Perspective

Principles of Management of Extremity Skeletal Metastasis

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Abstract

Understanding the epidemiology of extremity skeletal metastasis and the factors deciding the treatment decision-making are essential in developing a diagnostic and treatment strategy. This leads to optimum care and reduces disease-related burden. With the evolution of medical, radiation therapy, and surgical methods, cancer care has improved the quality of life for patients with improved survival and functional status in patients with skeletal metastasis. Based on the currently available literature, we have described a step-wise evaluation and management strategy of metastatic extremity bone disease. The present review article addresses various aspects and related controversies related to evaluation, staging, and treatment options in the management of extremity bone metastasis. This article also highlights the role of multidisciplinary involvement in management of extremity skeletal metastasis.

Keywords: Angioembolization, endoprosthesis, megaprosthesis, pathological fracture, radiotherapy, skeletal metastasis

Introduction

Bone is the third most frequent site of metastatic disease and primary tumors from breast, lung, prostate, renal cancers and thyroid are the most common cause of bone metastases.[1] The primary presentation is pain and pathological fracture in 9%–29% of cases, with about 90% of pathological fractures requiring intervention.[2,3] The orthopedic management of these bone metastasis have a major impact on both quality of life and probably survival rates.[4]

In this article, we review extremity bone metastases which accounts for 66% of skeletal metastasis. Extremity metastases are one of the first presentations of disease in lung cancer, renal cancer, myeloma, and lymphoma,[5] with a median survival from diagnosis of: 6 months in melanoma, 6–7 months in lung, 6–9 months in bladder, 12 months in renal cells carcinoma, 12–53 months in prostate, 19–25 months in breast, and 48 months in thyroid. The treatment involves a multidisciplinary team input which includes an orthopedic surgeon, orthopedic oncologist, radiologist, radiation oncologist, medical oncologist, and other health-care personnel. The treatment varies on the specific site of involvement and is important that health-care personnel, especially orthopedic surgeons, are updated with recent trends in the management of skeletal metastasis. In this article, we highlight the principles of management and decision-making in treatment of skeletal metastasis in the extremity.

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Mechanisms of Metastasis to Bone

Commonly involving the axial skeleton, bone metastasis present at multiple sites.[3] This could be in relation to the hematopoietically-active red bone marrow and the paravertebral network that may play a role in metastasis.[5] Apart from the favorable microenvironment for tumor cell survival, the following are needed ones the tumor cells are in circulation[3,5-7]

- Extravasation and adhesion to vascular tissues
- Microenvironmental support: As per the seed-and-soil hypothesis, for growth and survival of cancer cells, the fertile ground (the soil) is provided by the microenvironment
- Epithelial–mesenchymal transition: When the normal epithelial cells lose their epithelial features and transform into mesenchymal cells, they can migrate into new environments. This process of epithelial–mesenchymal

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transition occurs during embryogenesis. When the cancer cells undergo the same transition, they transform into an invasive phenotype.

Presentation and Evaluation

The golden rule stating that a complete workup must precede surgery, should be respected in the setting of a pathological fracture.[8] It can present as the first sign of an unknown primary or be seen in cases with an established primary diagnosis. In cases with an established primary, the diagnosis of a second primary bone tumor as a differential diagnosis should always be considered. Clinical features of multiplicity and typical axial preference point toward bone metastases. Biopsy should, however, be done to confirm the diagnosis before planning any intervention.

A painful solitary bone lesion without history of metastatic disease or a primary malignancy needs a more extensive metastatic workup which include laboratory investigations and imaging before the biopsy. Some of the commonly used laboratory investigations are: β_2 microglobulin, urine for Bence–Jones proteins and serum electrophoresis for multiple myeloma, CA-19.9 for pancreatic and biliary tumors, CA-125 for ovarian cancer, prostate-specific antigen (PSA) for prostate cancer, CA-15.3/CA-27.29 for breast cancer, carcinoembryonic antigen for colorectal and breast cancer, and calcitonin for medullary thyroid cancer. Imaging includes plain radiographs, bone scan, computerized tomography scan (CT), magnetic resonance imaging (MRI), and fluoride/fluorodeoxyglucose-positron emission tomography (PET) scan. Imaging may reveal an easier to access biopsy site or direct the tract for a percutaneous biopsy.[9] Possibility of bone sarcomas should be considered in cases with a history of prior radiation exposure such as Paget's disease and fibrous dysplasia. The final management and survival depend on the primary tumor.

