Pathological hip fracture in the elderly: review and proposal of an algorithm

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Summary

Objective. Current Italian guidelines recommend surgery within 24 hours from admission for hip fractures of the elderly. In such patients, a pathologic fracture of the proximal femur is not an uncommon event and may be consequent to bone metastases or primary tumours. This paper aims to investigate the current literature and to propose an algorithm to manage patients more securely.

Methods. A review of the literature on diagnostic and therapeutic tools in pathologic fractures of the hip was conducted. Evidence from the literature was merged to define a flow-chart for a safe clinical-diagnostic pathway.

Results. Proper imaging is essential in the management of bone metastases, along with appropriate laboratory tests and within a multi-disciplinary setting. While bone metastases are the expression of a systemic disease, bone sarcomas have an extremely aggressive local course and an incorrect surgical procedure could heavily affect prognosis of the patient. The surgeon should not rush to treat a suspicion of a pathological fracture without having performed all necessary investigations.

Conclusions. Orthopaedists must doubt a pathologic fracture. An algorithm could help standardise procedures and provide a tool for safe management of these patients.

Key words: pathologic fracture, hip fractures, metastasis, neoplasm, orthopaedic surgery

Introduction

Proximal femoral fractures in elderly patients are a widely diffused entity in orthopaedic scenery. In fact, more than 250,000 hip fractures are estimated annually in the United States in people over 65 years old. The incidence is expected to increase each year due to increasing life expectancy. This condition is associated with increased morbidity and mortality, with estimated 1-year mortality rates between 14 and 36% 1-4. This is due to patient-related factors such as pre-existing chronic comorbidities and fracture-related factors like bleeding, anaemia and exposure to proinflammatory conditions that can worsen prognosis 5,6. Since 2008, the Italian Ministry of Health has introduced the rate of proximal femoral fracture treated within 48 hours as one of the indexes of hospital efficiency 7. Early treatment aims to minimise the length of time a patient is confined to bed rest, thereby reducing the risk for associated complications, such as pressure sores, deep vein thrombosis (DVT) and urinary tract infections (UTI). A recent meta-analysis conducted by Moja that included over 190,000 patients reported that early surgery for hip fracture provides a survival benefit in comparison with later intervention. Moreover, prompt intervention is associated with a significant reduction in pressure sores 8,9.
Even if it is widely accepted that hip fractures in this group of patients should be treated surgically as soon as possible, there is no consensus about the effective timing of surgery. In clinical practice, it is not unusual to delay surgical procedures in elderly, as many variables can interfere with early treatment: daily therapy with oral anti-coagulant or anti-platelet drugs, on course infections, comorbidities like cardiac or renal disease which often require additional preoperative treatments and tests that take time. This unavoidable delay keeps the patient in bed, increasing the risk of pulmonary, skin and urinary tract infections. The timing issue for hip fractures in the elderly can be even more challenging for the orthopaedic surgeon if a pathological fracture is suspected. Managing pathological bone fractures in patients with either primary or metastatic bone tumours represents a difficult task even for the most experienced surgeons. Their management may alter prognosis and affect quality of life and survival of these patients. This kind of pathology can be secondary to either benign lesions (such as Paget disease or giant cell tumour) or malignancies. The latter can be either primary (i.e. osteosarcoma or chondrosarcoma) or secondary in case of metastatic disease, multiple myeloma, or bone lymphoma. The most frequent conditions in the elderly are metastatic diseases and multiple myeloma; local recurrences of a primary bone tumour are not uncommon and secondary sarcomas including pagetic and post-irradiation sarcomas (occurring as late as 20 years after the initial diagnosis) must be considered as a possible diagnosis. Furthermore, entities like aggressive benign bone tumours or tumour-like conditions such as fibrous dysplasia, simple bone cyst, aneurysmal bone cyst and giant cell tumour increase the risk for pathological fracture in the proximal femur, with an incidence at the time of diagnosis of about 12%. In addition to fracture-related factors that can worsen prognosis, other factors must be considered such as adjacent joint, soft tissue, nerves and vessel contamination by haematoma formation, or distant haematogenous dissemination due to microcirculation damage. In selected cases, an incorrect surgical approach can help to disseminate the malignancy with progression of disease. The orthopaedic traumatologist in the Emergency Department is often the first physician to deal with a patient with a pathologic fracture. A systematic approach to these patients is critical and must be aimed at avoiding complications that could compromise limb salvage or, at worst, affect overall survival/oncologic disease related prognosis. This study aims to investigate the literature about pathological fractures of proximal femur in elderly people and to propose an algorithm improved with reasonable timing to manage such patients in a safer way, and deciding on the effective need for surgery within 48 hours.

