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Osteosynthesis in Metastatic Disease of Long Bones

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Abstract

Prompt evaluation and effective treatment of long bone metastasis are a priority in the management of cancer patients. The main goals are to achieve local tumor control, pain relief, prevention and treatment of fractures, and maintenance of patient independence and quality of life.

Prognosis estimate, cross-sectional extent of bone destruction, and anatomic site of the bone lesion are clinical and radiographic features used by orthopedic surgeons in the decision-making process.

Treatment principles are the same regardless of the skeletal location. A construct should ideally provide enough stability to allow immediate full weight-bearing with enough durability to last the patients expected lifetime. Adequate mechanical stabilization by intramedullary interlocking nailing or plating and screws may address the vast majority of lesions of long bone diaphyseal and meta-diaphyseal portion in the presence of an adequate proximal and distal bone stock for fixation.

However, there are many additional aspects to consider in this setting as the need for biopsy, the evaluation of the extent of bone destruction and stability of the implant, dedicated and specific instruments for tumor surgery, the risk of perioperative bleeding and consideration to preoperative selective arterial embolization, cancer sensitivity and timing of postoperative radiation, possible tumor curettage, and use of local adjuvant and cement to improve tumor control and mechanical strength of the construct.

Keywords

Long bones metastasis · Impending fracture · Pathological fracture · Intramedullary nailing · Plating

12.1 Introduction

Goals of the surgical treatment of long bone metastasis are pain control and relief, function restoration, and prevention of tumor progression and complications for the patient lifespan [1–3]. For most cancer patients, a pathological fracture heralds the end-stage of their disease; on the other hand, the improvement of early diagnosis and the implementation of multidisciplinary therapies for primary tumors have resulted in prolonged life

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expectancy, thus increasing the incidence of bone metastases and skeletal-related events of patients with metastatic disease.

Surgery for bone metastatic cancer is generally indicated for patients with an expected survival at least of 3–6 months, although clinical judgment remains a key factor and may lead to more individualized management outside this timeframe [4].

When life expectancy related to histotype, staging, and general health condition is poor, the treatment aims to be palliative for pain control and prevention or treatment of mechanical complications. Conversely, if the patients' prognosis is favorable, the treatment of the metastases should be more aggressive and long-lasting and therefore can follow the principles of excisional surgery [5]. Regarding to the use of osteosynthesis in the treatment of long bone metastases, it is well known that the curative purpose is effectively achieved when the fixation is combined to wide or marginal resection or curettage and cement reconstruction. Therefore, the surgical strategy will depend on both the prognostic factors and the biological and mechanical features of metastatic disease and is conditioned by five key points [3–5]: (1) prognosis, good or poor; (2) histotype and its chemo-radio sensitivity, sensitive or resistant; (3) number of lesions, solitary or multiple; (4) location in the bone segment, diaphysis or metaepiphysis; and (5) pathological fracture, actual or impending.

12.2 Clinical and Prognostic Evaluation

The most common site for pathological fractures is the femur, followed by the humerus, and the tibia [1, 6–8]. Clinical course of long bone metastatic disease is variable, but pain is the most common symptom and complaint at onset. It is usually described as a night pain, typically deep and gnawing. Sharp pain increasing with weight-bearing is a concern for impending pathological fractures. Painless lesions are usually diagnosed during routinely follow-up at bone scan or CT-PET in patients with a known history of carcinoma. However, in 5–10% of cancer patients, a bone metastasis can be discovered as an incidental finding, thereby representing the first onset of a primary carcinoma. In a consecutive retrospective series of 139 pathological fractures, of which 36 from metastases, Hu et al. [9] focus on the statistically significant presence of prodromes before actual fracture in metastatic patients such as lump, soreness, and swelling. The evaluation of past medical history is mandatory along with a physical examination of the involved limb and palpation of the principal lymph node chains (axillary, supraclavicular, and inguinal).

