UNIVERSIDAD PERUANA CAYETANO HEREDIA | Facultad de MEDICINA

MANEJO QUIRÚRGICO DE FRACTURAS PATOLÓGICAS SUBTROCANTÉRICAS: MODALIDADES DE TRATAMIENTO Y DESENLACES ASOCIADOS

SURGICAL MANAGEMENT OF METASTATIC PATHOLOGIC SUBTROCHANTERIC FRACTURES: TREATMENT MODALITIES AND ASSOCIATED OUTCOMES

TESIS PARA OPTAR POR EL TÍTULO PROFESIONAL DE MÉDICO CIRUJANO

AUTORA

MARIA LUCIA INCHAUSTEGUI RIVASPLATA

ASESORA

DRA. GUILIANA MAS UBILLUS

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ASESORA DE TESIS

Dra. Guiliana Mas Ubillus

Departamento Académico de Medicina

ORCID: 0000-0002-3276-5759

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Dedicado a mis abuelos Susana Rivas, María Luisa Zevallos y Juan Inchaustegui.

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TABLA DE CONTENIDO

RESUMEN

Antecedentes: Las fracturas patológicas (FP) subtrocantéricas ocurren en aproximadamente un tercio de las metástasis óseas de fémur. **Objetivo:** Analizar las estrategias quirúrgicas para las FP metastásicas subtrocantéricas y sus tasas de revisión. **Métodos y Materiales:** Revisión sistemática utilizando las bases de datos Pubmed y Ovid. Reoperaciones como resultados de complicaciones se analizaron según la modalidad de tratamiento inicial, tumor primario y tipo de procedimiento de revisión. **Resultados:** 544 pacientes, 405 con FP y 139 con fractures inminentes. La edad promedio de la población fue 65.85 años con un ratio varones/mujeres de 0.9. Las FP subtrocantéricas manejadas clavo intramedular (CIM) (75%) presentaron una tasa de revisión no-infecciosa de 7.2%. Las manejadas con reconstrucción protésica (21%) presentaron una tasa de revisión no-infecciosa de 8.9% para endoprótesis estándar y de 2.5% para endoprótesis tumoral ($p < 0.001$). Las tasas de revisión por infección fueron 2.2% para estándar y 7.5% para endoprótesis tumoral. No hubo infecciones dentro del grupo de CIM y placa/clavo ($p=0.407$). La localización más común para el tumor primario fue la mama (41%) con la tasa de revisión más alta (14.81%). Las reconstrucciones protésicas fueron el tipo más común de procedimiento de revisión. **Conclusión:** No existe consenso sobre el manejo quirúrgico. CIM es más simple, menos invasivo e ideal para pacientes con menor sobrevida. Endoprótesis tumoral puede ser más adecuado para pacientes con menores sobrevidas. El tratamiento debe ser ajustado al paciente considerando tasas de revisión, expectativa de vida y expertise del cirujano.

Palabras claves: fractura subtrocantérica, fractura patológica, tratamiento.

ABSTRACT

Background: Subtrochanteric pathological fractures (PFs) occur in approximately one-third of femur bone metastases. **Objectives**: We seek to analyze surgical treatment strategies for subtrochanteric metastatic PFs and their revision rates. **Methods:** A systematic review was performed using the PubMed and Ovid databases. Reoperations as a result of complications were analyzed according to initial treatment modality, primary tumor site, and type of revision procedure. **Results:** We identified a total of 544 patients, 405 with PFs and 139 with impending fractures. The study population's mean age was 65.85 years with a male/female ratio of 0.9. Patients with subtrochanteric PFs who underwent an intramedullary nail (IMN) procedure (75%) presented a noninfectious revision rate of 7.2%. Patients treated with prosthesis reconstruction (21%) presented a noninfectious revision rate of 8.9% for standard endoprostheses and 2.5% for tumoral endoprostheses ($p < 0.001$). Revision rates because of infection were 2.2% for standard and 7.5% for tumoral endoprostheses. There were no infections within the IMN and plate/screws group ($p = 0.407$). Breast was the most common primary tumor site (41%) and had the highest revision rate (14.81%). Prosthetic reconstructions were the most common type of revision procedure. **Conclusion:** No consensus exists regarding the optimal surgical approach in patients with subtrochanteric PFs. IMN is a simpler, less invasive procedure, ideal for patients with a shorter survival. Tumoral prostheses may be better suited for patients with longer life expectancies. Treatment should be tailored considering revision rates, patient's life expectancy, and surgeon's expertise. **Key Words**: subtrochanteric fracture; pathologic fracture; treatment.