Materials and methods

An electronic literature search available up to December 2019 of PubMed, Embase and the Cochrane Review system was performed. The search terms used were “(pathological fracture OR pathological fractures OR pathologic fracture OR pathologic fractures) AND (hip OR femur OR femoral OR long bones)”. Identification and selection of the studies was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis criteria (www.prisma-statement.org). The PI(C)O model was as follows: the population consisted of elderly patients with a pathological fracture of the proximal femur (P) who underwent orthopaedic surgery (I). Outcomes of interest were perioperative outcomes and durability at follow-up (O). Filters were added to restrict the search to studies on humans, which were published between January 2003 and December 2019 and whose full text was composed in one of the following languages: English, Italian, French, Spanish and Portuguese. Title and abstracts were first reviewed to ascertain whether they would potentially meet inclusion criteria. For those passing the first screening, a full-text analysis was performed to confirm inclusion. Studies without primary data (letters to the editor or authors, case reports, opinion articles, technique descriptions, and commentaries) as well as conference abstracts were not considered. References of collected studies were manually reviewed to find additional studies of interest. A second electronic literature search was conducted to clarify the validation of 48 hours as a cut-off time for treatment.

Furthermore, the authors propose to design an algorithm for diagnostic and management of elderly patients with a suspicion of pathologic hip fracture, using evidence from the literature, in order to treat these patients even outside a reference centre for musculoskeletal tumour surgery. This research article was approved by the United Ethical Committee of “Città della Scienza e della Salute”, Turin, Italy and was in accordance with the Declaration of Helsinki.

Results

1912 articles were identified from the search engines. These articles were critically reviewed for evidence according to the PRISMA protocols (Fig. 1). Studies focused solely on impending fractures were ignored and articles on bisphosphonate fractures were excluded: the main entities considered in this study are listed in Table I. Six additional items were identified through other sources, so that 14 articles were finally considered pertinent for the aim of the study. Very few studies focused on the preoperative management of these patients, while almost none concentrated on the timing for surgery. Unfortunately, no guidelines were pertinent as well as a consistent portion of the literature. Given the mostly non-comparative design of the studies identified, the evidence was performed in a descriptive and narrative manner and summarised in Table II. Moreover, several studies concerning traumatic hip fractures explained the importance of performing the treatment as soon as possible to avoid complications that could worsen the outcome, but hardly any studies clarified the exact timing.
Discussion

Even though the concern about pathologic fracture has progressively increased over the last decades, the literature is still quite poor and rarely provides management algorithms validated by large international studies. Most of the literature is focused on the specific options for surgical treatment, while there is a lack in establishing applicable guidelines or algorithms that can help the surgeon in the preoperative general investigation of the patient. In 2004, Jacofsky and Haidukewych suggested a diagnostic and treatment algorithm of a patient with a pathologic fracture of the hip and no history of cancer. The protocol concentrates on the preoperative steps that the patient should undergo, yet lacks a reasonable timing for each of the steps. The authors of this study critically merged evidence from the

Table I. Main entities considered in the study.

<table>
<thead>
<tr>
<th>Benign and tumour-like lesions</th>
<th>Benign aggressive lesions</th>
<th>Malignant lesions</th>
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<tbody>
<tr>
<td>Non-ossifying fibroma</td>
<td>Desmoplastic fibroma</td>
<td>Metastases</td>
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<tr>
<td>Enchondroma</td>
<td>Fibrous dysplasia</td>
<td>Osteosarcoma</td>
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<tr>
<td>Unicameral bone cyst</td>
<td>Osteoblastoma</td>
<td>Chondrosarcoma</td>
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<tr>
<td>Aneurysmal bone cyst</td>
<td>Chondromixofibroma</td>
<td>Ewing's sarcoma</td>
</tr>
<tr>
<td>Paget disease</td>
<td>Chondroblastoma</td>
<td>Malignant fibrous histiocytoma</td>
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<tr>
<td></td>
<td>Giant cell tumor</td>
<td>Multiple myeloma</td>
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<td></td>
<td></td>
<td>Bone lymphoma</td>
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</table>
lit review and proposal of an algorithm

