

Cemented versus cementless megaprosthesis in proximal femur metastatic disease: A systematic review

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Abstract

The proximal femur is the long bone most commonly affected by metastatic disease. There are many treatment options, such as hip megaprotheses. A topic still widely debated in literature is the use of cemented or uncemented megaprotheses in this kind of patients. The purpose of this review is to examine both these surgical options to understand which of them should be preferred in metastatic patients. Twelve articles were finally included in the review. Eight authors used cemented megaprotheses, two cementless megaprotheses and two authors used both techniques. Better functional outcomes and lower infection rates were found in cementless megaprotheses. More studies have to be performed to choose the better technique and improve patients' quality of life.

Introduction

Bone metastasis are frequently observed in upper and lower limb, spine and pelvis.^{1,2} The proximal femur is the long bone most commonly affected by metastatic disease.^{3,4} Bone metastases weaken the bone destroying the bone architecture and increase the risk of pathological fractures.⁵ Bone metastases could produce pain, worsened by weight bearing, or be completely asymptomatic; the pain usually can be treated with radiation therapy or drugs.⁶ The impending fractures or the pathological fractures have to be surgically treated ensuring local control of the disease, pain control and good functional and clinical outcomes.^{7,8}

There are many kinds of surgical strategies to treat a proximal femur

metastasis, such as intramedullary nailing, resection and reconstruction by a standard prosthesis or a megaprosthesis, open reduction, curettage and internal fixation.³ In a recent review the safety of megaprosthesis in the management of metastasis in the proximal femur is confirmed.⁹

A topic still widely debated in literature is the use of cemented or uncemented megaprotheses in this kind of patients. Most of authors prefer the cementation because had lower rates of revision for loosening.¹⁰ Moreover, a cemented megaprosthesis does not need the osteointegration for a total weight bearing, so this condition allows patients to start chemotherapy as soon as possible.¹⁰ Must be considered that usually there were multiple metastasis in the femur, so the cementation guarantees a better grip.

Other authors, like Bischel *et al*, stated that the biomechanical status of a metastatic femur can be compared to the bone loss that can be found in aseptic loosening.¹¹ As well as we search a distal grip without cementation in hip prosthesis surgical revision of aseptic loosening, the authors in their paper demonstrate the validity and safety of uncemented stem positioning in metastatic femur.¹¹

Besides cementation needs longer surgical time that increased infection risk and in literature "bone cement implantation syndrome" was described, characterized by hypoxia, hypotension, cardiovascular collapse and an increased risk of pulmonary embolism.^{12,13} Lastly the presence of a cemented megaprosthesis could aggravate subsequent revision surgery.

In this paper we performed a systematic review of the literature about the use of cemented or uncemented hip megaprosthesis in the treatment of proximal femur metastasis.

Materials and Methods

A systematic review of the literature indexed in PubMed, MEDLINE and Cochrane Library databases using as search-terms ((modular prosthesis) OR (modular prostheses) OR (endoprotheses) OR (megaprosthesis) OR (prostheses)) AND ((metastasis) AND ((femur) OR (femoral) OR (hip) OR (limb))) was performed. The Preferred Reporting Items for Systematically Reviews (PRISMA) was follow as reported in Figure 1.

Only English publications were evaluated.

The following criteria of eligibility were used: demographic features, disease localization, type of megaprosthesis,

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possible complications and clinical outcomes. Abstracts and full texts were independently screened by two authors (R.V. and G.R), any discordance was solved by consensus with a third author (A.Z.). At the end of the screening of abstracts and full-text papers 30, 12 manuscripts were included in our review, since they met our inclusion criteria.

Results

Twelve articles were finally included in the review (Table 1).

All the studies were case-series without randomization except one that was a case-report.

1137 patients were present in all the studies; due to the non-homogeneity of the papers is not possible to calculate how many patients were affected by proximal femur metastasis treated by excision and replacement by megaprosthesis.

In two studies were used uncemented megaprotheses and in eight studies were used cemented ones; in only two studies was carried out a comparison between cemented and uncemented megaprosthesis.

The most frequent primary tumor were breast, lung, myeloma and kidney cancer.