I. INTRODUCTION

Metastases are the most common cause of morbidity and death among oncological patients. Pathological fractures (PFs) in oncological patients cause pain, loss of function, and psychological problems, thus compromising patient function and quality of life. (1) Survival among patients with metastatic bone disease has increased in recent decades leading to a successive increase in the incidence of pathological and impending fractures. (2,3) Long bones in the lower limbs tend to be a common site for skeletal metastases with an incidence of 56%. (4) The subtrochanteric region of the femur is involved in one-third of all pathological femur fractures requiring surgical intervention. (4) This region is subject to large forces causing malunion, delayed union, and mechanical failures after surgical treatment. (3,5)

Optimal management of metastatic lesions of the subtrochanteric femur region remains controversial. The literature is scarce with most studies only including a limited number of patients from this specific femoral region. (6) Current management is based mostly on the surgeon's experience and consists of either fixation with an intramedullary nail (IMN) or reconstruction with a standard or tumoral endoprosthesis. These approaches present different complications and mechanical failure rates. In the setting of increasing survival times, the risk of failure of conventional surgical techniques is also higher. (3)

II. OBJECTIVES

This systematic review seeks to identify the treatment modalities avail- able for subtrochanteric pathological femur fractures and evaluate the revision rates according to treatment modality and primary tumor site. In addition, individualized cases are presented, and types of revision procedures are described.

III. MATERIALS AND METHODS

Article Selection

A systematic review of the literature was conducted on November 11th , 2022, on the PubMed and Ovid databases using the following terms and Boolean operators: “pathologic” or “impending” AND “fracture” AND “metast” OR “cancer” AND “fem” OR “hip” OR “subtrochanteric” AND “surg” OR “operat” OR “intramedull” OR “fixation” OR “prosth” OR arthroplas.”

Articles that met the following inclusion criteria were considered eligible: (1) the article was published in an Index Medicus peer-reviewed journal, (2) the language of the manuscript was English or Spanish, (3) clinical and/or surgical outcomes were specific to sub- trochanteric PFs, and (4) variables include revision rate and cause of treatment failure.

The search resulted in 390 titles in PubMed and 598 titles in Ovid. Two independent reviewers reviewed all titles (M.L.I. and K.R.). We excluded 823 articles after title screening. The abstracts of the remaining 119 articles were reviewed after the exclusion of 46 duplicates. Thirteen abstracts were excluded because of language incompatibility. A total of 106 full texts were revised, and 88 records were excluded, 71 because of nonspecific subtrochanteric data and 17 because the variables of study were not of interest. Finally, 3 manuscripts were added after a review of cited works (Fig. 1).

Given the scarce literature on this topic, case reports and case series were included. Reviews of literature, letters to the editor, expert opinions, posters on congress, proceedings, and other non– peer-reviewed publications were excluded from the analysis. A total of 21 articles were finally included for quality assessment.

Quality Assessment

An adequate assessment of the quality of the included studies was performed independently by 2 reviewers (M.L.I. and K.R.). In case of disagreement, the senior author (J.P.-M.) made the final decision. The Strengthening the Re- porting of Observational Studies in Epidemiology (STROBE) statement and the CARE Case Reports Guidelines (CARE) were used to conduct the quality assessment of the studies included. Most of the studies were case reports and case series; hence, the CARE checklist was primarily used.

For the 14 studies that were case reports, the CARE checklist was used (Table I). We used 8 of the 13 items of the CARE checklist for the methodological assessment. All items were assigned scores from 0 to 2 points. A poorly described item received 0 point, a partly described item received 1 point, and a well-described item received 2 points. Articles with a cumulative score ≥14 were included in our analysis. One study was excluded.

The remaining 7 studies were assessed with the STROBE checklist, following the strategy published by Bryce-Alberti et al. (7) (Table II). For this checklist, 10 of the available 22 items were used, following the same point system described for the CARE checklist. Only 6 articles analyzed achieved a score higher than 14 and were included. A total of 19 studies were included in our analysis. All studies included had a Level of Evidence IV.

Data Extraction

Two independent reviewers (M.L.I. and K.R.) conducted the data extraction from the 19 included manuscripts. All variables of interest were extracted from the manuscripts into established spreadsheets. This study was registered at PROSPERO.

