JSES International 8 (2024) 446–450

Contents lists available at ScienceDirect

JSES International

journal homepage: www.jsesinternational.org

Treating pathological metastatic fractures of the humerus by compound osteosynthesis: a retrospective cohort study

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ARTICLE INFO

Keywords:
Pathologic fractures
Compound osteosynthesis
Internal fixation
Cement augmentation
Humerus
Competing risk analysis

Level of evidence: Level IV; Case Series; Treatment Study

Background: The number of malignant tumors is increasing as are bone metastases, such as those in the humerus. Arm function is important for an independent everyday life. In this study, compound osteosynthesis of metastatic fractures of the humerus is examined for its suitability in light of the competing risk of death.

Methods: This retrospective monocentric study includes a cohort of tumor patients who underwent primary compound osteosynthesis for pathological humeral fractures. The main endpoint was the continued existence of compound osteosynthesis using competing risk analysis to contrast failure and death. Failure was defined as mechanical failure of the osteosynthesis construct like refracture or plate-and-screw dislocation or loosening, which provides an indication for reintervention. Other complications are also described.

Results: We included 36 consecutive patients (64% male, mean age: 71.6 yr) from September 2007 to October 2020. In 58% of the cases, the left humerus was fractured. Lung carcinoma was the most common cause of bone metastases (27.8%). Compound osteosynthesis was performed with a median delay of 5 days after diagnosis of the pathologic fracture. Postoperative complications occurred in 7 of the 36 patients (19.4%): radial nerve palsy (n = 3), postoperative hematoma (n = 2), refracture (n = 2), and screw loosening (n = 1). Few mechanical failures (8.3%) occurred within the first year; only 1 patient needed revision of the osteosynthesis (2.8%). Median patient survival after compound osteosynthesis was 26.6 weeks. Competing risk analysis showed that for up to 2 years, the risk of death is clearly dominant over the risk of osteosynthesis failure from surgery.

Conclusion: Our study shows that compound osteosynthesis of the humerus is a suitable option for patients with pathologic humerus fractures. Compound osteosynthesis of the humerus usually survives the duration of malignant tumor disease.

Humeral shaft fractures are often caused by low-energy trauma in elderly patients and mainly related to osteoporosis.[4] Moreover, pathologic fractures also occur more frequently with increasing age.[22] Almost 10% of humerus shaft fractures are metastatic pathologic fractures.[4] The number of patients reaching the metastatic stage is steadily increasing due to the aging population and advanced oncological therapies.[20] Although some cancers, such as renal cell, breast, or prostate cancer, preferentially metastasize to bone, virtually any malignancy has the potential to develop bone metatases.[3,12] Osseous metastases are most commonly spread through hematogenous dissemination.[15,18] Regardless of the primary tumor location, carcinomas frequently metastasize to the spine, the diaphyseal region of the femur, and the proximal third of the humerus.[9,18] These affected bony structures are prone to pathologic fractures.[8]

Compound osteosynthesis is one treatment option in patients with impending or actual pathologic humeral fractures and refers to internal plate or nail fixation augmented with bone cement to create a more stable construct.[13] It provides immediate pain relief through reposition and stable fracture fixation ensuring rapid postoperative mobilization.[11] Thus, activities of daily living could be resumed as soon as possible.[11] This technique is mainly used for long tubular bones including the humerus.[13]

In cancer patients, postoperative complications leading to reoperation should be avoided as far as possible.[7] The performance of compound osteosynthesis for pathologic fractures of the

This study has been approved by the Ethical Committee of Eastern Switzerland, Switzerland (study ID: BASEC No. 2021-02019).

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https://doi.org/10.1016/j.jseint.2023.12.002

proximal humerus is not sufficiently covered in the literature. Therefore, the aim of this retrospective study was to review a cohort of patients with compound osteosynthesis for this specific indication. The primary goal was to assess all complications or reoperations and to determine the success of the fracture therapy until death (considering the competing risks of death and the failure of osteosynthesis).

