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Functional outcomes after megaprosthesis for neglected proximal femur pathological fractures: a retrospective case series

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Abstract

Purpose All pathological fractures secondary to cancer represents a clinical challenge. The management of neglected pathological fractures, which are those left untreated for extended periods, remains especially poorly defined. The aim of this study was to evaluate functional outcomes in patients with neglected proximal femur pathological fractures (NPFPF) surgically managed with a modular megaprosthesis.

Methods This was a retrospective analysis of 12 patients with NPFPF presenting at least twelve weeks of progression since initial diagnosis. Clinical, pathological, and demographic data, together with functional and survival outcomes, were assessed. In all cases, a modular megaprosthesis was used for reconstruction after *en bloc* resection.

Results Eight patients (66.7%) were female and four (33.3%) were male, with a median (IQR) age of 57(51.75;71.75) years. Fractures were caused by breast metastasis (n = 4/33.3%), lung metastasis (n = 3/25.0%), chondrosarcoma (n = 3/25.0%), angiosarcoma metastasis (n = 1/8.3%), and malignant giant cell tumor of bone (n = 1/8.3%). Prior to surgery, nine patients (75.0%) were bedridden and three (25.0%) were in a wheelchair, while after surgery four patients (33.3%) were in a wheelchair and eight (66.7%) were able to walk with crutches. The median (IQR) pre-operative ECOG was 4(4;4), and the median (IQR) post-operative ECOG was 2(2;2.75), with a pre-operative median (IQR) VAS of 9(9;9) and a median (IQR) post-operative VAS of 3(2.25;3).

Conclusion Our study supports surgical reconstruction with modular megaprosthesis to improve function and pain in patients with NPFPF. To our knowledge, this is the first study to report patient´s clinical outcomes in this clinical scenario, offering unique insights into appropriate management strategies in the absence of standardized protocols.

Level of Evidence: IV

Introduction

Pathological fractures represent significant events for patients with cancer, as they increase morbidity, reduce quality of life, and are associated with poor clinical outcomes [1–3]. Primary and metastatic lesions to the proximal femur are not uncommon, often requiring surgical treatment to promote bone tumor clearance and to manage impending or actual proximal femur pathological fractures [4, 5]. Of the different available surgical methods of treatment, the use of proximal femur modular megaprostheses is particularly promising [4]: they provide excellent pain relief and satisfactory functional improvement, together with a relatively low complication rate, after pathological fractures in the acute setting [6]. For most patients, proximal femur megaprostheses also provide a durable reconstruction and low rates of revision surgery [7]. Therefore, this surgical technique is considered one of the most valuable strategies for managing proximal femur pathological fractures [8, 9].

Despite the need to optimally manage all pathological fractures caused by cancer, the best approach for neglected and chronic pathological fractures remains uncertain [10–13]. In resource-rich Western countries delivering high-quality medical care, neglected pathological fractures are uncommon, as patients can generally access timely and appropriate preventative care [12]. Conversely, in low- and middle-income countries (LMICs) lacking adequate treatment resources, neglected and chronic pathological fractures are more prevalent [14]. Understanding the unique characteristics and context of neglected pathological fractures is crucial, as they pose distinct challenges to acute pathological fractures. Their appropriate management requires a comprehensive and multidisciplinary approach to address the underlying cancer and plan comprehensive surgical management on a background of an uncertain evidence base.

Drawing from our experience managing these unusual cases, here we analyzed functional outcomes of a series of patients presenting with neglected proximal femur pathological fractures (NPFPF) managed with modular megaprosthesis.

Materials and methods

Study design. This was a retrospective analysis of data retrieved from our prospectively maintained institutional database. Inclusion criteria were adult patients (≥ 18 years) with NPFPF caused by cancer who underwent *en bloc* proximal femur resection and reconstruction with a modular megaprosthesis.

Neglected proximal femur pathological fractures definition. NPFPF was defined as any proximal femur pathological fracture secondary to the presence of primary or metastatic cancer that had not received any surgical treatment for over twelve weeks since fracture occurrence or identification. Proximal femur pathological fracture was first identified based on simple X-rays films made in patients' first attending hospitals.

Patients' eligibility for reconstruction with modular proximal femur megaprosthesis. NPFPF presenting extensive bone destruction, and/or soft tissue extension rendering internal fixation unsuitable. All included cases were transferred to our center from other Portuguese hospitals or Portugal's former African colonies such as Mozambique, Cabo Verde, or Guiné-Bissau.