Survival Prediction

Irrespective of the primary tumor, presence of skeletal metastases, visceral metastases, and multiplicity is associated with poor prognosis.[10-12] Prognosis in metastatic bone cases depends on various factors. For those arising from breast cancer, the extraosseous disease, disease-free interval, performance status, estrogen receptor status, age, and histologic grade play a role in prognosis. While in skeletally metastatic prostate cancer, the performance status, extraosseous disease, fall in alkaline phosphatase, and PSA levels are well-approved prognostic factors.[13]

In multiple myelomas, β2 microglobulin and C-reactive protein are the main independent prognostic factors with the median survival of 6 months for those with high levels and 54 months for those with low levels.[14]

Using predictive models like Bayesian Belief Network,[15] patient's survival can be predicted which helps us in deciding the final treatment plan. The clinical data are used to calculate survival at 3 and 12 months. For those with survival < 3 months, surgical management is not recommended, those with 3–12 months of survival may require less invasive procedures without long rehabilitation and those with > 12 months of survival, a more durable reconstruction method is recommended.[16]

In a study done by Bauer, it was reported that the overall survival of those who underwent fixation for pathological fracture was <6 months and was similar to those who received radiotherapy (RT) for bone pain.[8,17] The incidence of solitary metastases is lower compared with those with multiple metastases, with solitary metastases having better prognosis than those with multiple metastases.[18,19]

Five-year survival rate of skeletal metastasis is shown in Table 1.[2]

Mechanical strength prediction

Prediction of mechanical strength and the risk of pathological fracture are considered to be an important variable for decision-making when managing bone metastases. Mirel's scoring system is one of the most commonly used systems to predict the risk of pathological fracture [Table 2].[20] The risk of fracture was 33% for a patient with a score of 9, 15% for a patient with a score of 8, an 4% for a patient with a score of 7. Excessive pain is one of the most significant indicators for an impending pathological fracture. At times, plain radiography alone is not diagnostic or a predictor of impending fractures. More than 50% of trabecular bone should be destroyed to be evident on radiograph. In such cases, significant pathological fracture risk should be considered. Cases with lesser trochanter avulsion indicate an impending hip fracture.[21] CT rigidity analysis (CTRA) is a novel method of predicting the pathological fracture probability, wherein the density of the bone and the cross-sectional area at maximal weakness point are recorded to estimate bending, torsion, and axial rigidity. The data are then compared with a gender- and size-matched normal femur CT. Reduction in axial, bending, or torsional rigidities >35% was considered a significant risk for fracture.[22]

CTRA reported better sensitivity, specificity, and PPV and NPV over Mirel's Scoring System.

Table 1: Incidence and median survival of various primary malignancies with skeletal metastasis

	Incidence advanced disease (%)	Median survival (months)	5 years survival (%)
Myeloma	95-100	20	10
Breast	65-75	24	20
Prostate	65-75	40	25
Lung	30-40	6	5
Kidney	20-25	6	10
Thyroid	60	48	40
Melanoma	14-45	6	5

Table 2: Mirel's Scoring System

Variable	1	2	3
Site	Upper limb	Lower limb	Peritrochanter
Pain	Mild	Moderate	Functional
Lesion	Blastic	Mixed	Lytic
Size	<1/3	1/3-2/3	>2/3

Management

Skeletal metastases are seldom an emergency. The goal of treatment would be to get the patient back to their previous activity level. The following are the treatment strategies available.