The clinical evaluations of the outcomes were performed by MusculoSkeletal Tumor Society rating (MSTS), walking recovery and use of crutches and Karnofsky Performance Status (KPS); the pain evaluation was performed by visual analogic scale (VAS).

Several types of megaprotheses were used, such as GMRS® (Stryker), MUTARS® (Implantcast) and MRP® (Gruppo Bioimpianti).

The most frequent complications recorded were infection (surgical site infection and deep infection), dislocation, aseptic loosening and internal pathologies (pulmonary embolism, myocardial infarction, deep vein thrombosis, pneumonia).

Discussion

Clinical outcomes

Consulting the literature, it is possible to find different studies involving patients undergoing salvage limbs surgery on neoplastic lesions.

Many of these studies focused on analyzing functional outcomes following this surgery, but none of them compared directly functional outcomes in cemented and cement less endoprosthetic replacement, while other distinctions were made, as the nature of the lesion (primary vs secondary) or the type of surgical treatment adopted (nailing vs prosthesis).^{6,14}

The most frequently adopted rating

scales have been Karnofsky Performance Status (KPS) and MusculoSkeletal Tumor Society rating (MSTS).

According to Potter, the cohort of patients treated with cemented megaprosthesis, has a MSTS score that was 66.8% for metastatic disease. Potter analysis demonstrated that both patient age and diagnosis were significant independent predictors of MSTS functional scores.¹⁴

Bischel treated patients with cemented

prostheses. Both Karnofsky index and MSTS score improved from pre-operative to post-operative period, and this result was confirmed also by Angelini *et al* in their study. The use of a Trevira tube did not influence the functional outcome.⁵

According to Piccioli, who analyzed a cohort of predominantly metastatic patients (66%) treated with cementless prosthesis, the MSTS score increased after surgery from 29.3% to 82.5% and SF-36 from 41.2 to

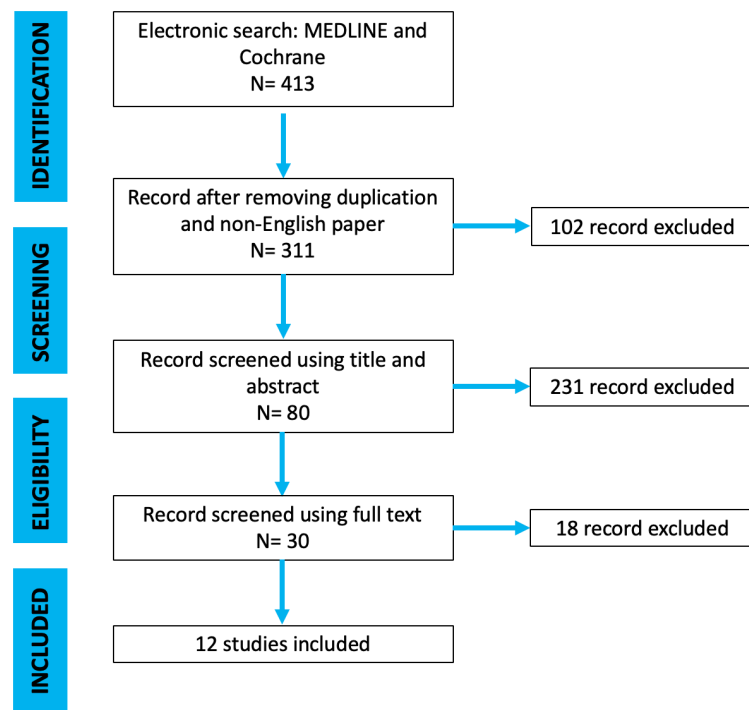


Figure 1. PRISMA flowchart.

Table 1. Review of the literature.