Life expectancy evaluation is a key factor to conceive the feasibility of prophylactic fixation in case of impending fracture. Several prognostic factors can help the prediction of life expectancy as shown by the study of Forsberg et al. [10]: Eastern Cooperative Oncology Group (ECOG) "performance status" [11], presence of visceral metastasis, surgeon's estimate patient survival, number of bone metastasis, hemoglobin concentration, absolute lymphocyte count, and completed pathological fracture. A multicenter Italian and American scientific collaboration has recently resulted in the validation of Bayesian method to assess that the presence of a pathological fracture affects more significantly the survival of patient with worst prognosis (<12 months) than patients with better life expectancy (>12 months); in other words, patient selection and meticulous considerations of expected survival, benefits, and potential risk from surgical choice are a paramount concern [10, 12].

12.3 Evaluation of Mechanical Stability

Along with the prognosis, the assessment of the risk of fracture is important for the choice of the most appropriate surgical procedure. As well as preventing complete fractures, surgery at the stage of impending fracture is of significantly shorter duration and often technically simpler [2]. Evaluation of the mechanical stability is challenging even for an experienced surgeon. Plain radiographs provide the insight into the

Table 12.1 Studies defining the fracture risk in the setting of impending fracture evaluation

Authors	Recommendations for prophylactic fixation
Fidler [14]	>50% cortical destruction
Harrington [15]	– Lesion >25 mm – >50% cortical destruction – Persistent pain after radiation therapy
Mirels [16]	Variable points: (1), (2), (3) *Site*: Upper limb (1), lower limb (2), peritrochanteric (3) *Pain*: Mild (1), moderate (2), functional (3) *Lesion type*: Blastic (1), mixed (2), lytic (3) *Size as a proportion of shaft diameter*: <1/3 (1) 1/3–2/3 (2) >2/3 (3) >9 points = high risk of fracture

structural integrity of cortex and the presence of an alteration in the intracortical and medullary bone. Computed tomography (CT) scan defines in a detailed way the cortical structure and the extent of cortical compromise. Magnetic resonance imaging (MRI) shows the intramedullary extent of the tumor and any soft tissue extension. MRI is valuable to find spot lesions at the femoral neck or in the trochanter region, not well detected at a standard X-ray study [13]. Metastasis located at the long bones requires plain radiographs, CT, and/or MRI of the entire extent of the bone to exclude the possibility of additional lesions and aimed to the surgical planning. Missed metastasis, proximal or distal to the level of fixation, could determine pathological fractures at weight-bearing at the surgical treated extremity.

Although neither objective criteria nor guidelines exist, several studies have provided clinical and radiographic parameters to provide an algorithm for prophylactic fixation (Table 12.1).

12.4 Preoperative Planning

It is important to confirm the diagnosis of bone metastasis with a biopsy. A lesion in a patient with a known primary tumor should not be assumed to be from the patient's known primary tumor. Most of all, a biopsy is recommended if a bone lesion is solitary and if the primary tumor is unknown. Biopsy may be performed with a fine needle, a CT-guided or open procedure. In case of uncertain diagnosis when a surgical fixation has been planned for an impending or displaced pathological fracture, an open biopsy with frozen section should be performed immediately before the fixation, and the surgeon should not proceed until the pathology report has confirmed the metastatic disease. If the frozen specimen is inconclusive, the operative time should be stopped until the definitive pathology report is returned [17].

Angiography can be used preoperatively to embolize hypervascular lesions such as clear cell kidney carcinoma, thyroid, and liver carcinomas or myeloma reducing intraoperative bleeding at the time of fixation, thereby minimizing the postoperative anemia [18]; embolization can be expected to be effective in approximately 90% of cases [19, 20].

Bone pain could be treated by narcotic analgesics and radiation therapy, usually external beam irradiation. Also bisphosphonates have been shown to impact on pain and to contribute to the reconstitution of the bone stock [3, 21]. As Cheung [17] shortly assessed, the surgical indication and the kind of fixation should suit the following conditions: acceptable perioperative life risk and a shorter recovery time than the expected patient life; the construct must ensure immediate functionality, mechanical resistance to potential metastatic progression in the bone segment, and postoperative radiotherapy.

12.5 Treatment

12.5.1 General Considerations and Principles

The indications for operative treatment of long bone metastasis include impending and pathological fractures and intractable pain [3, 7, 8]. Patient's survival, the location of the lesion, skeletal complications, and response to nonsurgical therapies guide the choice of the surgical procedure (Fig. 12.1).