1. Medical management
2. RT
3. Surgery.

Medical management

The most common debilitating symptom of a malignancy is pain which causes significant impact on the daily activity and social life. Pain can be due to osteoclast activation, substances produced by tumor cells, surrounding inflammatory reaction due to tumor growth and invasion into surrounding tissues and nerve compression. Pain management has various treatment modalities along with histology-specific treatment, namely, nonsteroidal anti-inflammatory drugs, bisphosphonates, opioids, tricyclic antidepressants, RT, and surgical management.[23]

Osteoclast activation has an essential role in the destruction of bone with metastases. Receptor-activated nuclear factor kappa-B ligand (RANKL) attracts tumor cells into the bone to produce more RANKL.[24] This increases the osteoclasts leading to accelerated bone destruction. Bisphosphonates therapy has become commonly used to reduce morbidity among patients with skeletal metastases. However, they benefit the patient by only 30%–40% with complications such as osteonecrosis of the jaw and may require intravenous administration.[25]

Denosumab, a monoclonal antibody against RANKL has shown improved efficacy in blocking osteoclast formation and osteoclast-mediated bone destruction.[26] It is administered subcutaneously and is not excreted through the kidney, an advantage for patients with chronic kidney disease. Denosumab was reported to be superior to zolendronic acid with relation to reduction of the skeletal-related events. Both had similar results regarding the quality of life, pain, and overall survival. However, bisphosphonates have an additional antitumor action which may add to survival, especially in breast cancer.[26]

Radiotherapy

RT is frequently used for palliation of pain in bone metastases with reports of complete pain relief in one-third of the patients. More than 50% of them have pain relief beyond 6 months.[27] Studies have shown that short-course regimen with 8 Gray (Gy) as single fraction dose is as effective as the long-course RT regimens. Jeremic *et al*. have compared short course RT regimens (4 Gy vs. 6 Gy vs. 8 Gy) and concluded that 8 Gy is the "lowest" optimal single fraction.[28]

Hartsell *et al*. compared the 8 Gy in a single fraction with 30 Gy in 10 fractions in 898 patients and reported comparable results with regard to pain and narcotic relief. The risk of pathologic fracture was 5% in 8-Gy group and in 4% in 30-Gy group. However, the 8-Gy group had a retreatment rate higher than the 30-Gy group (18% vs. 9%, $P < 0.001$).[29]

The protective role of RT from pathological fractures has not been well defined. Comparison between the outcomes of the surgical fixation of pathological fractures with or without RT has been done with a conclusion that postoperative RT is the only significant predictor for a successful outcome.[30]

RT starts within 2 weeks postoperative and covers the entire operative field and the whole length of the implant.[31] However, the role of RT is limited in those cases with endoprosthesis replacements with one study reporting poor bone remodeling distal to prosthesis and less new bone formation around the prosthesis.[32]

Surgical management

Depending on the aim of intervention, intralesional curettage, marginal excision, or wide excision can be done. Preoperative embolization can be done while dealing with vascular tumors such as skeletal metastases from renal cell carcinoma or simply to facilitate *en bloc* excision. Solitary lesions should be treated with curative intent with added emphasis on functional recovery and pain control.

The general rule in reconstruction is to protect the whole length of the bone to avoid failure in cases of recurrence. Plating, nailing, or endoprosthesis can be used. Locked compression plates fixed using minimally invasive techniques have maximal benefits in metastatic fixations. Locked plates reduce the risk of pullout or loosening with reduced postoperative morbidity due to minimally invasive approach.[33]

Since the lesion is not expected to heal, bone cement is used for augmentation of the fixation instead of allografts and biological cement types. Bone cement facilitates early weight bearing[34] with improved postoperative pain and function.[35]

For lesions involving the diaphysis, intramedullary nailing can be done. Titanium nails have the advantage of improved mechanical strength with smaller diameter. Repair or reconstruction of the capsule and reattachment of surrounding soft tissue to the implant (rotator cuffs, external rotators) should be done to achieve good functional strength, range of movement, and joint stability. 15% to 20% of those treated with surgery will have disease progression and loss of fixation, thus postoperative radiation is recommended.[30]

Pelvis

Enneking classified the pelvis into three distinct zones.[36] Zone 1 and 3 are nonweight bearing and expendable bones. Lesions involving Zone 2 alone or in combination with adjacent bones,

require curettage with cementing or reconstruction with custom made or modular mega prosthesis, saddle prosthesis, or total hip replacements combined with multiple Steinmann pins and cement (Harrington technique).[37] In lesions requiring resection of Zone 2 and 3, an inverted ice cream cone prosthesis or pedestal cup can be used.[38]