Authors	Mean Age	Sex	Type of Study	Cases	MSTS (improvement)	Infection	Dislocation	Cemented /Cementless	Followup (months)
FDonati (2016)	61.6	31M/37F	Retrospective	68	0	8	0	Cementless	46.5
E. Pala (2013)	47	122M/110F	Retrospective	232	0	20	2	48 cemented 10 cementless	28
A.Angelini (2018)	63.6	11M/29F	Prospective	40	22.4	2	3	Cemented	10.2
Johannes KM Fakler (2013)	69.8	9F/11M	Retrospective	20	0	2	0	Cemented	25
Grzegorz Guzik (2018)	69.5	77F/45M	Retrospective	122	19.8	0	0	22 cemented 53 cementless	27
Stein J. Janssen (2016)	62	163m/254f	Retrospective	417	0	6	1	48 Cemented 54 Cementless	4
P.E. Ferrara (2001)	61,7	7m/14f	Retrospective	21	65	6	0	Cementless	12
Oliver E. Bischel (2020)	58.7	26f/19m	Retrospective	45	54.9	1	6	Cemented	16.4
Chandra Prakash Pal (2012)	65	1F	Case Report	1	0	0	0	Cemented	11
Andreas F. Mavrogenis (2012)	63.5	53M/57F	Retrospective	110	0	3	1	Cemented	18
Piccioli (2016)	56.2	14M/16F	Retrospective	30	82.5%	5	2	Cementless	38.8
Benjamin K. Potter (2008)	58	33M/26F	Retrospective	61	71.7%	6	4	Cemented	55.4

46.7, respectively.¹⁵ The same kind of patients were analyzed by Ferrara *et al* in their study, in which they observed the trend of the values of various scales of functional outcomes assessment over a year.¹⁶ The MTST reached the peak value six months after the intervention thanks to early rehabilitation.

The improvement of ROM and muscle strength was progressive, like the self-sufficiency and psychophysical conditions.

Guzik *et al.* observed exclusively metastatic patients and used both surgical techniques. Cemented proximal femur modular stem was used in 22 cases (GMRS-Stryker) and cementless in 53 cases (MUTARS- Implant Cast).¹⁷ Mean MSTS score was 6.4-19.8 points before and after-surgery respectively, but no clear distinction was made between the two considered categories.

Complications

In this review we analyzed 12 articles about the use of cemented or cement less stems in PFR.

Six authors used cemented mega prostheses, 3 both cemented and cement less ones, 2 authors used cementless ones, one author doesn't report any complications.

In the group of cemented mega prostheses Potter *et al* treated 39 patients with PFR and mega prostheses for metastatic disease.¹⁴ The main complication were infections (4,9%), dislocations (6,6%) and aseptic loosening. It is not specified if the patients affected by these conditions were treated for primary or metastatic bone tumors. Also in the study of Angelini *et al* overall complication rate was 22,5% (9/40 patients), most of all infections and dislocations.¹

Bischel treated metastatic patients with hip megaprosthesis. Implant removal was performed on one patient due to infection.⁵ Six patients suffered from prosthetic dislocation and 4 needed an open reduction. In these four cases, 3 were total hip arthroplasties. The author specifies that the dislocation was found in patients with soft-tissue deficiency in which Trevira tube was used, while none of the patients with sane soft-tissue suture suffered from prosthesis dislocation.

Janssen treated 70 patients with proximal femur metastatic disease with PFR among 417 patients.³ He reports 2 intraoperative deaths during endoprosthetic reconstruction (one of them with modular prosthesis) with cemented femoral implants. This is the first study in which death during cemented implantation is described, though many authors described an increase of cardiovascular dysfunction or embolic

syndrome during this kind of procedure, most of all in metastatic patients. Jansen also describes that pneumonia, myocardial infarction, pulmonary embolism and sepsis occurred in his patients, even if we can not know if they were metastatic patients or not.^{12,13} The only authors that report few complications are Mavrogenis *et al* and Pal *et al.* Mavrogenis treated 42 metastatic patients with PFR and had one case of dislocation solved with a close reduction while Pal *et al* reported no complications in their patient affected by proximal femur metastatic adenocarcinoma at 1 year follow-up.^{6,10} In the group of cementless megaprosthesis Donati treated 68 patients, 45 of them with metastatic disease. He reported complications in 14 cases (20,6% of the population), with 11,8% of infections.¹⁸ It is impossible to state if the complication occurred in the primary bone tumor or metastatic group.

