

A systematic review of endoprosthetic replacement versus cement spacer in reconstruction of proximal humerus following proximal humerus metastasis

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Background

The choice between cement spacer and endoprosthesis in the treatment of metastatic lesions to the proximal humerus is increasingly controversial. However, it may be easier to categorize the patients, and their socioeconomic and perioperative parameters into two groups.

Aim

This work aims to review the available literature on the topic of endoprosthetic replacement versus cement spacer in the reconstruction of the proximal humerus following metastatic lesions to the proximal humerus regarding the surgical technique, its indications, its advantages, and limitations.

Patients and methods

We followed the preferred reporting items for systematic review and Meta-analysis (PRISMA) statement guidelines during this systematic review and performed all steps according to the Cochrane Handbook of Systematic Reviews of Intervention.

Results

Four studies were included in this systematic review, and a total of 100 patients were included (22 of which had cement spacer and 78 had endoprosthesis). Several parameters were compared in the reviewed studies including the MSTS score of the patients; the primary tumor; postoperative complications; the patients' age; follow-up periods; and the presenting symptoms of the patients.

Conclusion

This systematic review suggests that the cement spacer technique is not inferior to endoprosthetic replacement of the proximal humerus in cases of metastases. Therefore, we suggest that determining whether to use an end prosthesis or a cement spacer depends on categorizing the patients into two groups. Endoprosthetic replacement will be an appropriate choice for patients with preserved deltoid and axillary nerve function following resection, solitary and nonaggressive metastatic lesion, and long-life expectancy with minimal co-morbidities. We believe that cement spacer is a more appropriate choice in patients with nonfunctioning deltoid or axillary nerve following resection; multiple and aggressive metastatic lesions; short life expectancy with many co-morbidities, and poor socioeconomic status.

Keywords:

cement spacer, endoprosthetic replacement, proximal humerus metastasis, proximal humerus

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Introduction

The proximal humerus is the third common site for primary and metastatic tumors of bone [1]. Multiple treatment options have been reported recently. In most cases, surgery is a major component of therapy. Patient acceptance for limb-preserving treatments is high.

Therefore, amputation of the shoulder girdle should be avoided if possible [2,3]. The unpredictable life expectancy of patients with metastases [1,4], accompanied by often high failure rates after internal fixation with or without intralesional resection and radiotherapy [5,6], has led to more aggressive surgical

techniques being researched to resect and reconstruct the proximal humerus [7].

Many reconstruction techniques may be implemented to reconstruct the proximal humerus following its resection. The most commonly used reconstructive techniques after resection of the proximal humerus following metastatic disease are endoprosthetics and cement spacers. Other techniques may be used for

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the reconstruction of the proximal humerus following the resection of a primary tumor such as allograft–prosthesis composite, osteoarticular allografts, and autograft–prosthesis composite [7].

Risks vary depending on the choice of reconstruction. Biological reconstruction may be complicated by the incidence of infection, subchondral collapse, and fracture, leading to implant removal or revision especially following extensive chemo and radiotherapy to the site of reconstruction. Also, difficulties with an endprosthesis involve consequences of surgical resection of the deltoid and the rotator cuff. These involve proximal instability, subluxation and a reduction in the functional range of motion [2,3,8–10].

Wide end bloc intra-articular excision and reconstruction of the defect with a nail cement spacer is a palliative therapy option for metastatic lesions to the proximal humerus [11]. The advantages of this method is that it is a low cost, and a relatively easy surgical procedure with rapid recovery of limb function [12].

Aim

This work aims to review the available literature on the topic of endoprosthetic replacement versus cement spacer in the reconstruction of the proximal humerus following metastatic lesions to the proximal humerus regarding the surgical technique, its indications, its advantages and limitations. In addition to an evaluation of its effectiveness in improving the patients' quality of life by decreasing postoperative pain, allowing satisfactory limb function and not being a major financial burden on the patient and being an appropriate economical choice.