Lower limb

The proximal femur is the most common site for bone metastases involving a significant risk of mechanical failure, hampering the quality of life. For lesions involving head or neck of the femur [Figures 1 and 2] the choice of treatment is typically a bipolar hemiarthroplasty with a long stem. For lesions involving the acetabulum or associated with large mass (e.g., trochanteric and peri trochanteric regions), endoprosthesis gives best results. This facilitates early weight bearing and return to function with a lower failure rate.[38,39]

For femoral and tibial diaphyseal lesions, nailing [Figure 3] can be done along with curettage and cementing. To avoid failure due to recurrence in the neck, reconstruction nails can be used and the entire length of the bone should be spanned.[9] In lesions involving the distal femur [Figure 4] and proximal tibia, composite total knee replacement can be done. For lesions involving the proximal tibia, the management principles are essentially similar to the femur and depend on the size of the lesion varying from curettage to resection and megaprosthesis.[40]

Upper limb

The humerus is the second most common site of long bone metastases after the proximal femur. Mechanical stress on the humerus is far less than on the lower limb, and this is the reason why humeral bone metastases can be managed nonoperatively by external beam irradiation.[30] Proximal humerus hemiarthroplasty can be used in cases with lesions, involving the proximal humeral head or neck provided the greater tuberosity, lesser tuberosity, and axillary nerve are intact. Proximal humerus endoprosthesis [Figure 5] or nail cement spacer with meshplasty can be done in large lesions involving proximal half of the humerus. Subluxation of the humeral head can be avoided by soft-tissue repair.[41] For lesions spanning 2–3 cm distal to greater tuberosity and 5 cm proximal to olecrenon fossa, intramedullary nailing is recommended. Distal humeral metastases can be managed with plating and cement augmentation or total elbow replacement for large lesions involving joint. Nail cement spacer can be used for segmental defects of long bones. More than 90% of patients with humeral metastases have pain relief and functional restoration for activities of daily living irrespective of the management method. Functionally, they have restricted range of movements of the shoulder with normal functioning of the elbow and wrist.[42] Lesions involving the scapula, a total or partial scapulectomy, can be planned based on the extent of involvement. The forearm is a relatively uncommon site for metastasis which may require resection of the involved bone.

Minimal invasive modalities

Radiofrequency ablation, cryoablation, and high-intensity focused ultrasound and microwave therapy are the percutaneous modalities which can be used to relieve the pain and improve bone strength without additional risk of morbidity from open surgery.[43,44] Cementoplasty plays a vital role in lesions involving the pelvis [Figure 6]. They

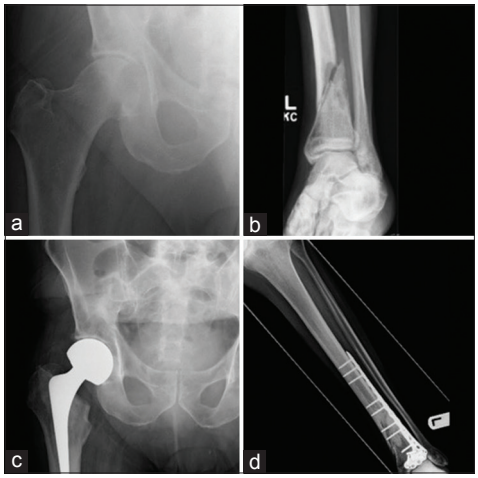

Figure 1: A 70-year-old male with metastatic clear cell renal carcinoma. (a and b) Lytic lesion involving the proximal femur and pathological fracture of the distal tibia. (c) Wide excision followed by hemiarthroplasty done for the proximal femur. (d) Cementing and plating done for distal tibia lesion