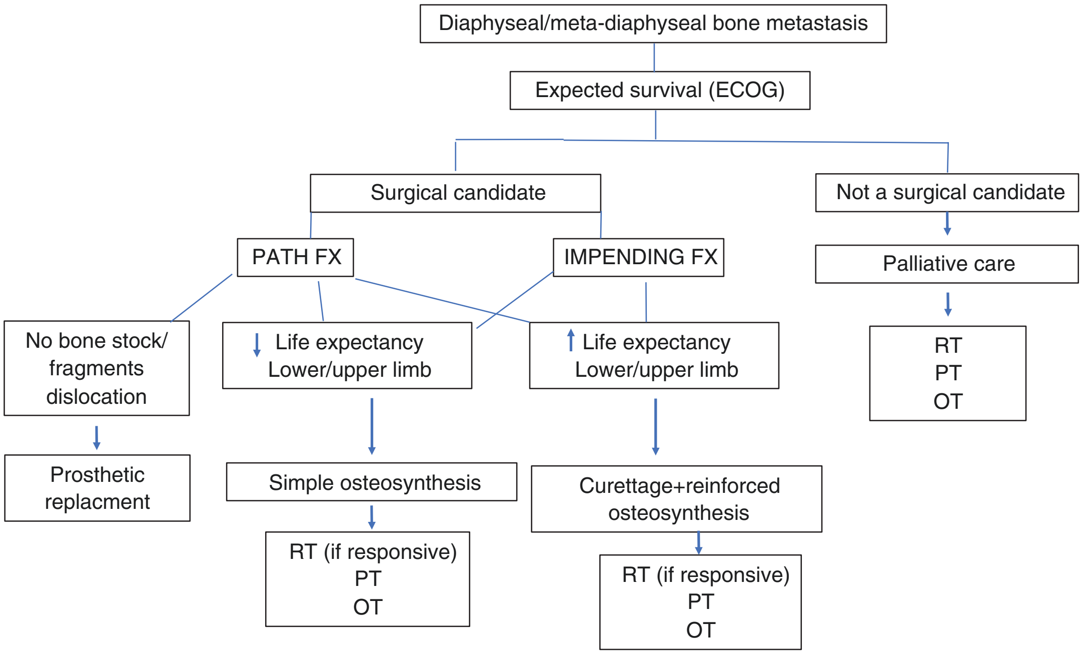

Fig. 12.1 Treatment strategy for long bone metastasis. *RT* radiation therapy, *PT* pain therapy, *OT* osteoprotective therapy

A construct should ideally provide enough stability to allow immediate restoring of the function, with enough durability to overcome the patients expected survival, which may be prolonged for patients with breast, prostate, or renal cancer [3, 6]. The procedures used for osteosynthesis are conceived to ensure early full weight-bearing of the lower extremities and to stabilize the upper extremities to allow common activities.

Plating, as a load-bearing device, is suggested in metaphyseal and epiphyseal lesions in the case of intact articular surface and sufficient adjacent bone stock [22]. Indeed, plate fixation requires adequate cortical bone proximal and distal to the fracture. Fixation with side plates is appropriate for lesions located at the upper extremity, for example, the humeral diaphysis, which is not subjected to considerable weight-bearing, or in places where it is difficult to use an intramedullary device such as the proximal tibial metaphysis. Conversely, reamed intramedullary nails have a neutral axis almost identical to that of the bone in which they are placed [23]. Considering that a normal bone healing cannot be expected, this load-sharing device, with a small moment arm and low transmission of torque, can withstand the mechanical loads and support the entire length of the affected bone [3, 22]. Intramedullary nailing is the most accepted method of fixation in diaphyseal metastasis, because of its ease of insertion, less invasiveness and limited bleeding, load-sharing properties, and low costs [24, 25]. Cemented or not, reamed or not, intramedullary fixation should be long enough to reinforce the entire length of the bone and to prevent the breakdown from potential contiguous lesions. The nail should be of the greater possible diameter, proximally and distally locked with static holes and interlocking screws to control distraction and torsion stresses, and to early gain function [13, 22, 26].