At admission, clinical history and anamnesis should be examined accurately to detect the pathologic nature of the fracture. History of non-traumatic injury and previous weight-loss should be judged as suspicious, if the patient presents a negative oncological anamnesis. Radiologic imaging is the first and crucial step for diagnosis: these patients must undergo mandatory X-ray evaluation with both anteroposterior and lateral radiographs of the affected entire femur \cite{32,39,41} and the pelvis at admission, along with the routine preoperative tests. The evaluation of the entire affected bone has remarkable importance to detect multiple lesions or possible skip lesions within the same bone. Management is difficult and immobilisation hard to achieve: if necessary, skin or trans-tuberosity skeletal traction are preferred to avoid compartmental contamination \cite{42}. If a myeloma is suspected, serum protein electrophoresis (SPEP) should be always requested and if abnormal peaks are detected, Bence-Jones proteinuria (BJP) should be investigated. A systematic skeletal radiographs or whole-body low-dose computed tomography (WBLDCT) \cite{32,39,43} need to be performed to stage the disease and investigate its extent. Even if its role is debated \cite{44}, bone scintigraphy may be helpful to screen for additional skeletal lesions if the patient has a positive oncological medical history \cite{32,39}. An oncological/haematological examination should be also performed. Such general evaluations should be accurately run in any trauma centre within two days from admission; patients with solitary lesions ideally referred to orthopaedic oncologists and multiple lesions should be treated within four days.

Apart from those affected by multiple myeloma, all patients should undergo computed tomography (CT) of the chest and abdomen to investigate a possible primary malignancy and for staging purposes \cite{32,34,35,39,40,42}. A CT scan of the brain could be performed if the primary tumour is at high risk for brain metastases (e.g. lung cancer). Imaging workup must be completed with CT and/or MRI scan of the affected limb to evaluate the local extension of the lesion and conditions of the cortical bone \cite{35,42}. Furthermore, chemical blood analysis along with oncological markers (CEA, Ca 19.9, Ca 125, Ca 15.3, AFP, PSA) should be run. SPEP and BJP should be requested in a selected

Figure 2. Implemented Jacofsky and Haidukewych’s diagnostic and treatment algorithm.
A group of patients. Even if indications for surgery in this patient population are well described in the literature\(^{45-47}\), an oncologist could help the surgeon with no expertise in musculoskeletal surgery and metastatic disease – or in case of doubt – to address the patient to palliative care, medical treatments, or surgery. Alternatively, the case should be discussed in the local multidisciplinary team (MDT) for bone metastases.\(^{29-32,34,35,39-42}\) Whenever surgery is advocated within two days from admission,\(^{7,8}\) the authors consider the same timing as reasonable for all the above-mentioned workups to avoid incorrect surgeries and guarantee the most adequate treatment for each patient. It must be considered that some primary bone tumours, such as chondrosarcoma, frequently affect the proximal femur and it is not uncommon for patients to undergo an intramedullary nailing stabilisation or a hip replacement, with the pathologist eventually reporting a primary bone sarcoma.\(^{41}\) Even if it is widely accepted that early surgery increases the probability of walking again after femur fracture, the 48 hour deadline for surgery seems arbitrary timing\(^{18,19}\) and not completely suitable as a performance indicator for good practice: a recent study\(^{17}\) including two major Italian hospitals reported 5 to 6 days between surgery and returning to ambulation for elderly patients treated for a hip fracture even if surgery was performed within 2 days from admission.

When choosing the best treatment for each patient, several variables should be considered. Towards this end, Willeumier et al.\(^{46}\) defined a flowchart (OPTIMAL) for stratification of patients with long bone metastases with different levels of prognosis depending on the clinical profile, Karnofsky score and presence of visceral/brain metastases. Piccioli et al.\(^{47}\) recently validated another tool (PATHFx) for estimation of survival in patients with metastatic bone disease in the Italian population. Furthermore, if the patient is eligible for surgery, a recent questionnaire survey study to institutions participating in the Bone and Soft Tissue Tumor Study Group of the Japan Clinical Oncology Group\(^{36}\) listed a number of factors influencing the type of surgery and pathologic fractures of the proximal femur reported in Table II.