Demographic Characteristics

Mean age and male/female ratio were reported for the 544 cases of both sub-trochanteric PFs and impending fractures. Most studies reported these parameters including other non- subtrochanteric fractures; thus, these parameters are not subtrochanteric specific.

Revision Rates According to Treatment Modality

To avoid confounding factors and to focus on clinical significance, treatment modalities and their respective revision rates were analyzed only for the 405 PFs, excluding the 139 impending fractures from analysis. Treatment modalities were classified into 4 categories: IMN, endoprosthesis, plate/screws, and others.

The IMN implant type was recorded. Endoprosthetic reconstructions included standard endoprosthesis and tumoral endoprosthesis, the latter sub- classified as proximal femoral megaprosthesis or total femoral megaprosthesis. We define standard endoprosthesis as all prosthetic reconstructions that are composed of a long stem implant that bypasses the PF and do not include tumor resection. Tumoral endoprosthesis, on the other hand, composes all prosthetic reconstructions that include tumoral resection with a proximal femur reconstruction or total femoral reconstruction. Other treatment modalities included procedures that were not described in the included manuscripts. Adjuvant treatment including chemotherapy and/or radiotherapy was not assessed in the analysis because they were not reported in most included manuscripts.

A revision was defined as any reoperation performed as a result of complications that compromised the implant or were directly associated with the initial procedure. Two types of revision rates are presented: (1) noninfectious revision rates and (2) infectious revision rates. Noninfectious revisions are defined as a loss of normal function of the implant and/or relationships between the implant components and adjacent bone and soft-tissue attachments. (8) Infectious revisions are defined as reoperations for infections in which at least the implant/prosthesis or plate was retained, but a surgical procedure was performed. Revision rates are presented for each treatment modality. The significance between IMN, standard endoprosthesis, and tumor endoprosthesis revision rates was calculated. Weiss et al. described their study population including both impending and displaced pathological subtrochanteric fractures. (6) Based on their population proportions, we estimated the number of PFs that received each treatment modality and their respective revision rates. Reasons for failure are described within each treatment modality category. IMN reasons for failure include noninfectious events such as nail breakage because of nonunion, symptomatic nonunion, tumor progression, and mechanical failure. Mechanical failure includes nail protrusion, cutout of the cephalic screw, refracture, immediate failure, and all mechanical causes not related to nonunion or tumor progression. Endoprosthesis reasons for failure are described using the Henderson classification of segmental endoprosthetic failure. (8) Although this classification was originally designed for tumor endoprosthesis, we extrapolated it to our population, including both standard and tumoral endoprosthesis. Henderson et al. described 5 types of failure modes classified in 2 groups: mechanical and nonmechanical. Mechanical failure includes soft-tissue failure (Henderson 1), aseptic loosening (Henderson 2), and structural failure (Henderson 3). Non mechanical failure includes infection (Henderson 4) and tumor progression (Henderson 5). (8)

Revision Rates According to Primary Tumor Site

Primary tumor site was defined as the location from where the initial malignant tumor cells emerged and metastasized to the subtrochanteric femoral region. Primary tumor site was described for the 244 patients (5,9–17) for whom these data were available. Revision rates according to primary tumor were calculated using only 138 patients with actual PFs from the study by Weiss et al. (6) This population represents 34% of our sample and is the only one with enough data to calculate the revision rate according to primary tumor site.

Revision Procedures

Individualized data were retrieved from 27 patients (6,11,14,18–20) that presented a PF with failed treatment, required a revision procedure, and had individualized information about the revision procedure performed. Primary surgery and the type of revision procedure were described for each individual patient. Primary surgery was classified into 3 categories: IMN, endoprosthesis, and plate/screws. Revision procedures were classified into 4 categories: IMN, endoprosthesis, plate/screws, and others. The details regarding the revision procedure are described following the same definitions previously described.

Data Analysis

Descriptive statistics were used to pre- sent demographic, clinical, and therapeutic approach data. Median and interquartile ranges were used to describe quantitative data because of the non- normal distribution of the values. Non- parametric tests were implemented to compare quantitative variables. The Fisher exact value statistics was used to evaluate significance between the revision rates ac- cording to treatment modality. A p ,0.05 was considered statistically significant. Statistical analysis was performed using Stata software (StataCorp LLC).