Simple closed osteosynthesis, without open curettage, may be considered for patients in a poor general health condition, and for lesions with favorable predicted response to radiotherapy. Closed nailing is done in patients affected by impending or actual pathological fractures with minimal bone destruction and fragment displacement.

Fractures involving the proximal femur are the most common surgical issues in the management of long bone metastasis. Of all long bone pathologic fractures, 60% involve the femur. Of these, 80% involve the proximal portion: the femoral neck (50%), the subtrochanteric region (30%), and the intertrochanteric region (15%) [27]. Anterograde reconstruction nail is recommended to prophylactically and simultaneously stabilize the neck, intertrochanteric region, and shaft. Reconstruction nailing provides resistance to torsional stresses as well as to angular displacement through the full length of the femur, and fixation with static screws gives the adequate stability to allow for immediate postoperative function [13, 24]. Tanaka et al. [25], among 186 surgically treated femoral metastasis cases, retrospectively reviewed 80 consecutive nailing procedures in 75 patients, including 14 pathological and 66 impending fractures. In this cohort, only three intramedullary nails broke through their proximal parts, where the fracture site was in the subtrochanteric region; the 2- and 3-year postoperative survivals were 14.2% and 8.4%, respectively, whereas the implant survival rate was 94.0% at both 2 and 3 years; however, it dropped to 62.8% at 50 months. They proposed a much broader indication for the use of intramedullary devices including the trochanteric part of the femur as a sufficient fixation system for a few years, demonstrating several advantages and wider indications compared to prosthetic reconstruction implants, and sufficient durability and revision options.

A more aggressive approach, as reinforced osteosynthesis with cement augmentation, is indicated in patients with a good prognosis and in case of scarce response to adjuvant therapy. Open exposure may be required in cases of pathological fractures with considerable bone destruction. Bone cement increases the structural stability, enables the patient to withstand the stress of immediate motion and function, and enhances the local control after debulking of the tumor; the disadvantages include longer surgical times, risk of wound healing compromise, and local bleeding [4, 5]. Pairing intralesional curettage with the use of local adjuvant treatment, such as liquid nitrogen, alcohol and phenol, and argon probes, improves the debulking of the tumor deposit and helps to prevent the local progression of disease. Cementing requires the use of low-viscosity PMMA, minimal pressurization, clean canals, and adequate patient hydration to reduce the risk of fat emboli [17, 18].

Immediate functionality of the construct is important in this setting because the patient's lifespan may be limited.

Therefore, construct that rely on allograft healing, bone healing, and ingrowth into stems and cups are discouraged in favor of cemented constructs. Large destructive lesions, intra- or periarticular, may require prosthetic replacement [28].

Indications for different implants and features to obtain adequate stabilization of long bone metastases are summarized in Table 12.2.

Table 12.2 Options and features of osteosynthesis for long bone metastases

Construct	Indication	Features
Plating	Proximal humerus, distal femur, distal tibia and distal humerus <50% diameter, radio and ulna	Adequate length Periarticular
	Open surgery, curettage or tumor resection, use of cement	
	Preexisting implants or prosthesis	
Nailing	All diaphyseal lesion, femoral neck, and trochanteric impending lesion	Anterograde, long, interlocking, recon, reamed, greater diameter, flexible in radio and ulna
	Patients with poor prognosis	
Cemented osteosynthesis (nail or plate)	Patients with good prognosis	Low-viscosity PMMA, low pressurization, repeated clean canals
	Clear cell kidney carcinoma and thyroid histotype (CHT-RT resistance)	
	Trend in pathological fracture more than impending	

12.6 Impending and Complete Pathologic Fracture

From the Scandinavian Skeletal Metastasis Registry for patients with skeletal metastasis of the extremities surgically treated between 1999 and 2009, the complete fracture was the major reason for surgery in 74.2% of the cases while an impending fracture in 18.3% of cases [8].

