello, Evelina Lamberti, Virginia Pozza. Analysis was performed by Marco Maruzzo, Antonella Brunello, Anna Roma, Cristina Falci, Ugo Nena, Sara Galuppo. The first draft of the manuscript was written by Marco Maruzzo, Chiara Pittarello, Antonella Brunello. All the authors read and approved the final manuscript.

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Data availability The dataset generated for the present paper will be available online via Zenodo (EU Open Research Repository).

Declarations

Ethics approval This study has been performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Istituto Oncologico Veneto (23Jan2023).

Competing interest The authors declare no competing interests.

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