Methodology

We followed the preferred reporting items for systematic review and Meta-analysis (PRISMA) statement guidelines during this systematic review, and performed our research in accordance with the Cochrane Handbook of Systematic Reviews of Intervention [13]. Search Strategy and Study Selection, We searched PubMed, Science Direct, Cochrane Library, Scopus, and Google Scholar. The search interval is from May 2000 to December 2022. A variety of Medical Subject Headings (MESH) was used: ('proximal humerus metastasis*' OR 'proximal humerus secondaries*' OR 'proximal humerus neoplasm*' OR 'Proximal humerus tumor*' OR 'proximal humerus cancer*') AND (Endprosthesis* OR 'Joint replacement*' OR 'arthroplasty*').

Also the MESH ('proximal humerus metastasis*' OR 'proximal humerus secondaries*' OR 'proximal humerus neoplasm*' OR 'Proximal humerus tumor*' OR 'proximal humerus cancer*') AND 'cement spacer*' was used and the following free text words were used: 'Proximal Humerus Metastasis' combined with 'Cement Spacer' or 'Endprosthesis Replacement Humerus'. Additional search for more contemporary content along with previous reviews, examination of previously cited references and expert opinions was carried out. Only a Systematic Review was conducted and not a meta-analysis as there was insufficient material to conduct a meta-analysis.

Types of participants

Inclusion Criteria: Patients with proximal humerus metastasis or pathological fractures of the proximal humerus as a result of metastasis

Exclusion Criteria: Patients with diseases to the proximal humerus other than metastasis such as osteoarthritis or traumatic fractures to the proximal humerus or primary tumors.

Type of intervention

Endoprosthetic replacement of the proximal humerus, cement spacer with Hackethal, Rush and Seidel Rods of the proximal humerus; or intramedullary nails

Types of outcome measures

Musculoskeletal Tumor Society System (MSTS), radiological assessment using antero-posterior and Lateral radiography Radiographs as well as CTs (Computed Tomography) and MRI (Magnetic Resonance Imaging), clinical assessment of shoulder mobility and function, the functional assessment of cancer therapy-general (FACT-G).

All published articles were screened with no restrictions for data of search. Titles and abstracts were done in two parts, followed by full-text screening. Reference lists of the included studies were manually screened to find any other eligible studies that may be omitted from previous steps.

Results

Literature search results

The initial search resulted in 109 articles from five databases including PubMed, Science Direct, Cochrane Library, Scopus, and Google Scholar. 0 studies are retrieved from additional databases. The total number before duplicates removal is 109 records. Of these 109 articles, we excluded 29 articles due to duplication. 80 articles underwent title and abstract screening, and 76 were excluded because they did not

meet the inclusion criteria. The remaining 4 articles underwent full-text screening. A total of 4 studies were finally included for the final qualitative synthesis and the quantitative analysis. Exclusion from the full-text screening was due to the papers comparing the use of cement spacers and endprosthesis in the reconstruction of the proximal humerus in primary tumors not in metastatic lesions (Fig. 1).

A systematic review of the literature was conducted and not a meta-analysis as there was insufficient material to conduct a meta-analysis as only 1 paper was found comparing the cement spacer and endprosthesis in the reconstruction of the proximal humerus following a metastatic lesion. Therefore there was no measure of association and the cumulative odds ratio couldn't be calculated.

Baseline characteristics of included studies

A total of four studies were included Casadei *et al.* [14] Guo *et al.* [15], Rovere *et al.* [16], Scotti *et al.* [13]. The baseline clinicodemographic characteristics of included