IV. RESULTS

A detailed flowchart of the search strategy and selection process is represented in Figure 1. The aggregate data comprised a total of 544 patients of the 19 studies finally included in our analysis. (2,5,6,9,11–25)

Study Population

The aggregate data set comprised 544 patients from the 19 studies selected. The mean age was 65.85 years, and the male/female ratio was 0.9 (Table III). Demographic analysis included 139 impending fractures and 405 PFs. Further analysis was performed in the patients with PFs. The mean follow-up ranged from 0 to 24 months. Revision rates ranged from 0% to 100%. A compound revision rate of 8.2% was calculated for the PFs.

Revision Rates According to Treatment Modality

The 4 treatment modality categories are presented in Table IV. Of the patient population, 304 underwent IMN (75%), 85 endoprosthesis (21%), 11 plate/screws (2.7%), and 5 other procedures (2.3%). Revision rates are presented in Table V. IMN presented an infectious revision rate of 0% and a noninfectious revision rate of 7.2%. Nail breakage because of nonunion was the most common reason for failure (40.9%). Regarding treatment with an endoprosthesis, standard endoprosthesis was the most common type of endoprosthesis procedure (53%). Tumoral endoprosthesis included only proximal femur reconstruction in 39 fractures and total femoral reconstruction in 1 case. Standard endoprosthesis presented an infectious revision rate of 2.2% and a noninfectious revision rate of 8.9%. Conversely, tumoral endoprosthesis presented an infectious revision rate of 7.5% and a noninfectious revision rate of 2.5%. There was a statistically significant difference among treatment groups because of non- infectious revision rates ($p < 0.001$) while this difference was not observed because of infectious revision rates ($p = 0.407$).

Plating had a noninfectious revision rate of 9.1% (1 of 11) because of plate breakage. Only 2 types of procedures were performed: insertion of a double plate with cementation in 10 patients and a 95- angled plate in 1 patient.

Revision Rates According to Primary Tumor

Primary tumor site was described for 244 patients. (5,9–17) The most frequent primary tumor sites were breast (41%), prostate (15.2%), lung (11.9%), and kidney (10.2%).

Revision rate according to primary tumor was calculated for 138 patients from the study by Weiss et al.6. Breast cancer presented the highest revision rate (14.8%), followed by the kidney (14.3%), prostate (7.7%), and lung (6.7%).

Revision Procedures

Individualized patient data are presented for 27 cases (6,11,14,18–20,23,24) of subtrochanteric PFs that required a revision procedure (Table VI). IMN was the primary surgery in 17 cases, prosthesis in 9 cases, and plate in 1 case. Among patients treated with IMN in the primary surgery, revision procedures were diverse. The most frequent were endoprosthesis (47%), IMN (18%), plate fixation (10%), and others (25%).

The most frequent type of revision procedure was 1-stage revision to an endoprosthesis (noninfectious failures), extensive washout with hardware retention, drainage of hematoma, and open reduction with internal fixation. Because of their low frequency, all these procedures were classified within the “others” group.

One patient had a plate insertion as the primary surgery; the reason for failure was breakage of the plate with resection and reconstruction with tumoral endoprosthesis as revision procedure.

V. DISCUSSION

Our study represents the first systematic review of subtrochanteric PF, with the largest study population to date (544 patients). The best surgical approach to subtrochanteric metastatic disease is not clear and varies greatly among orthopaedic surgeons. (3,10,18,22)

Study Population

The mean age of 65.85 years is reported for our study population, in agreement with previous reports of PFs of the proximal femoral region. (3,19,26) Similarly, a female predominance has been previously reported for PFs of this region (3,6,10,27–29) Our study population is composed of 405 PFs and 139 impending PFs. PFs are most frequently reported in the subtrochanteric femoral area because of being subject to long-term cyclical loading forces. (2,3)

The reported rate of progression of skeletal metastasis to PFs is between 2% and 3%. (2) Compared with impending fractures in long bones, displaced fractures directly affect patient survival and are associated with a higher risk of revision after surgical management (22) and is for this reason that our analysis focused on displaced PFs.