Patients and methods

The survival and complications of compound osteosynthesis for pathologic humeral fractures performed at the Kantonsspital St. Gallen between September 2007 and October 2020 were studied in this retrospective monocentric cohort study. The most recent data on survival were collected on January 1, 2022, and the dataset completed. Inclusion criteria were impending or complete pathologic humeral fracture, primary surgical treatment with compound osteosynthesis, and complete radiological records. As shown in the CONSORT flowchart of patient selection in Fig. 1, 1 patient who explicitly denied further use of his data was excluded. The local ethics committee granted the approval for use of patient data without their consent for deceased patients and for patients treated before 2015 who could not be contacted.

Surgical techniques and implants

With the patient in a beach-chair position, the affected arm was draped so that it could be held by an assistant and moved freely in all directions. The standard deltopectoral approach (for more proximal metastases) and subsequent distal extension into an anterolateral approach (for more mid-shaft and distal metastases) were used. After deep dissection to the bone, the tumor mass was thoroughly curetted in the sense of an intralesional tumor resection and specimens collected for histology as well as bacteriology. The fractures were anatomically reduced and, if necessary, temporarily fixed with Kirschner wires. A locking plate of appropriate length (LCP or long Philos plate) was then applied, all screws tightened and the positioning controlled using an image intensifier. Bone cement was applied through the fenestration used earlier for curettage, and its intramedullary distribution was controlled with an image intensifier. Alternatively, the screws were partially retracted, the cement was applied, and then the screws were tightened again. Unintentional cement leakage through the screw holes or the defect zone of the pathological fracture were fluoroscopically controlled and removed if necessary. The wound was drained, sutured, and dressed as usual. The postoperative recommendation was passive, and active-assisted mobilization of the shoulder for 6 weeks at the maximum permitted abduction and flexion of 90° to protect the construct.

Fig. 2 illustrates an example of preoperative and postoperative imaging.

Data collection

We created a case report form with all variables necessary for descriptive and survival analysis using competing risk analysis (CRA). Data were extracted from our institutional patient management system containing written reports and radiographs. When needed, missing reports from external follow-up examinations were requested from general practitioners or other hospitals. The data of the follow-up visits were collected and recorded as long as available or until the patient's death. Final information was collected January 1, 2022.

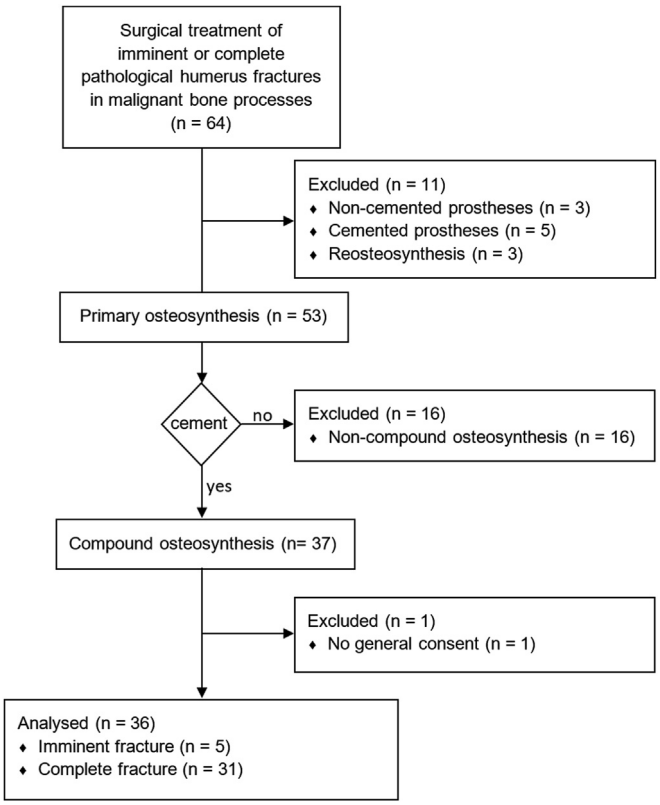

Figure 1 The flowchart of patient selection. *LCP*, Locking Compression Plate; *AP*, anteroposterior; *T1*, T1-weighted MRI scan.

Statistical analysis

All statistical analyses were performed using R (R: A language and environment for statistical computing; R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics included counts and proportions for categorical data and means and standard deviation for numeric data. By performing the CRA (R-package "cmprsk", version 2.2-11), the 2 events "failure of osteosynthesis" and "death" were differentiated within the survival analysis.