The pathologic fracture is one of the adverse prognostic factors in the lifespan of a metastatic patient [29]. General indications for surgery are a life expectancy of 1–3 months for a fracture of a weight-bearing bone and 3 months or more for fracture of a non-weight-bearing segment; adequate bone stock to support the construct; a benefit from surgery in terms of pain, patient mobilization, and general care [1].

Although potentially simpler than stabilization of an actual fracture, prophylactic fixation of an impending fracture requires peculiar considerations and planning.

Plating with cement augmentation is the surgical choice for metaphyseal and epiphyseal lesions, but it requires an intact articular surface and sufficient bone stock to stabilize the interested bone portion. At least one intact cortex is required to achieve rigid fixation and allow full weight-bearing in a short time postoperatively in this setting [30]. Intramedullary nailing is the most common treatment for diaphyseal lesions at risk of fracture of the upper and lower limbs. It is contraindicated when there is a substantial periarticular involvement, when the bone stock is inadequate (a load-bearing device such as endoprosthetic replacement is preferable in these cases), and when the life expectancy is less than 6 weeks (Fig. 12.2).

Usually it is recommended to completely excise the metastatic cancer deposit, followed by using local adjuvants (alcohol, liquid nitrogen, phenol, peroxide) to sterilize the lesion cavity. The defect, after performing the curettage should be filled with cement [31].

It is important to preserve the soft tissue attachments to the bone and articular surfaces to improve its function and to lower the infection risk in immune-depressed patients.

Fractures involving different portions of long bones are treated with different forms of fixation (Table 12.3). In general, intramedullary devices are the choice in pathological fracture allowing to stabilize all the anatomical segments reducing the risk of failure due to progression of the disease and permitting an easier return to normal life [26].

If epiphyseal and diaphyseal lesions benefit from well-established fixation systems (prosthetic replacement for epiphyseal fractures and intramedullary nail for diaphyseal fractures), metaphyseal fractures provide a more significant surgical challenge [32].

There are instances in which nailing is contraindicated, such as sclerotic lesions or when there are metaphyseal fragments that cannot be reduced

Fig. 12.2 Proximal femur metastatic impending fracture lesion in lung tumor. Last pictures show 6 months' follow-up

Table 12.3 Osteosynthesis options by segmental location

Bones	Site	Fracture	Osteosynthesis
Femur	Proximal (trochanteric)	Impending	Long cephalomedullary nail
		Complete	Cemented long cephalomedullary nail
	Diaphysis	Impending	Long cephalomedullary nail (with or without cement)
		Complete	
	Distal	Impending	Distal femoral plate
		Complete	Cemented distal femoral plate
Humerus	Proximal	Impending	Plate or long proximal humeral nail
		Complete	Cemented long proximal humeral nail
	Diaphysis	Impending	Long humeral nail (with or without cement)
		Complete	
	Distal	Impending	Distal humeral plate
		Complete	Cemented distal humeral plate
Tibia	Proximal	Impending	Proximal tibial plate or cemented K-wires
		Complete	Cemented proximal tibial plate
	Diaphysis	Impending	Long cephalomedullary nail (with or without cement)
		Complete	
	Distal	Impending	Cemented distal tibial plate
		Complete	
Radio	Proximal	Impending	Small fragment T plate
		Complete	
	Diaphysis	Impending	Small fragment plate or flexible nail (with or without cement)
		Complete	
	Distal	Impending	Distal radius plate (with or without cement) or wrist fusion to ulna
		Complete	
Ulna	Proximal	Impending	Olecranon plate
		Complete	
	Diaphysis	Impending	Small fragment plate or flexible nail (with or without cement)
		Complete	
	Distal	Impending	Small fragment plate (with or without cement) or resection
		Complete	
Fibula	Proximal	Impending	Not surgical
		Complete	
	Diaphysis	Impending	
		Complete	
	Distal	Impending	Distal fibular plate or retrograde screw
		Complete	Distal fibular plate or ankle fusion
Phalanx	Any	Any	Small fragment plate vs K-wire fixation

without opening the site of fracture that are not permitting a good stabilization of the fracture site. In these setting plating is more indicated (Fig. 12.3). When the bone stock at the fracture site of a metaphyseal unique lesion is inadequate, it is important to consider the prosthetic replacement. This could guarantee a better stability and debulking of local disease. Diaphyseal fractures are best treated with intramedullary nailing. To stabilize the fracture, it is recommended to use a long, interlocking nail and to cement the defect. When the fracture involves both the diaphyseal and metaepiphyseal portion, a cemented prosthetic replacement is the best device to stabilize the fracture sites.