Revision Rates According to Treatment Modality

Revision rates are a crucial factor in the selection of treatment. The decision between surgical or other palliative treatment is based on the location, tumor type, the extent of the tumor, and the patient's comorbidities. Weiss et al. reported that a life expectancy of at least 2 months is usually required for surgical intervention and that stabilization of long bone fractures is always justified unless the patient is at a terminal stage with imminent death. (6)

IMN was the most common treatment modality of our study, being used in 304 patients (75%) (2,5,6,13,18,25) IMNs act as internal splints with load-sharing properties, bearing most of the load initially and then transferring it to the bone as the fracture gradually heals. The goal of these devices is not to bear the patient's weight for the remainder of the patient's lifetime; as patient survival increases and healing is not achieved because of tumor burden, the risk of IMN failure increases as well. (10) Nevertheless, intramedullary nailing offers several advantages: The procedure is quick and simple, with low morbidity and provides immediate stability. (2) IMN devices are reported as the best treatment by some authors (30,31); however, there is poor evidence on whether patients benefit from more aggressive metastatic resection followed by reconstruction or from minimally invasive intramedullary stabilization. (19)

We found a 7.2% noninfectious revision rate when IMN was used, which is in agreement with previous reports ranging from 0% to 14%. (6,22,31,32) Nonetheless, other studies report revision rates as high as 26% for IMN. (10,33,34) Implant failure or other surgical complications are dependent on different factors, including the amount of stress the patient is subject to, with impaired patients reporting lower implant failure rates. (25) Willeumier et al. identified a high frequency of revision once the patient had a first revision procedure. (22) The infectious revision rate found was 0%, probably because the characteristics of the implant and procedure represent a lower infection risk. (8)

The most common reason for failure in IMN reported in our study was nail breakage because of nonunion. PF in the subtrochanteric region of the femur is exposed to eccentric loading forces, combined with the loss of bone substance and strength seen in metastatic lesions, making internal fixation difficult. (2,5,13,21,23) Nonunion is common in PFs and leads to increased stress and eventual failure of the fixation device. Tumor progression, another reason for failure described in our study, also generates fatigue in the IMN material and ultimately leads to failure. (5,13)

Endoprostheses were used in 21% of cases included, with standard endoprosthesis as the most frequent procedure (53%). Both standard and tumoral endoprostheses are major procedures associated with intraoperative complications and mechanical complications, including high dislocation rates. (6,21,33)

Infectious revision rates were higher in tumoral endoprosthesis (7.50%) than in standard endoprosthesis (2.5%). Larger endoprosthesis have a higher failure rate because of infection than smaller implants; this is explained by more extensive dissections and longer operative times. (8,35,36) They could also be explained by confounding factors such as diverse surgical techniques and postoperative care followed in the diverse institutions of the studies included.

Standard endoprosthesis presented one of the highest noninfectious revision rates (8.9%) (6,8,16,25) However, the noninfectious revision rate of 2.5% of tumoral endoprosthesis was lower than that of standard ones and IMN ($p < 0.001$). Multiple studies have indeed reported lower revision rates in endoprosthetic replacements than in IMN. (6,10,21) Resection of tumor tissue with a proximal or total femur resection offers the advantage of removing the source of structural failure.

These findings highlight the importance of individualizing patient treatment according to factors such as survival and surgeon's expertise. In patients with limited life expectancy, less invasive procedures with fewer complications, such as

IMN, are indicated. In patients with a higher survival rate, invasive procedures with more durable implants such as tumoral prostheses are better suited. (6) Although specific indications for each method have not yet been established, life expectancy and postoperative function must be considered.

Finally, plating represented only 3% of our treatment modalities. Plating is no longer the treatment of choice because it lacks load-sharing properties and control of bending forces. Although the revision rate we found was 9.1%, rates as high as 23% have been reported. (2) The low rate reported by us is probably explained by our limited sample of 11 patients, making our revision rate less accurate. All 11 cases included came from the study by Broos et al. published in 1992. (20)

Revision Rates According to Primary Tumor Site

We found that breast was the most frequent primary tumor site (41%), followed by prostate (15.2%), lung (11.9%), and kidney (10.2%). In a retrospective study of 142 metastatic fractures of the femur, Sarahudi et al. reported a similar distribution pattern, with breast (46.5%), bronchial carcinoma (9.9%), prostate (7.7%), and kidney (4.9%) as the most common locations. (31) Furthermore, breast had the highest revision rates according to primary tumor (14.81%), followed by kidney (14.29%), prostate (7.69%), and lung (6.67%). No previous study has reported revision rates according to primary tumor site, and further studies with larger populations are necessary to evaluate this finding.

Revision Procedures

Revision procedures described for the 27 individualized patients were diverse. Endoprosthetic replacement was the most common type of revision procedure.