Data collection. Demographic and clinical information, functional status before and after surgery, pain before and after surgery, and oncologic outcomes were obtained from 12 consecutive patients with NPFPF who underwent surgery between January 2018 and December 2022. To better understand the clinical context of these patients, we also collected data on the underlying cancer including histopathological diagnosis, stage at presentation, quality of surgical resections, current oncologic status, and overall survival. Time since fracture occurrence and treatment, tumor dimensions, and tumor volume were also collected.

Multidisciplinary team discussion. All patients were discussed at our multidisciplinary team meeting (MDT), where patients had their oncological diagnosis confirmed and prognosis discussed. Patients

presenting with NPFPF and significant functional impairment, pain, and a survival prognosis of at least three months or more, were considered surgical candidates. Relative contraindications to surgery included other metastasis in the affected limb and if patients were deemed medically unfit for surgery.

All cases were treated by the same two Orthopedic Oncology consultants (JSB and JP). All patients provided written informed consent for study participation. The study was conducted in accordance with the Declaration of Helsinki and received approval from the local Research Ethics Committee (Comissão de Ética do Centro Académico de Medicina de Lisboa; ref. 325/25).

Functional outcomes and pain assessments. Functional outcomes were assessed using the Eastern Cooperative Oncology Group (ECOG) performance status (PS) scale and our own subjective classification system, where patients were characterized as bedridden, able to sit, using a wheelchair, walking with crutches, or walking without aids (**Supplementary Table S1**). The ECOG PS scale is a widely adopted, five-point scale used in clinical oncology to assess functional status and overall well-being, where scores range from 0 (fully active) to 5 (patient dead), with 4 corresponding to a completely disabled patient [15].

Pain was evaluated using a visual analog scale (VAS), a commonly used psychometric response scale for quantifying subjective characteristics or attitudes that cannot be directly measured [16]. The VAS is widely used for pain assessment in the clinical setting, allowing patients to graphically represent their pain intensity along a continuum [17].

Oncological outcomes. Oncological outcomes were evaluated based on the quality of surgical resection (R0 – no microscopic disease at the surgical margins; R1 – surgical margins with microscopic disease; R2 – surgical margins with macroscopic disease); patient status (AWD – alive with disease; AAWD – alive and without disease; DOD – dead of disease); and overall survival (OS). OS was the time since the oncological diagnosis until the latest follow-up evaluation or moment of death.

Statistical analysis. Statistical analysis was carried out using SPSS v24 (IBM Statistics, Armonk, NY). As data were not normally distributed, groups were compared with the signed-rank test. Overall survival was analyzed using the Kaplan-Meier methods. A p-value < 0.05 was considered significant.

Results

Between January 2018 and December 2022, 12 patients (eight female, 66.7%), with median (IQR) age 57 (51.75; 71.75) years, were surgically managed for NPFPF (**Table 1**). All patients underwent *en bloc* resection and reconstruction using a proximal femur modular megaprosthesis in a single surgical procedure (Fig. 1).

The underlying causes of pathological fractures were breast metastasis (n = 4, 33.3%), lung metastasis (n = 3, 25.0%), chondrosarcoma (n = 3, 25.0%), angiosarcoma metastasis (n = 1, 8.3%), and malignant giant cell tumor of bone (n = 1, 8.3%). The median (IQR) time from fracture occurrence to treatment was

14 (12; 24.75) weeks. Causes for delay in treatment were “delayed diagnosis” in 7 (58.3%) patients, “inability to provide treatment” in 4 (33.3%) patients, and “need for pre-operative medical optimization” in one patient (8.3%). Tumors were extensive in all cases, presenting with a median (IQR) volume of 469.3 (248.6, 1083.2) cm^3. Only three patients presented with localized disease.

Prior to surgery, nine patients (75.0%) were bedridden and three (25.0%) were in a wheelchair. After surgery, four patients (33.3%) were in a wheelchair and eight (66.7%) were walking with crutches, equating to a subjective functional improvement for all patients after surgery. The median (IQR) pre-operative ECOG was 4 (4;4), and the median (IQR) post-operative ECOG was 2 (2; 2.75), representing a significant decrease in ECOG from the pre-operative to post-operative period ($p = 0.002$). Pain significantly improved for all 12 patients after surgery, with a pre-operative median (IQR) VAS of 9 (9; 9) and a median (IQR) post-operative VAS of 3 (2.25; 3) ($p = 0.002$) - **Table 2**.