In another study, Piccioli *et al* involve 30 patients, but just 11 of them are treated for PFR, while the others have other district involved (total femur, proximal tibia, proximal humerus).¹⁵ Also in this case complications presented in 30% of the population with an infection rate of 16,7%. It is not specified if the proximal femurs were treated for primary tumor or metastatic disease and if complications occurred in PFR, due to the variously treated patients. Also authors that used both techniques, cemented and cementless megaprosthesis, presented delayed wound healing, infection and aseptic loosening.^{10,17} While Guzik used 22 cemented and 53 cementless prosthesis, Pala used 48 cemented stems and 10 cementless stems.^{10,17} Pala is the only author that compares these techniques and reports that infections and aseptic loosening are higher in cemented mega prosthesis replacements.¹⁰ It is peculiar to observe that although cementation is the preferred techniques by almost all the authors only Jansen refers the occurrence of one intraoperative death due to cementation procedure. As already said, it is described that in metastatic patients this kind of complication can reach the 8% of all patients but is not described in the considered studies.^{12,13}

In addition to that it is possible to notice that complications are similar in the cemented and cementless megaprosthesis, and this is probably mostly due to the surgical aggressiveness and to the kind of treated patients. Infection is the most common complication in this kind of surgery. Most of the authors treated this redoubtable event with antibiotics in post-operative period, but only two of them specify what kind of pre-operative

prophylaxis has been used. Potter *et al* used a first generation cephalosporin continued for 48h post-operatively.¹⁴ Pala *et al* preferred a pre-operative prophylaxis with teicoplanin and amikacin prolonged for 5 days after surgery.¹⁰ Piccioli *et al* and Donati *et al* used a prophylaxis with cefazolin, that seems to be safe as pre-operative prophylaxis in orthopaedic oncologic surgery.^{15,18,19}

Bischel in his study associates prosthesis dislocation to the soft tissue deficiency and the use of Trevira tube.⁵ This kind of statement counteracts with other studies that affirm that Trevira tube can lower dislocation rate in hip mega prostheses, thanks to its capability to improve left soft tissue adhesion on its surface, not increasing infection rate.^{18,20,21}

Survival rate

The mean survival after modular endoprosthetic replacement was almost two years in many articles.¹⁷

In 2013, Pala *et al.* retrospectively analyzed 232 patients treated with lower limb salvage surgery and reconstruction using cemented and cementless endoprostheses and the overall survival at 60 months was 64 and 78% respectively.¹⁰

In literature overall survival rate at 1 year in cemented implant ranges from 42% to 75% and these data were confirmed by the study of Angelini (58% survival at 1 year) and Bischel *et al* (52.9% one year survival rate).^{1,5} Bischel found also no difference between survival rates of patients with solitary or disseminated disease.⁵ Fakler retrospectively studied cemented prosthesis in 8 patients who had a survival rate at six and twelve months of 45.0% and 35.0%, respectively.²² This datum is lower, if compared to the survival rate of Angelini and Bischel.^{1,5}

The 1-year survival is related to type of tumor both in cemented and cementless stems: it is higher for patients with renal cancer metastasis and myeloma, compared to breast cancer (mean survival time 10 months) or lung cancer (mean survival time 13 months).^{1,6,15,16}

In terms of patient survival rate, it is very difficult to estimate the role of the surgical method or the choice of implant. Many cofactors may influence patient survival as age, gender, BMI, preoperative general health status, type of cancer, location of metastasis, solitary versus multiple metastases, radiation therapy and chemotherapy.

But in lots of studies with multivariate analysis, cement/cementless type of stem fixation was also the only significant variable for predicting survival.^{6,10,15,22}

According to E. Pala *et al* in 2013 there is a positive trend on survival with the use of chemotherapy rather than radiotherapy, but this can depend on the fact that most of patients who made radiotherapy treatment had metastatic disease.¹⁰

In addition, combination of radiation therapy with chemotherapy sensitizes normal tissues to radiation, and this may cause more complications in relation to radiation therapy alone.¹⁰

Conclusions

In consideration of the analyzed literature, the stem cementation of hip megaprotheses is preferred. The comparison between cemented and cement less megaprotheses in proximal femur metastases is still poor.

Despite this, it appears that more and more data are supporting the use of cementless hip megaprotheses; in fact they seem to guarantee better functional outcome, longer implant survival and lower rates of complications.

In the future, more studies should be focused on the comparison between these two surgical techniques, and how they can affect patients' quality of life.

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