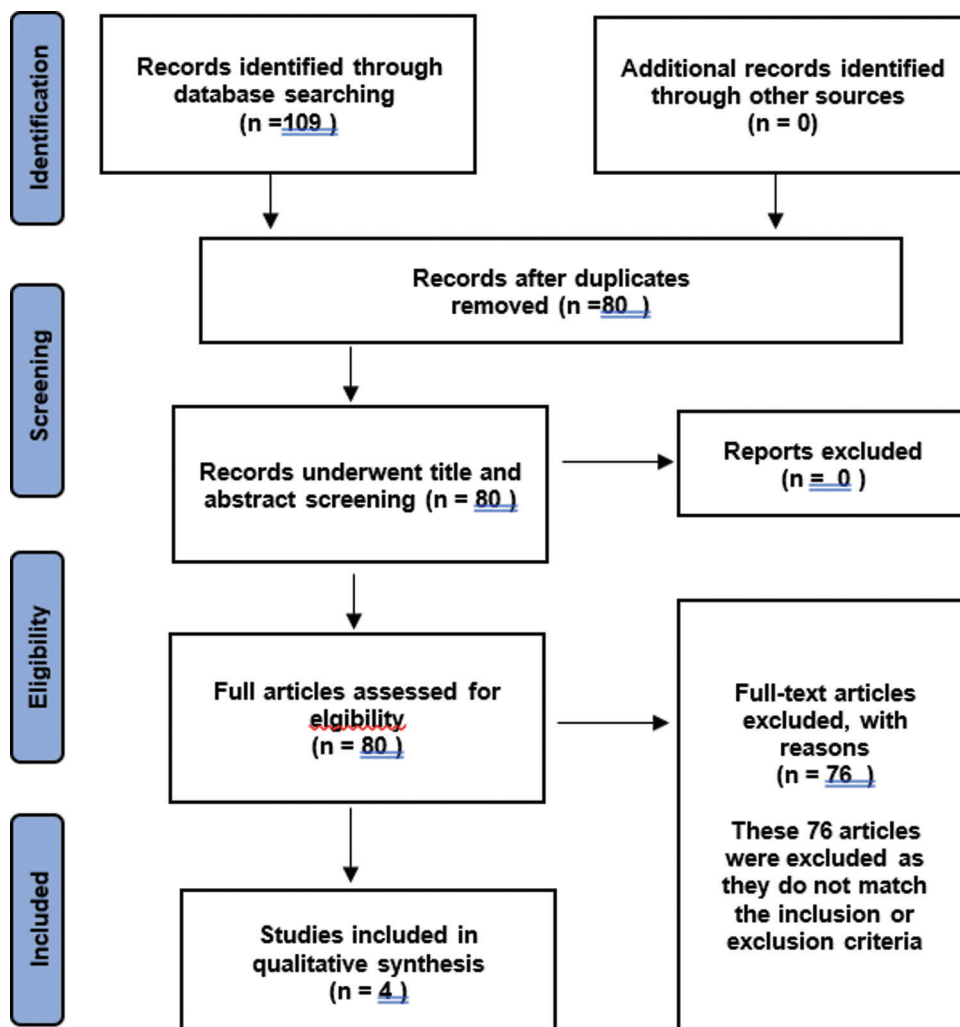
studies and patients were summarized in Table 1. A total of 100 patients were included in the final analysis, distributed as follows: 78 in the endoprosthesis group and 22 in the cement spacer group.

The age of included patients ranged from 56 to 67 years, with an average age of 61 years. The follow-up period ranged from 22 to 42 months in the endoprosthesis group and from 5 to 42 months in the cement spacer group.

Clinical characteristics of included patients

Patients who underwent cement spacer were more likely to present with a pathological fracture as compared with those in the endoprosthesis group (100% vs. 55%). In terms of primary treatment of the pathological fractures, 44.9% (35/78) of patients in the endoprosthesis group underwent resection, while the rest had the endoprosthesis span and internally splint the fracture site; this is compared with 0% of patients in the cement spacer group, where debulking and spacer application were done primarily. This showed a

Figure 1



PRISMA (preferred reporting items for systematic review and Meta-analysis) flow diagram for study selection.