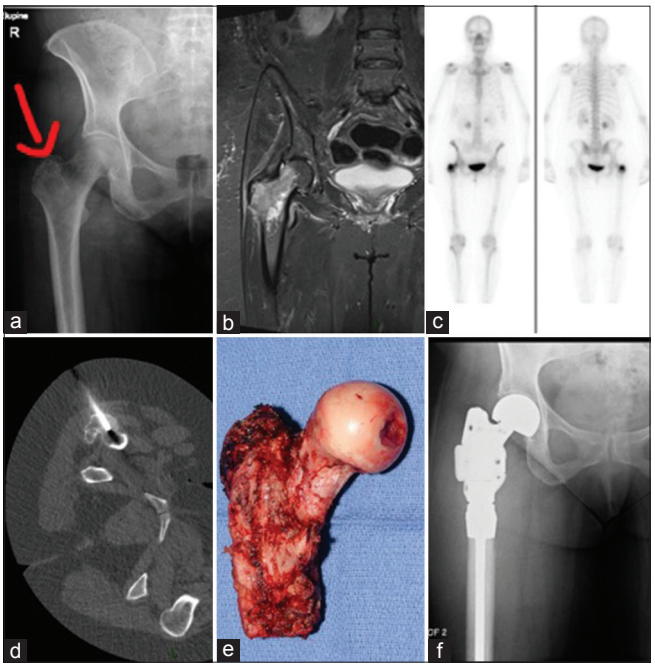

Figure 2: A 60 year-old female metastatic carcinoma of the breast. (a and b) X-ray and magnetic resonance imaging showing metastatic lesion involving proximal femur. (c) Bone scan showing solitary lesion. (d) Computerized tomography-guided biopsy done to confirm metastases. (e) Resected specimen. (f) Postoperative radiography showing reconstruction with megaprosthesis

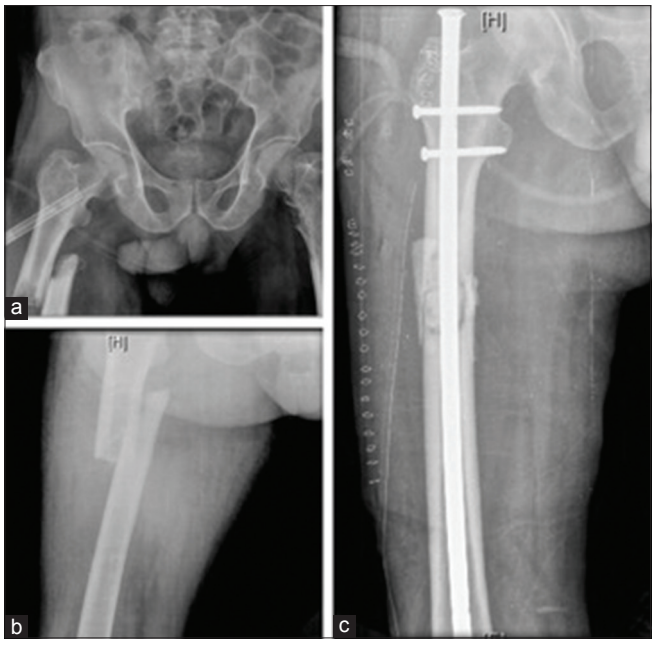

Figure 3: A 50-year-old male with metastatic adenocarcinoma of the lung. (a and b) Radiograph showing pathological fracture involving the proximal femur. (c) Fixation done with IMIL nail and bone cement

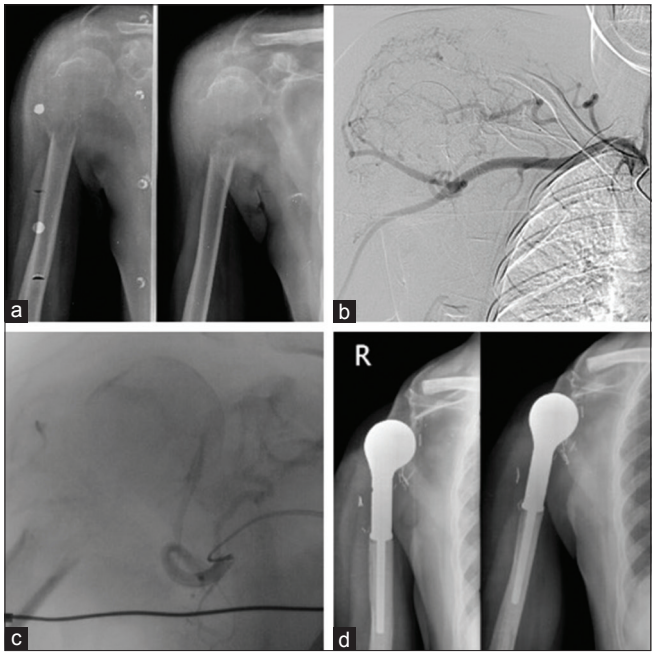

Figure 5: A 55-year-old male, metastatic renal cell carcinoma. (a) Lytic lesion involving the proximal humerus in a case of renal cell carcinoma. (b and c) Pre- and post-angioembolization. (d) Wide excision followed by reconstruction with proximal humerus megaprosthesis