Results

This study includes 36 patients [23 men (64%) and 13 women (36%)] treated operatively with compound osteosynthesis of the humerus. Complete fracture was found in 31 patients (86%), whereas 5 patients (14%) had an impending fracture. Demographics and baseline clinical data are in Table I.

In our patient cohort, lung carcinoma (27.8%) was the most common primary tumor. In 21 cases (58%), the left humerus was fractured. Approximately $^{2}/_{3}$ of the fractures were in the shaft region, $^{1}/_{3}$ proximal, and only rarely was the fracture localized more distally. In 50% of the patients, the pathologic fracture occurred within 12 months of the tumor diagnosis. More than 65% of the patients included had already reached the metastatic stage at initial diagnosis. In 5 cases of impending but symptomatic fractures, compound osteosynthesis was performed prophylactically. In 78% of the cases, the fracture extended through the medial and lateral cortex in the conventional AP X-ray. The lateral cortex was affected in 89% of the cases in which only 1 cortex was involved.

Surgical treatment was mainly elective; however, in 8 cases (22%), it was performed as an emergency procedure. The average duration of surgery was 117 minutes. Two different types of plates

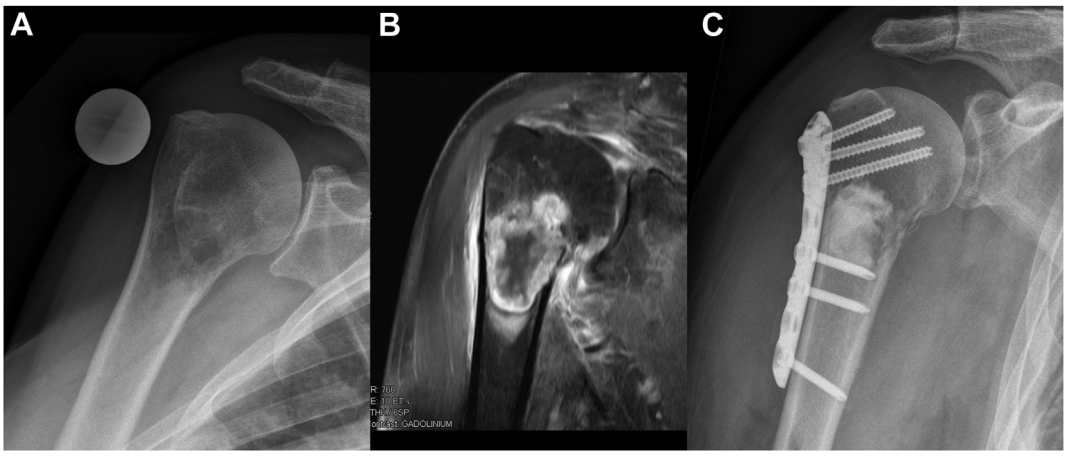

Figure 2 Case of a 53-year-old male patient with a renal cell carcinoma diagnosed 11 years before the fracture occurred. (**A**) Preoperative anteroposterior view showing osteolytic osseous metastasis metaphyseal below the humeral head. (**B**) Magnetic resonance imaging: Gadolinium-enhanced fat-suppressed T1-weighted coronal view showing bone metastases in the proximal humeral metaphysis with medial minimally compressed pathologic fracture. (**C**) Postoperative anteroposterior view after compound osteosynthesis. The bright, patch-like areas in the bone are cement-filled regions.

Table I
Patient characteristics.

	Total N = 36	Complete fracture N = 31	Immediate fracture N = 5
Age, y Median (min, max)	71.6 (47.5, 93.9)	71.5 (47.5, 93.1)	71.7 (52.9, 83.0)
Gender (%)			
M	23 (63.9%)	19 (61.3%)	4 (80%)
F	13 (36.1%)	12 (38.7%)	1 (20%)
Side (%)			
L	21 (58.3%)	19 (61.3%)	2 (40%)
R	15 (41.7%)	12 (38.7%)	3 (60%)
Primary tumor (%)			
Pulmonary	10 (27.8%)	7 (22.6%)	3 (60.0%)
Breast	7 (19.4%)	7 (22.6%)	0 (0.0%)
Hematologic	6 (16.7%)	5 (16.1%)	1 (20.0%)
Prostatic	4 (11.1%)	4 (12.9%)	0 (0.0%)
Other (kidney, gastrointestinal, bone)	5 (13.9%)	5 (16.1%)	0 (0.0%)
Primary tumor of unknown origin	4 (11.1%)	3 (9.7%)	1 (20.0%)

were used for stabilization during the observed period: the Philos plate (DePuy Synthes, Raynham, MA, USA) and the LCP plate (DePuy Synthes, Raynham, MA, USA). Regarding the number of used plates, 2 plates were used in only 8 cases, mainly from 2018 onward. In the other cases, only 1 plate was used. The postoperative hospital stay ranged from 2 to 27 days (median = 7.5 days).