Owing to the lower risk of non- infectious failure, prosthetic replacement is the most commonly used method after treatment failure. (10,21)

Limitations

Several limitations were noted. Subtrochanteric PFs specific data were not explicit in most studies, and certain inferences had to be done to obtain the data. Revision rates according to primary tumor site were reported in only one article. Thus, there were not enough individualized data reports on this topic. Finally, there was a lack of information regarding whether adjuvant treatment, chemotherapy or radiation therapy, was administered. Conversely, our study has many strengths, mainly that it represents the first systematic review of subtrochanteric PFs with a study population of 544 patients. Similarly, we report useful data regarding revision rate according to treatment modality and primary tumor site, which can hopefully assist orthopaedic oncologists in their decision-making process.

VI. CONCLUSIONS

Management of subtrochanteric PFs remains challenging because of higher-than-normal revision rates and lack of consensus on optimal surgical approach. IMN has a noninfectious revision rate of 7.2% and an infectious revision rate of 0%. Tumoral endoprostheses have the lowest noninfectious failure revision rate (2.5%) and are ideal option for patients with longer life expectancy. Revision rates in standard endoprostheses were considerably higher (8.9%) for which it would not be an ideal implant to use. In oncologic patients with subtrochanteric PF, breast was the most common primary tumor site with the highest revision rates. Revision procedures are most often done with endoprosthetic reconstructions.

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VIII. TABLES AND FIGURES

Table I. Quality assessment using CARE Checklist Items (2 = Well-described, 1 = Partly described, 0 = Poorly described

Study Name	Tittle	Key words	Abstract	Introduction	Patient Information	Clinical findings	Timeline	Diagnostic assessment	Therapeutic Intervention	Follow-up & Outcomes	Discussion	Patient Perspective	Informed consent	Included in Analysis
Broos PL	Poorly	Poorly	Well	Well	Partly	Well	Partly	Well	Well	Well	Well	Poorly	Poorly	**Yes**
Chesser TJ	Poorly	Poorly	Well	Well	Partly	Well	Well	Well	Well	Partly	Well	Poorly	Poorly	**Yes**
Datir SP	Well	Partly	Well	Well	Well	Well	Partly	Well	Well	Well	Well	Poorly	Poorly	**Yes**
Dayer R	Well	Poorly	Poorly	Well	Well	Well	Well	Well	Well	Well	Well	Poorly	Poorly	**Yes**
Karachalios T	Poorly	Poorly	Well	Well	Well	Partly	Well	Well	Well	Partly	Well	Poorly	Poorly	**Yes**
Koskinen EV	Poorly	Poorly	Partly	Well	Well	Well	Partly	Partly	Well	Partly	Well	Poorly	Poorly	**NO**
Lim CY	Well	Partly	Well	Well	Well	Partly	Well	Well	Well	Partly	Partly	Poorly	Poorly	**Yes**
Najibi S	Partly	Poorly	Partly	Partly	Well	Well	Well	Partly	Well	Well	Well	Poorly	Poorly	**Yes**
Nargol AV	Poorly	Poorly	Well	Well	Well	Well	Partly	Well	Well	Well	Partly	Poorly	Poorly	**Yes**
Ramakrishnan M	Poorly	Partly	Well	Well	Partly	Partly	Partly	Well	Well	Well	Well	Poorly	Poorly	**Yes**
Samsani SR	Poorly	Poorly	Well	Well	Partly	Partly	Partly	Well	Well	Well	Well	Poorly	Poorly	**Yes**
Van den Brink	Well	Poorly	Well	Well	Well	Partly	Partly	Partly	Well	Partly	Partly	Poorly	Poorly	**Yes**
Vermesan D	Well	Partly	Well	Well	Well	Well	Well	Well	Well	Well	Well	Poorly	Poorly	**Yes**
Weikert DR	Poorly	Poorly	Partly	Well	Well	Well	Partly	Well	Well	Well	Well	Poorly	Poorly	**Yes**

Table II. Quality assessment using STROBE Checklist Items (2 = Well-described, 1 = Partly described, 0 = Poorly described)

Study	Setting	Participants	Variables	Data sources	Statistical Methods	Participants	Descriptive data	Outcome data	Main results	Limitations	Included in Analysis
Edwards SA	Well	Well	Well	Well	Poorly	Well	Partly	Well	Well	Poorly	**Yes**
Forsberg AG	Well	Well	Partly	Poorly	Well	Partly	Partly	Partly	Well	Well	**NO**
Tanaka T	Well	Well	Well	Well	Well	Well	Well	Well	Well	Partly	**Yes**
Weiss RJ	Well	Well	Well	Well	Well	Well	Well	Well	Well	Well	**Yes**
Willeumier JJ	Well	Well	Well	Partly	Well	Well	Well	Well	Well	Well	**Yes**
Zacherl M	Well	Well	Well	Well	Well	Partly	Well	Well	Well	Well	**Yes**
Zickel RE	Well	Well	Well	Partly	Poorly	Well	Well	Well	Well	Poorly	**Yes**