If the surgery is feasible in a peripheral hospital or a standard traumatological unit, such as in case of multiple lesions or single lesion from a poor prognosis solid neoplasm,\(^{32}\) it should be reasonably performed within 4 working days from admission.

### Table II. Resume of the literature considered pertinent with the study.

<table>
<thead>
<tr>
<th>References</th>
<th>Study design</th>
<th>Main concerns</th>
<th>Main findings</th>
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<tbody>
<tr>
<td>Araki et al., J Orthop Sci, 2017</td>
<td>Questionnaire survey to Japanese BSTTSG</td>
<td>Factors influencing the type of surgery in PPFF</td>
<td>Factors listed in descending order: life expectancy, performance status before fracture, degree of bone loss, walking ability before fracture, general complications, number of bone metastases in other sites, and visceral metastasis status</td>
</tr>
<tr>
<td>Chandrasekar et al., ISRN Oncology, 2012</td>
<td>Retrospective study</td>
<td>PPFF in osteosarcoma</td>
<td>Poor prognosis and scarse possibility of limb salvage surgery Avoiding preoperative CHT in a lytic lesion at high risk for fracture should be considered to avoid a PF</td>
</tr>
<tr>
<td>Ebeid et al., Cancer Control, 2005</td>
<td>Retrospective case series</td>
<td>Middle-term complications in PF from primary bone tumours</td>
<td>A pathologic fracture of primary bone tumor is not a contraindication for limb salvage The oncologic outcome appears acceptable (study from 2005)</td>
</tr>
<tr>
<td>Errani et al., Eur J Orthop Surg Traumatol, 2017</td>
<td>Systematic review and proposal of algorithm</td>
<td>Treatment in LBPF</td>
<td>IMN in generally preferred HHA reconstruction in multiple lesions or metaphyseal defects Isolated bone metastases require en bloc resection</td>
</tr>
<tr>
<td>Faisham et al., Med J Malaysia, 2003</td>
<td>Retrospective study</td>
<td>Middle-term complications in PPFF</td>
<td>Good quality of life for treated patients, even if no improve in survival (study from 2003)</td>
</tr>
<tr>
<td>Guzik, BMC Surgery, 2018</td>
<td>Retrospective study</td>
<td>Oncological and functional outcome after PPFF</td>
<td>Patients need to be studied preoperatively in a multidisciplinary approach Good outcomes in resection of tumor and implant modular prostheses</td>
</tr>
</tbody>
</table>
after all due workups and if comorbidities and daily therapies allow. For all other conditions, such as a solitary metastasis from a primary tumour with good prognosis (e.g. thyroid or renal cancer), single myeloma lesion, primary tumour uniden-

ified, or solitary lesion or suspicion of sarcoma, the patient should be referred to the closest centre for orthopaedic oncology within 4 working days from admission. The outcome and overall survival of patients with a solitary bone metastasis