Complications and revisions

At hospital discharge, 81% of the patients were oligosymptomatic. Complications recorded were neurological deficits (radial paresis, n = 3) and postoperative hematoma (n = 2), none of these requiring revision. All of the 3 radial nerve palsies were not preexisting but occurred postoperatively. One of these recovered completely over time, with persistent radial paresis in 5.6% of patients. Two patients died during hospitalization due to their underlying neoplastic disease. During follow-ups, screw loosening (n = 1) and refractures (n = 2) were registered as failures (8.3%); these were accompanied with limited mobility and pain during movement; 2 of these were treated conservatively, and 1 underwent revision surgery (2.8%). These complications occurred in 7 of 36 patients (19.4%) and are considered not specifically related to the index surgery. In 1 patient, 2 complications were recorded: postoperative hematoma and screw loosening. The mechanical failure occurred between 4 and 9 months postoperatively, with all using 1 plate in the initial surgery. These plates did not extend over the entire length of the bone. In the 3 investigated failures, bone metastases were located in the humeral shaft or at the proximal end, whereas the tumor entity differed between lung carcinoma, breast carcinoma, and prostate carcinoma.

The median survival after this surgical intervention was 26.6 weeks (186 days). However, 4 patients died within the first 30 days after compound osteosynthesis. Comparing impending and complete fractures, no statistical difference of the time between cancer diagnosis and death ($P = .576$) or the time from compound osteosynthesis and death ($P = .238$) was found.

The CRA showed that there was no censoring for reasons other than death. During the first 2 years, the competing event of death was frequent, and substantially reduced the cohort at risk (Fig. 3). Failures of osteosynthesis occurred early—usually within the first year.

Discussion

In this study, compound osteosynthesis of the humerus was a valid therapeutic option for patients with impending or complete pathologic humerus fractures. The failure rate (8.3%) was low and occurred usually during the first year after surgery. In the vast majority of cases, the fracture could be stabilized until the end of life with only 1 surgical reintervention in the whole series.

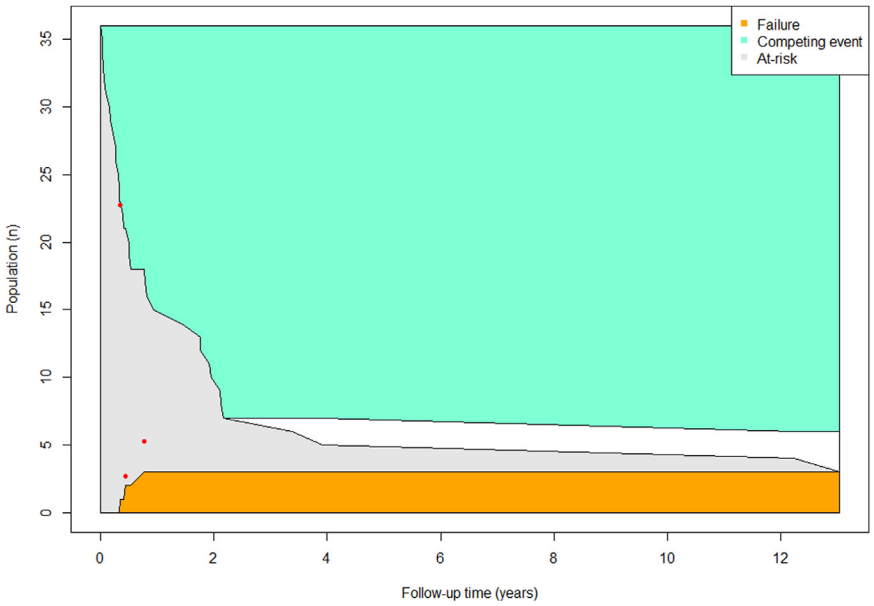

Figure 3 Competing risk analysis plot. Gray: at risk; orange: failure; green: deceased; red dots: revision events (refracture or screw loosening).