help by preventing a fracture and provide significant pain relief and functional improvement in 80% of cases.[45] In endovascular techniques, angioembolization can provide devascularization and tumor necrosis.[46] Embolization coupled with antimitotic agents (mainly adriamycin and platinum) prolongs the analgesia and can produce partial-to-complete tumoral remission.[47]

Figure 4: A 87–year-old male with metastatic carcinoma of the bladder. (a and b) Lytic lesion involving the distal femur. (c) PET scan showing metastases in the distal femur. (d and e) Wide excision followed by reconstruction with distal femur megaprosthesis

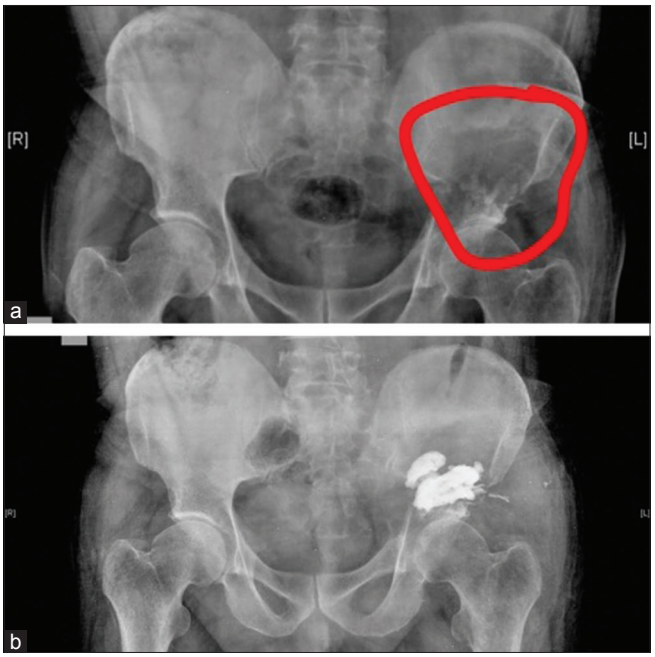

Figure 6: A 55-year-old female, metastatic papillary carcinoma of the thyroid. (a) Lytic lesion seen in the supra-acetabular region. (b) Acetabuloplasty followed by radiotherapy given

Conclusion

Extremity metastases require adequate work-up and a biopsy to confirm the diagnosis. Management involves a multidisciplinary approach and cannot be generalised. It depends on the primary tumour and the expected survival.