Resection margins were R0 in three cases (25.0%), R1 in eight cases (66.7%), and R2 in one case (8.3%). The median (IQR) overall survival was 25 (16.25, 36.25) months. At final follow-up, three patients (25.0%) were alive and disease-free, three were alive and had disease (25.0%), and six patients (50%) were dead due to the underlying cancer.

Postoperative complications included post-operative anemia in 12 cases (100%) and infection and dislocation (8.3%) in one case (both in the same patient). All 12 patients needed blood transfusions.

Discussion

Pathological fractures are typically caused by bone fragility due to unbalanced bone remodeling towards osteolysis [18]. These fractures often occur due to bone metastases, although primary bone tumors are also less commonly a cause. Due to the morbidity and increased mortality caused by pathologic fractures, most are managed surgically [19–21]. There is growing evidence supporting endoprosthetic replacement as the preferred surgical option for pathological fractures, with the lowest rates of implant failure for proximal femur pathological fractures [5, 22].

In developed countries, patients with pathological fractures are usually managed in the acute phase to stabilize the fracture, relieve pain, and regain weight-bearing capacity [23]. However, several factors may justify a delay in treatment, such as the need for medical optimization before surgery or, in cases where the pathological fracture is the presenting feature of a previously undiagnosed cancer, the need for staging [4, 24]. Nonetheless, treatment delays of several months are uncommon in western countries with developed healthcare systems.

Despite being in Europe, our sarcoma center in Portugal serves a unique and highly diverse demographic that not only includes typical European patients but also migrants from Portugal's former African colonies. This latter group often present with more biologically aggressive tumors and advanced disease, including neglected pathological fractures, due to significant diagnostic delays and limited access to appropriate treatment in their countries of origin. Even in some underserved areas of Portugal,

immediate and optimal management are not readily available, delaying diagnosis and treatment [25]. These patients are often complex and present significant management challenges, since for most of them reconstructive techniques are no longer an option, and they require ablative surgery. Despite this unfavorable scenario, a small group of these patients may benefit from arthroplasty reconstruction with megaprosthesis.

Herein, two-thirds of patients developed NPFPF on a background of metastatic disease, mainly breast and lung carcinomas. Chronic fractures developed due to a lack of capacity for adequate treatment in their home institutions, exacerbated by inadequate referral systems, which prevented timely intervention. As such, the underlying tumors represented large, high-volume disease in almost all cases.

Pathological fractures are associated with a high morbidity risk and significantly impact on QoL. As demonstrated in this series, these clinical scenarios imply severe functional impairment and pain. However, megaprosthetic replacement had a positive impact in this group of patients. The observed functional improvement, together with pain relief, seems to be sufficient motivation to recommend surgery for these high-risk, late-stage patients. Despite a significant number of observed complications, the outcomes were similar to acute clinical contexts [9, 23]. The most frequent post-operative complication was indeed post-operative anemia requiring transfusion, which was expected, since most patients presented with advanced oncological disease. However, there was only one major complication: a megaprosthesis dislocation and subsequent infection requiring revision.

Regarding oncological outcomes, we observed a low median overall survival, nonetheless, this result is not meaningful given the small mixed cohort analyzed, which includes different tumor biology and staging at presentation.

Taken together with the favorable outcomes, our experience favors megaprosthetic replacement for patients with NPFPF whenever feasible. Although a relatively small case series, reporting these patients' outcomes shares valuable experience managing a neglected group of complex clinical scenarios. It also provides an opportunity to raise awareness of the unique challenges and considerations involved in addressing NPFPF to guide multidisciplinary decision-making.

Conclusions

Here we present a rare group of patients on whom there is little reported surgical experience. As chronic pathological fractures caused by cancer remain rare in western societies, standardized management strategies are still lacking. Our data support surgical reconstruction, particularly with modular megaprosthesis, for functional and pain improvement in this rare and complex clinical scenario.

Declarations

Financial support and sponsorship

The authors declare no financial support of any kind.

Conflicts of interest:

The authors declare no competing interests.

Ethics approval:

The study was conducted in accordance with the Declaration of Helsinki and received approval from the local Research Ethics Committee (Comissão de Ética do Centro Académico de Medicina de Lisboa; Reference number of approval is 325/25).