Table III. Study population. PF: Pathological Fracture, IMN: Intramedullary nail, LGN: Long gamma nail, MUH: Modified unipolar hemiarthroplasty, UFN-SB: Unreamed femoral nail with spiral blade, NA: Not available

*Average age refers to the mean age in years with the exception of *absolute value of 1 patient

**Data displayed in Mean follow up (months) refers to the mean time in months with the exception of ^median, “range, and ¨until death.

Study	Age	Male/Female ratio	Impending fracture	PF	Mean follow up (months)	PF Type of Treatment	Treatment Details	PF Revision Rate	PF Reason for Failure
Broos PL	62	3/8	0	15	NA	Endoprosthesis (4), Plate (11)	Tumor prosthesis (4), 95 angled plate (1), Compound double plate with cementation (10)	1/15 (6.7%)	**PLATE:** Plate breakage due to nonunion
Chesser TJ	63*	1/0	1	0	-	-	-	-	-
Datir SP	71	18/37	4	13	7	IMN (13)	Unreamed femoral nail with spiral blade UFN-SB	0/13 (0%)	No failure
Dayer R	79*	1/0	1	0	-	-	-	-	-
Edwards SA	68	4/5	11	11	18	IMN (11)	Long gamma nail	1/11 (9%)	Mechanical failure
Karachalios T	66.5	2/5	0	14	24	IMN (14)	Russel Taylor reconstruction nails (6), Uniflex reconstruction nail (7), Modified AO universal nail (1)	0/14 (0%)	No failure
Lim CY	61.8	2	0	4	Until death¨	Endoprosthesis (4)	Standard endoprosthesis (4)	1/4 (25%)	Non-mechanical:infection (Hernderson 4)
Najibi S	78*	0/1	0	1	12	IMN (1)	Long gamma nail	1/1 (100%)	Mechanical failure
Nargol AV	71	NA	0	6	6	IMN (6)	Variwall reconstruction Nail with no cement	0/6 (0%)	No failure
Ramakrishnan M	65	4/5	23	5	11.9	IMN (5)	Proximal Femoral Nail closed with percutaneous technique	0/5 (0%)	No failure
Samsani SR	65	4/5	28	11	3.5	IMN (11)	Long gamma nail	0	No failure
Tanaka T	60.1	1	2	44	11.4	IMN (44)	Trigen System or the Alta CFx IM rod system	1/44 (2.3%)	Nail breakage due to nonunion
Van den Brink	73	0/2	0	2	13	IMN (2)	Gamma nail + proximal lag screw	2/2 (100%)	Nail breakage due to nonunion
Vermesan D	64	5/6	0	6	24-84 "	IMN (5), Endoprosthesis (1)	Long gamma nail (4), Kuntscher nail (1), Standard endoprosthesis (1)	0/6 (0%)	No failure

Weikert DR	66.8	NA	0	10	6	IMN (10)	Russel Taylor reconstruction nail	0/10 (0%)	No failure
Weiss RJ	68	1	45	151	6^	IMN (83), Endoprosthesis (63), Others (5)	IMN not specified (83), standard endoprosthesis (45), tumoral endoprosthesis (18), others not specified (5)	17/151 (11.3%)	**IMN:** nail breakage due to nonunion (3), nonunion (2), tumor progression (1), mechanical failure (5). **PROSTHESIS:** mechanical failure technical failure (Henderson 3) (5), non-mechanical failure infection (Henderson 4) (1)
Willeumier JJ	65	2/3	13	50	14.4	IMN (63)	Type of IMN not specified (50)	3/50 (6%)	Not specified
Zacherl M	63.5	2/3	0	27	8^	IMN (14), Endoprosthesis (13)	IMN not specified (14), Tumoral endoprosthesis (13)	5/27 (18.5%)	**IMN:** mechanical failure (2). **PROSTHESIS:** non mechanical failure infection (Henderson 4) (3)
Zickel RE	63	1/5	11	35	NA	IMN (35)	Zickel intramedullary device without cement (35)	1/35 (2.9%)	Tumor progresion (1)
TOTAL	**65.85**	**0.9**	**139** **544**	**405**				**33/405 (8.2%)**	