The aim of treatment can range from pain relief by medical management or radiotherapy and curative intent in cases with solitary metastases. The final aim should of course be to improve the patient's quality of life.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Macedo F, Ladeira K, Pinho F, Saraiva N, Bonito N, Pinto L, *et al.* Bone metastases: An overview. Oncol Rev 2017;11:321.
2. Harrington KD. Orthopaedic management of extremity and pelvic lesions. Clin Orthop Relat Res 1995;(312):136-47.
3. Cecchini M, Wetterwald A, Pluijm G, Thalmann G. Molecular and biological mechanisms of bone metastasis. EAU Update Ser 2005;3:214-26.
4. Aaron AD. Current concepts review-treatment of metastatic adenocarcinoma of the pelvis and the extremities. J Bone Joint Surg 1997;79:917-32.
5. Berrettoni BA, Carter JR. Mechanisms of cancer metastasis to bone. J Bone Joint Surg Am 1986;68:308-12.
6. Jones DH, Nakashima T, Sanchez OH, Kozieradzki I, Komarova SV, Sarosi I, *et al.* Regulation of cancer cell migration and bone metastasis by RANKL. Nature 2006;440:692-6.
7. Langley RR, Fidler IJ. Tumor cell-organ microenvironment interactions in the pathogenesis of cancer metastasis. Endocr Rev 2007;28:297-321.
8. Bauer HC. Controversies in the surgical management of skeletal metastases. J Bone Joint Surg Br 2005;87:608-17.
9. Ogilvie CM, Fox EJ, Lackman RD. Current surgical management of bone metastases in the extremities and pelvis. Semin Oncol 2008;35:118-28.
10. Dijstra S, Wiggers T, van Geel BN, Boxma H. Impending and actual pathological fractures in patients with bone metastases of the long bones. A retrospective study of 233 surgically treated fractures. Eur J Surg 1994;160:535-42.
11. Sarahrudi K, Greitbauer M, Platzer P, Hausmann JT, Heinz T, Vécsei V. Surgical treatment of metastatic fractures of the femur: A retrospective analysis of 142 patients. J Trauma 2009;66:1158-63.
12. Hansen BH, Keller J, Laitinen M, Berg P, Skjeldal S, Trovik C, *et al.* The scandinavian sarcoma group skeletal metastasis register. Survival after surgery for bone metastases in the pelvis and extremities. Acta Orthop Scand Suppl 2004;75:11-5.
13. Robson M, Dawson N. How is androgen-dependent metastatic prostate cancer best treated? Hematol Oncol Clin North Am 1996;10:727-47.
14. Bataille R, Boccadoro M, Klein B, Durie B, Pileri A. C-reactive protein and beta-2 microglobulin produce a simple and powerful myeloma staging system. Blood 1992;80:733-7.
15. Forsberg JA, Eberhardt J, Boland PJ, Wedin R, Healey JH. Estimating survival in patients with operable skeletal metastases: An application of a Bayesian belief network. PLoS One 2011;6:e19956.
16. Forsberg JA, Sjoberg D, Chen QR, Vickers A, Healey JH. Treating metastatic disease: Which survival model is best suited for the clinic? Clin Orthop Relat Res 2013;471:843-50.
17. Bauer HC, Wedin R. Survival after surgery for spinal and extremity metastases. Prognostication in 241 patients. Acta Orthop Scand 1995;66:143-6.
18. Koizumi M, Yoshimoto M, Kasumi F, Ogata E. Comparison between solitary and multiple skeletal metastatic lesions of breast cancer patients. Ann Oncol 2003;14:1234-40.
19. Kobayashi T, Ichiba T, Sakuyama T, Arakawa Y, Nagasaki E, Aiba K, *et al.* Possible clinical cure of metastatic breast cancer: Lessons from our 30-year experience with oligometastatic breast cancer patients and literature review. Breast Cancer 2012;19:218-37.
20. Mirels H. Metastatic disease in long bones. A proposed scoring system for diagnosing impending pathologic fractures. Clin Orthop Relat Res 1989;(249):256-64.
21. Phillips CD, Pope TL Jr., Jones JE, Keats TE, MacMillan RH 3rd. Nontraumatic avulsion of the lesser trochanter: A pathognomonic sign of metastatic disease? Skeletal Radiol 1988;17:106-10.
22. Damron TA, Nazarian A, Entezari V, Brown C, Grant W, Calderon N, *et al.* CT-based structural rigidity analysis is more accurate than mirels scoring for fracture prediction in metastatic femoral lesions. Clin Orthop Relat Res 2016;474:643-51.
23. Ahmad I, Ahmed MM, Ahsraf MF, Naeem A, Tasleem A, Ahmed M, *et al.* Pain management in metastatic bone disease: A literature review. Cureus 2018;10:e3286.
24. Silva I, Branco JC. Rank/Rankl/opg: Literature review. Acta Reumatol Port 2011;36:209-18.
25. Mauri D, Valachis A, Polyzos IP, Polyzos NP, Kamposioras K, Pesce LL. Osteonecrosis of the jaw and use of bisphosphonates in adjuvant breast cancer treatment: A meta-analysis. Breast Cancer Res Treat 2009;116:433-9.
26. Kohno N. The treatment for cancer with bone metastases -whether to use zoledoronate or denosumab for bone metastases. Clin Calcium 2014;24:1229-36.
27. Chow E, Harris K, Fan G, Tsao M, Sze WM. Palliative radiotherapy trials for bone metastases: A systematic review. J Clin Oncol 2007;25:1423-36.
28. Jeremic B, Shibamoto Y, Acimovic L, Milicic B, Milisavljevic S, Nikolic N, *et al.* A randomized trial of three single-dose radiation therapy regimens in the treatment of metastatic bone pain. Int J Radiat Oncol Biol Phys 1998;42:161-7.
29. Hartsell WF, Scott CB, Bruner DW, Scarantino CW, Ivker RA, Roach M 3rd, *et al.* Randomized trial of short- versus long-course radiotherapy for palliation of painful bone metastases. J Natl Cancer Inst 2005;97:798-804.
30. Townsend PW, Rosenthal HG, Smalley SR, Cozad SC, Hassanein RE. Impact of postoperative radiation therapy and other perioperative factors on outcome after orthopedic stabilization of impending or pathologic fractures due to metastatic disease. J Clin Oncol 1994;12:2345-50.
31. Frassica DA. General principles of external beam radiation therapy for skeletal metastases. Clin Orthop Relat Res 2003;415 Suppl:S158-64.
32. Haentjens P, De Neve W, Opdecam P. Prosthesis for the treatment of metastatic bone disease of the hip: Effects of radiotherapy. Bull Cancer 1995;82:961-70.
33. Gregory JJ, Ockendon M, Cribb GL, Cool PW, Williams DH. The outcome of locking plate fixation for the treatment of periarticular metastases. Acta Orthop Belg 2011;77:362-70.
34. Yazawa Y, Frassica FJ, Chao EY, Pritchard DJ, Sim FH, Shives TC. Metastatic bone disease. A study of the surgical treatment of 166 pathologic humeral and femoral fractures. Clin Orthop Relat Res 1990;(251):213-9.
35. Weiss KR, Bhumbra R, Biau DJ, Griffin AM, Deheshi B, Wunder JS, *et al.* Fixation of pathological humeral fractures by the cemented plate technique. J Bone Joint Surg Br 2011;93:1093-7.
36. Enneking WF, Dunham WK. Resection and reconstruction for primary neoplasms involving the innominate bone. J Bone Joint Surg Am 1978;60:731-46.
37. Harrington KD. The management of acetabular insufficiency secondary to metastatic malignant disease. J Bone Joint Surg Am 1981;63:653-64.
38. Müller DA, Capanna R. The surgical treatment of pelvic bone metastases. Adv Orthop 2015;2015:525363.
39. Ratasvuori M, Wedin R, Keller J, Nottrott M, Zaikova O, Bergh P,