End of life occurred at a median of 26.6 weeks (186 days) after this primary surgical intervention though. Compared to other authors, this study showed a shorter survival after this surgery. Moura et al documented a mean survival time after the surgery of 309.29 ± 33.71 days in 86 fixations. Thirty-point five percent of their patients suffered from breast carcinoma.[14] In the study by Pretell et al, it was recorded that the mean postoperative survival time of 22.7 months in 23 cases with a pathological fracture of the humerus. Forty percent of their cases consisted of patients with multiple myeloma.[17] Toepfer et al reported a mean survival of 11.5 months after surgery. The most common tumor entities responsible for a pathological fracture were renal cell and breast carcinoma, accounting for 33% of all pathological fractures in their cohort.[20] Piccioli et al disclosed a mean survival of 8.3 months after surgery for pathological humeral fractures in 87 cases. In 39% of those cases, breast carcinoma or renal cell carcinoma was the primary tumor.[16] As previously stated by Wedin et al, the variations in survival rates may be explained, apart from other factors, by the differences in primary tumors, stage of the disease, number of impending fractures, and selection criteria.[23]

The literature on pathologic humerus fractures and compound osteosynthesis is sparse, and thus comparison of the results is difficult. One of the reasons for this is that the choice of treatment method is influenced by factors such as the tumor entity, its staging, and the prognosis associated with it. In general, rapid postoperative recovery of activities of daily living can improve personal autonomy, especially considering that the concept of the end of life has changed in the last decades. Today, with advances in systemic therapies metastatic disease often can be considered a chronic condition rather than a palliative one. This has led modern medicine to focus on the long-term well-being and autonomy of the patient. Correspondingly, the expectations of both patients and their families have become more important for medical decision making.[2] Furthermore, surgical stabilization of the weakened or fractured humerus significantly reduces pain and usually leads to a rapid reduction of analgesic treatment. This counteracts polypharmacy in patients who are already seriously ill.[10]

Cancer patients in the advanced metastatic stage have a reduced life expectancy.[21] Applying CRA we could show that from surgery and up to 2 years, the risk of death is clearly dominant over the risk of osteosynthesis failure. Therefore, it can be expected that patients will still have intact compound osteosynthesis until death caused by cancer. Probably due to the low number of impending fractures in our cohort, we could not confirm the findings of Groot et al that patients with impending pathological fractures of long bones have better secondary outcomes than patients with complete fractures.[6]

Our study has some limitations. First, due to the retrospective study design on nonstandardized data records, the information extracted has been reduced to chart reviews without any validated clinical scores. Second, the sample size was small and heterogeneous in terms of type of the primary tumor and different localization of the metastatic lesions in the humerus, which make it difficult to generalize and compare the results. More cases of pathological fractures caused by malignant tumors with a longer life expectancy could have significantly altered our results. The aim of any composite osteosynthesis should be to ensure permanent stability of the affected limb and to avoid premature implant failure. The longer the affected patient lives, the higher the risk of failure of the surgical treatment, as often no osseous healing of a pathological fracture can be expected.[5,19] The median overall survival after surgery in our cohort was low (26.6 weeks).

Therefore, double plate osteosynthesis in combination with bone cement augmentation of the bone defect and adjacent medullary canal should be discussed for all patients with a longer prognosis to avoid implant failure and revision surgery. From a biomechanical standpoint, 90-90 double plating is stronger than single plating and requires less soft tissue dissection compared to spanning plate fixation.[1] Oligoostotic or singular osseous metastatic manifestation in chronic malignant diseases with a good prognosis and systemic treatment options may even warrant wide resection and alloarthroplastic reconstruction, similar to primary malignant bone tumors.[16]

Additional statements on adjuvant therapy cannot be made because we do not have the complete data for this.

Conclusion

The present study shows that compound osteosynthesis of the humerus using locking plates is a suitable option for patients with pathological humeral fractures. Depending on the patient's life

expectancy, it is usually successful until the end of life and has a low rate of mechanical failure (or the need of subsequent revision) and an acceptable rate of complication.

Disclaimers:

Funding: No funding was disclosed by the authors.
Conflicts of interest: The authors, their immediate families, and any research foundation with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

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