<table>
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<tbody>
<tr>
<td>Jacofsky et al., J Orthop Trauma 2004</td>
<td>Review of literature and proposal of algorithm</td>
<td>Management of patients with a PPFF</td>
<td>Careful and multidisciplinary approach may give patients increased chances for a better prognosis. Delayed surgeries are acceptable if the case needs to be studied. Algorithms could help surgeons to manage patients in a safer way.</td>
</tr>
<tr>
<td>Khattak et al., Ann Med Surg (Lond), 2018</td>
<td>Review of literature</td>
<td>Management of patients with metastatic involvement of the hip</td>
<td>Careful preoperative study of the patient. Surgery must be planned in coordination with oncologists and physicians for comprehensive perioperative management.</td>
</tr>
<tr>
<td>Ruggieri et al., Injury, Int J Care Injured, 2010</td>
<td>Review of literature and proposal of algorithm</td>
<td>Management algorithm for LBPF</td>
<td>Treatment decision requires complete staging and oncological principles. Tumour response to CHT, RT, fracture union, and wide resection are significant predictive factors for overall survival and local disease control.</td>
</tr>
<tr>
<td>Szendrői et al., EFORT Open Rev, 2017</td>
<td>Review of literature and proposal of algorithm</td>
<td>Management of patients with bone metastatic disease</td>
<td>Few algorithms are proposed in literature and none of them has been validated. Type of surgical intervention could be crucial on patients’ prognosis.</td>
</tr>
<tr>
<td>Varady et al., J Surg Oncol, 2019</td>
<td>Multicentre retrospective study</td>
<td>Comparison between HHA-THA and IMN in PPFF</td>
<td>Trend in favour of IMN in the US. Longer preoperative time and hospitalization than for traumatic fractures. Need for more communication between orthopaedic oncologists and the rest of the orthopaedic community.</td>
</tr>
<tr>
<td>Varady et al., Clin Orthop Relat Res, 2019</td>
<td>Multicentre retrospective study</td>
<td>Short-term complications in delayed surgery in PPFF</td>
<td>No increase in short-term complication if surgery after more than 48 hours. The association between delayed surgery and complications seen for patients with standard hip fractures may not exist in PPFF.</td>
</tr>
<tr>
<td>Willeumier et al., EFORT Open Rev, 2016</td>
<td>Review of literature</td>
<td>Management and treatment of LBPF</td>
<td>Treatment highly depends on the fracture risk in relation to expected survival. A careful and multidisciplinary approach is advisable.</td>
</tr>
<tr>
<td>Zacherl et al., International Orthopaedics (SICOT), 2011</td>
<td>Retrospective, comparative, double-centre study</td>
<td>Type of surgery in PPFF</td>
<td>Study excluded head and neck fractures. Resection of bone metastases has no impact on overall survival. Long-term survivals are at risk of implant-related complications.</td>
</tr>
</tbody>
</table>

Note: BSTTSG: Bone and Soft Tissue Tumor Study Group; PPFF: pathologic proximal femur fracture; CHT: chemotherapy; PF: pathologic fracture; LBPF: long bone pathologic fracture; RT: radiant therapy; HHA: hip hemiarthroplasty; THA: total hip arthroplasty; IMN: intramedullary nailing.
treated with wide resection are claimed to be better in several studies, especially for primary tumours with good prognosis 48–51. Wide resection of the metastatic bone and megaprosthetic replacement of the joint is frequently performed by orthopaedic oncologist surgeons and should be performed in referral centres. The surgical treatment in orthopaedic oncology is a very delicate issue and care must be taken when approaching these patients. The definition of a decisional algorithm could be a useful tool to avoid the three most common mistakes in this surgery: incorrect operations (also known as “whoops surgery” 52), over- and undertreatment 53. Indeed, a preoperative biopsy is mandatory in patients with unknown malignancies and a solitary bone lesion as well as in patients with suspicion of a primary bone tumour. It is advisable to perform the biopsy in a specialized centre to identify the most correct type of biopsy (needle aspiration, core needle biopsy, or incisional biopsy) and avoid technical mistakes such as incorrect approach and compartmental contamination 54–56. Surgical procedures should be carefully selected for each patient avoiding overtreatment and undertreatment. On occasion, aggressive surgical treatments can worsen the patient’s prognosis: the goal is to maximise function and quality of life for the longest amount of time. Patients with short life expectancy may require less invasive surgery, including intramedullary nailing or other fixation techniques (plating and reinforcement with bone cement, mini-invasive photodynamic stabilisation). In contrast, patients with longer life expectancy are normally thought to require more durable reconstructive options that increase both perioperative risk and duration of rehabilitation 57–59. Nevertheless, in patients with long life expectancy, durable reconstructions are the best option to assure a long-lasting and good quality of life.

Conclusions

The surgeon must be aware of the indications for biopsy and the criteria for resection versus internal fixation, as well as the options for reconstruction. A diagnostic algorithm with a systemic approach along with workups and implemented with timing can help the surgeon to best deal with a patient affected by a pathologic fracture. Good clinical management of bone tumour or skeletal metastases improves pain management, can reduce disease progression and avoid errors that could harm or worsen prognosis. Surgery must be tailored to the patient and several options for reconstruction must be considered.

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