et al. Insight opinion to surgically treated metastatic bone disease: Scandinavian sarcoma group skeletal metastasis registry report of 1195 operated skeletal metastasis. Surg Oncol 2013;22:132-8.
40. Agarwal MG, Nayak P. Management of skeletal metastases: An orthopaedic surgeon's guide. Indian J Orthop 2015;49:83-100.
41. Sim FH, Frassica FJ, Chao EY. Orthopaedic management using new devices and prostheses. Clin Orthop Relat Res 1995;312:160-72.
42. Frassica FJ, Frassica DA. Evaluation and treatment of metastases to the humerus. Clin Orthop Relat Res 2003;(415 Suppl):S212-8.
43. Dupuy DE, Liu D, Hartfeil D, Hanna L, Blume JD, Ahrar K, *et al*. Percutaneous radiofrequency ablation of painful osseous metastases: A multicenter American College of Radiology imaging network trial. Cancer 2010;116:989-97.
44. Hoffmann RT, Jakobs TF, Trumm C, Weber C, Helmberger TK, Reiser MF. Radiofrequency ablation in combination with osteoplasty in the treatment of painful metastatic bone disease. J Vasc Interv Radiol 2008;19:419-25.
45. Moser TP, Onate M, Achour K, Freire V. Cementoplasty of pelvic bone metastases: Systematic assessment of lesion filling and other factors that could affect the clinical outcomes. Skeletal Radiol 2003;(415 Suppl):S212-8.
46. Moser T, Buy X, Goyault G, Tok C, Irani F, Gangi A. Image-guided ablation of bone tumors: Review of current techniques. J Radiol 2008;89:461-71.
47. Layalle I, Flandroy P, Trotteur G, Dondelinger RF. Arterial embolization of bone metastases: Is it worthwhile? J Belge Radiol 1998;81:223-5.