There is not a universal nail or plate in orthopedic oncology. Titanium is traditionally the material of choice for fixation constructs, and it reduces the infective risk in patient candidates to postoperative radiotherapy and chemotherapy. Carbon-fiber-reinforced (CFR) implants have been recently proposed as very valuable

Fig. 12.3 Pathological fracture in patient affected by multiple myeloma. After surgery X-ray. Last picture shows 2 years' follow-up

devices for osteosynthesis in musculoskeletal tumors, due to their peculiar biomechanical strength and for their advantages in combination with adjuvant radiotherapy and fracture monitoring during follow-up [33, 34]. It is not surprising that the first clinical application of a CFR-PEEK nail has been described for the treatment of long bone metastases. Collis et al. [33] reported the first case and technique of CFR nailing for treatment of a humeral metastasis from melanoma; the authors remarked the definition of "the invisible nail," focusing on its radiolucent properties. Zimel et al. [34] qualitatively and semiquantitatively assessed the differences between CFR-PEEK and titanium implant artifact seen on the MRI and CT imaging follow-up for recurrent oncologic disease in a phantom simulation. Moreover, the authors described the clinical application of CFR nails in eight cancer patients, reporting no immediate or short-term postoperative complications nor implant failure; the lower MRI distortion immediately adjacent to the implant allowed a better visualization of the surrounding marrow space, cortex, and bone–muscle interface.

IlluminOss® Photodynamic Bone Stabilization System (IlluminOss® Medical GmbH, Germany) is an innovative percutaneous stabilization device for diaphyseal fragility fractures of not weight-bearing long bones. This mini-invasive procedure incorporates the use of an inflatable polyethylene terephthalate (Dacron®) walled balloon catheter that is inserted into the previously reamed canal and then infused with a liquid monomer, so the balloon expansion fills the intramedullary canal with patient-specific anatomical conformation. The monomer-filled balloon is cured in situ and on demand using a fiber optic light source resulting in a stable and radiotransparent implant [35]. Overall complication rate, surgical time, and costs make IlluminOss® System a reliable system to stabilize pathological fractures and lytic lesions in the upper limb (Fig. 12.4). No intramedullary devices are to date available for the radial and ulnar shaft. Similarly to CFR devices, IlluminOss® System is radiotransparent, and moreover, it allows placement of locking screws anywhere along the length of the implant. Even if it is a good solution for diaphyseal bone, metaepiphyseal lesions are at high fracture risk with this technique and often require ancillary stabilization with plate and screws.