Table IV. Treatment modalities for pathological fractures. IMN: Intramedullary nail

Type of treament	
IMN (n = 304)	Trigen System or the Alta CFx intramedullary rod system (n=44) Zickel intramedullary device without cement (n=35) Long gamma nail (n=27) Russel Taylor reconstruction nail (n=16) Cephalocondylic intramedullary device (n=14) Unreamed femoral nail with spiral blade (UFN-SB) (n=13) Uniflex reconstruction nail (n=7) Variwall reconstruction nail (n=6) Proximal Femoral Nail (n=5) Gamma nail (n=2) Kuntcher nail (n=1) Modified AO universal nail (n=1) Not specified (133)
Endoprosthesis (n =85)	Standart endoprosthesis (n=45)
	Tumoral endoprosthesis (n=40) Proximal femoral megaprosthesis (n=39) Total femoral megaprosthesis (n=1)
Plate/Screws (n =11)	Double plate + cement (n= 10) 95% Angled plate (n= 1)
Others (n =5)	Not specified (n=5)

Table V. Revision rates according to treatment modalities. *IMN:* Intramedullary nail

Type of treament	Revisions (n)	Reason for failure	n	Infectious revision rate	Non-infectious revision rate
IMN (n = 304)	22	Nail breakage due to nonunion	9	0%	7.20%
		Mechanical failure	6		
		Symptomatic nonunion	2		
		Tumor progression	2		
		Not specified	3		
Standard Endoprosthesis (n = 45)	5	Mechanical structural failure (Henderson 3)	4	2.20%	8.90%
		Non-mechanical: infection (Henderson 4)	1		
Tumoral Endoprosthesis (n=40)	4	Non-mechanical: infection (Henderson 4)	3	7.50%	2.50%
Proximal femoral megaprosthesis (n=39)					
Total femoral megaprosthesis (n=1)		Mechanical structural failure (Henderson 3)	1		
Plate/Screws (n = 11)	1	Plate breakage due to nonunion	1	0%	9.10%

Others (n=5)	0	-	-	-	-
p-value				0.405	<0.001

Table VI. Revision procedures. IMN: Intramedullary nail, NA: not available

Patient Number	Study	Sex	Age	Primary tumor	Primary surgery (n)	Revision procedure (%)	Revision procedure details
1	Weiss RJ	F	67	Breast			
2	Weiss RJ	M	79	Kidney			
3	Weiss RJ	F	41	Breast			Standard endoprosthesis
4	Zacherl M	F	80	Breast			
5	Zacherl M	M	63	Kidney		Endoprosthesis (47%)	
6	Weiss RJ	F	57	Breast			Tumoral endoprosthesis
7	Weiss RJ	M	54	Kidney			
8	Tanaka T	F	58	Breast			Not specified
9	Van den Brink WA	F	67	Breast			Replacement of IMN
10	Van den Brink WA	F	79	Breast	IMN (17)	IMN (18%)	
11	Weiss RJ	M	67	Other			External fixation
12	Najibi S	F	78	Lymphoma		Plate (10%)	Open reduction and internal fixation with a 95-degree blade plate
13	Weiss RJ	M	78	Prostate			Glide screw plate
14	Weiss RJ	F	73	Other			
15	Weiss RJ	M	76	Breast			
16	Weiss RJ	F	61	Breast		Others (25%)	Not specified
17	Weiss RJ	F	73	Breast			
18	Weiss RJ	F	51	Breast			Standard endoprosthesis
19	Weiss RJ	F	62	Lung		Endoprothesis (33%)	
20	Weiss RJ	M	78	Prostate			Tumoral endoprosthesis
21	Weiss RJ	F	56	Breast		Plate (11%)	Not specified
22	Zacherl M	F	59	Vagina	Endoprosthesis (9)		One stage revision
23	Zacherl M	F	64	Lung			
24	Zacherl M	F	71	Angiosarcoma		Other (56%)	Extensive washout with hardware retention
25	Weiss RJ	M	81	Kidney			Excavation hematoma
26	Weiss RJ	M	38	Other			Open reduction
27	Broos PL	NA	NA	NA	Plate (1)	Prosthesis (100%)	Tumoral endoprosthesis

Figure 1. Flowchart for our literature search and selection of relevant articles. *Px*: patient, *ID*: identification, *ST:* subtrochanteric