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Figures

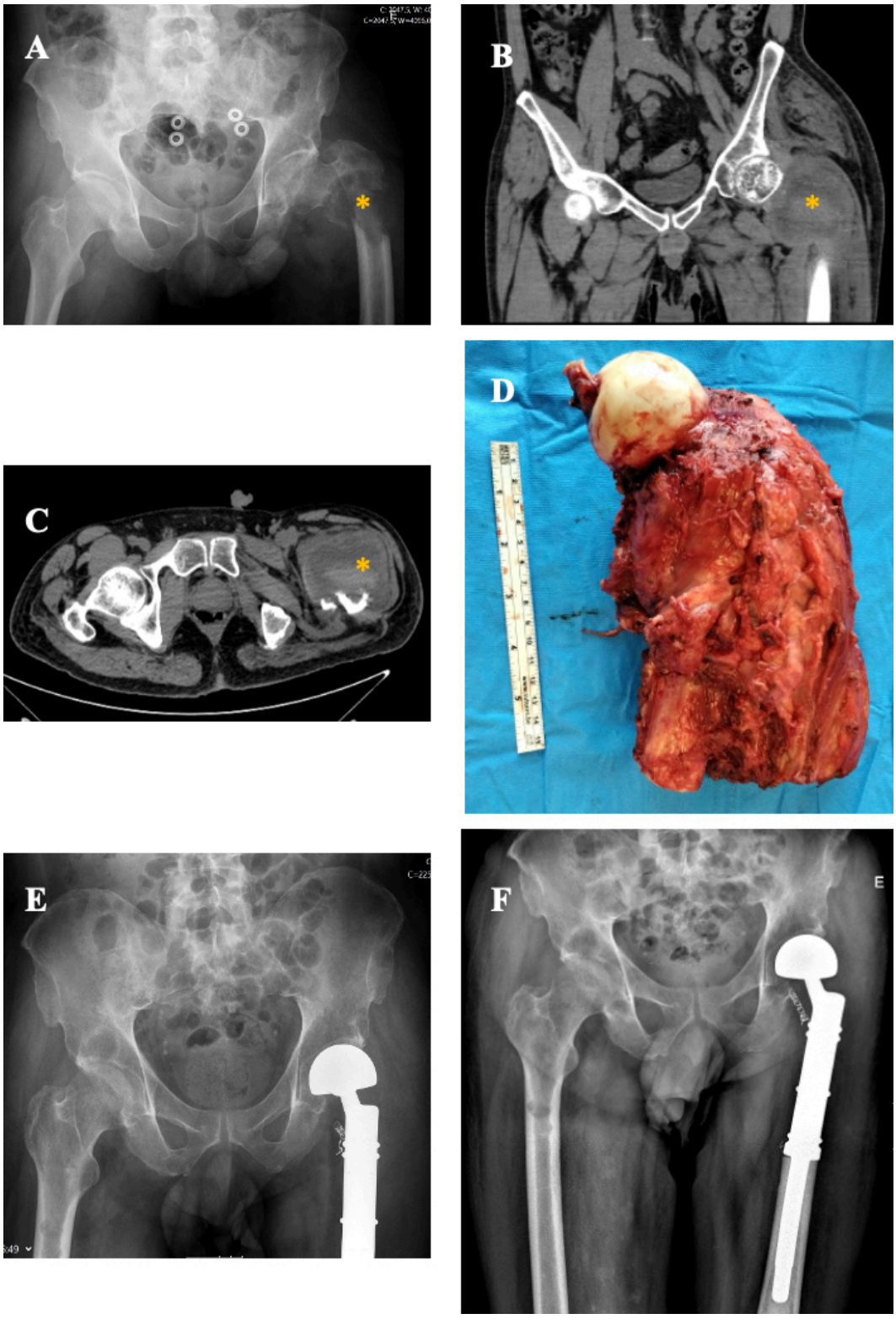


Figure 1

Figure 1. A: Antero-posterior pelvis X-ray imaging showing a left proximal femur neglected pathological fracture (*); B: Coronal computed tomography image of the same neglected pathological fracture (*) and significant associated soft tissue mass; C: Axial computed tomography imaging showing the significant soft tissue mass (*) associated with the pathological fracture; D: Photograph of the surgical specimen corresponding to the neglected pathological fracture presented in A, B and C, immediately after *en*

*bloc*resection; E: Post-operative antero-posterior pelvis X-ray imaging showing the proximal femur megaprosthesis used to reconstruct the resected bone segment. Another proximal femur metastasis can be seen within the contralateral limb; F: Post-operative antero-posterior pelvis X-ray imaging showing the same megaprosthesis and the cemented stem. Again, another proximal femur metastasis can be seen within the contralateral femur.

Supplementary Files

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- Table1.docx
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- SupplementaryTableS1.docx