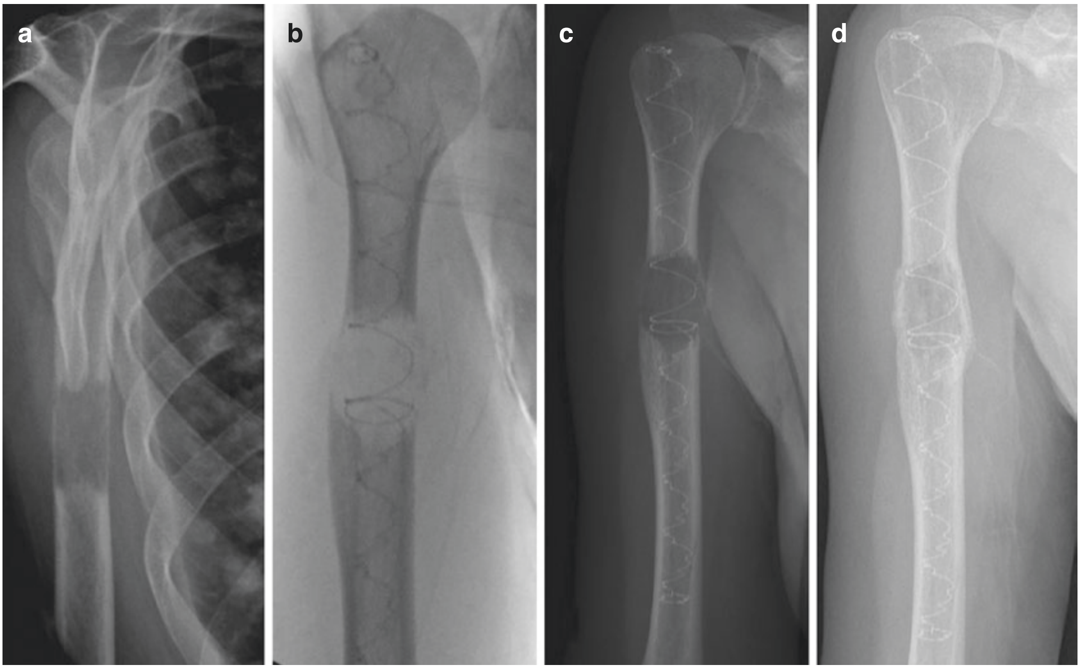

Fig. 12.4 Clinical case of a patient with a pathologic fracture of the humerus due to a metastasis from a solid tumor (**a**), fluoroscopic intraoperative picture of the Illuminoss® implant (**b**); 1-week postoperative X-ray (**c**); 90-day postoperative X-ray (**d**), after the performance of radiotherapy, showing partial healing of the fracture (Courtesy of IlluminOss Medical, Inc. East Providence, Rhode Island, USA)

12.7 Postoperative Treatment and Care

Following intramedullary fixation, early weight-bearing is encouraged as tolerated by the patient. The use of antibiotics therapies and deep vein thrombosis prophylaxis is dictated by postoperative course and by the level of mobility and comorbidities. Passive and active range of motion exercises of the adjacent joints should be performed as soon as possible as determined on the basis of the wound healing and the patient's ability. Early discharge from the hospital will generally enhance the patient's motivation and minimize the interruption of an ongoing oncological protocol.

Postoperative clinical and radiographic follow-up is then undertaken. Radiation therapy usually follows at 3–4 weeks from surgery, provided wound healing is complete. Townsend et al. [36] found that 15% of patients treated with surgery alone required a second surgery because of increasing pain or loss of fixation due to tumor progression, but only 3% of patients who received postoperative radiation therapy needed additional surgical procedures. The radiation field should cover the site of disease, the operative field, and also the entire fixation device.

The most frequent complications are wound dehiscence, deep infection, and fracture due to tumor progression otherwise post-actinic.

In case of plating and screws, the patient can be mobilized except for full weight-bearing that is prohibited indicatively for 30 days or more, depending on the progression of fracture healing.

12.8 Complications and Risk of Failure

Complications are reported in 11% (61/554) of plate and nailing procedures in the Scandinavian Sarcoma Group cohort: systemic complications, wound infections, deep infections, nail brakes, fractures next to implant, and nerve injuries, non-unions, and technical errors/immediate fails [8].

The long survival after surgery is the most important risk factor for failure of osteosynthesis secondary to disease progression, implant failure, or loss of fixation [22]. Failed surgery depends on implant breakage, tumor progression, stress fracture, and poor surgery.

By comparing different surgical procedures from a series of 57 patients with bone metastases secondary to breast cancer, Wegener et al. [7] assess that the procedure (nail, standard, or tumor endoprosthesis) had no impact on survival and the complication rate was 11%.

From the Scandinavian series, in plating and nailing procedure group, there were 6.1% reoperations because of either local tumor progression or failure of fixation [8].

Conclusions

Patients with metastatic disease at long bones pose a management challenge. A multimodality approach is mandatory in caring for these patients: oncologists, radiation therapists, radiologists, and pathologists' cooperation is needed to estimate the therapeutic program and their life expectancy. Because surgery has most frequently a palliative role for patients with limited life expectancy, unnecessary reoperations due to complications resulting from hardware failure are unwarranted. This should be kept in mind in surgical osteosynthesis, like intramedullary nailing and plating: a patient's survival should not exceed the durability of the construct.

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