Table 1 Baseline clinic-demographic characteristics of included studies

Author (YOP)	Sample Size, N		Age, years		Mean follow-up, months		Pathological Fracture, N (%)		Resection as primary treatment, N	
	Endoprosthesis	Cement Spacer	Endoprosthesis	Cement Spacer	Endoprosthesis	Cement Spacer	Endoprosthesis	Cement Spacer	Endoprosthesis	Cement Spacer
	Scotti <i>et al.</i> [13] (2008)	40	NA	67	NA	32	NA	12 (30)	NA	28 (70)
Casadei <i>et al.</i> [14] (2018)	29	NA	62	NA	22	NA	22 (76)	NA	7 (24)	NA
Guo <i>et al.</i> [15] (2019)	0	15	NA	56	NA	4	NA	NA	NA	0
Rovere <i>et al.</i> [16] (2022)	9	7	58	61	42	42	9 (100)	7 (100)	0	0

N, Number of Patients; NA, Not Available; YOP, Year of Publication.

significantly higher likelihood of undergoing primary resection in the endoprosthesis group compared with the cement spacer group.

Tumor characteristics of included patients

Regarding primary tumor site, we noted a substantial difference between those who underwent endoprosthesis and cement spacer. For instance, compared with cement spacer, patients who received the endoprosthesis management were more likely to have renal cell carcinoma (RCC) (10% vs. 65%), melanoma (0% vs. 2%), and plasmacytoma (0% vs. 2%), respectively. On the other hand, participants who received the cement spacer management were more likely to have breast cancer (21% vs. 12%), lung carcinoma (16% vs. 5%), liver cancer (10% vs. 0%), prostate cancer (10% vs. 4%), and gastrointestinal tract (GIT) cancer (5% vs. 0%).

Postoperative complications

Four main postoperative complications have been reported in individual studies, including dislocation, infection, local recurrence, and neurological injury. In the cement spacer group, no complications were reported. The patients in the endoprosthesis group had an infection rate of 4% (3/78). In the endoprosthesis group, local recurrence was commonly encountered during the postoperative period, accounting for 6% (5/78) of cases. Meanwhile, dislocation 3% (2/78) and neurological injuries 1% (1/78) occurred as rare events during the postoperative period in the endoprosthesis group.

Functional outcome (MSTS scale)

The Musculoskeletal Tumor Society (MSTS) scoring system was used to assess the functionality of patients who underwent either endoprosthesis or cement spacer. The MSTS scale is given a score ranging from 0 to 100%, is given to each patient. The mean MSTS score in the endoprosthesis group was 73.2% ranging from 64% in the study of Casadei *et al.* [14] to as high as 87.5% in the study of Scotti *et al.* [13]. Meanwhile, in the cement spacer group, the mean MSTS score was lower (69.1%), ranging from 57% as reported in the study of Guo *et al.* [15] to 81.65% as reported in the study of Rovere *et al.* [16].

Discussion

Literature is rich with studies on different techniques in the reconstruction of the proximal humerus following primary proximal humerus tumors, however there is still controversy regarding the optimal method of reconstruction of the proximal humerus following a metastatic lesion. Four studies were included in this systematic review, a total of 100 patients were

included (22 of which had cement spacer and 78 had endprosthesis).

The age groups of the patients studied ranged from 56 to 67 years in the studied groups (with a total average age of 61 years) so there wasn't a significant difference in the ages of the patients.

When comparing the mean period of follow-up, it was found that in studies of the endprosthesis group had a longer period of follow-up ranging from 22, 32 and 72 months according to Scotti *et al.* [13] Cassadei *et al.* [14] and Rovere *et al.* [16], respectively. However, in the cement spacer group a short follow-up period was conducted as in the case of Guo *et al.* [15] which had a mean follow-up period of 5 months. This maybe correlated to the fact that patients who were treated with cement spacers had a shorter life expectancy than those treated with endprosthesis, therefore denoting the difficulty in long term follow-up in patients with cement spacer. As according to Guo *et al.* [15] 64% of patients had a mean survival period of 11 months.

As much as it was necessary, it was difficult to compare the life expectancies and the mean survival periods of the patients included in the studies. This is because not all of the studies provided the data on the mean survival period of the patients.

As regards to the MSTTS score, the endprosthesis group averaged a slightly higher MSTTS score at 70.68% in comparison with the cement spacer group which averaged 69.25%. The lower MSTTS score in the cement spacer group was due to the study done by Guo *et al.* [15] where the MSTTS score averaged 57% at a mean follow-up period of 5 months. This was significantly lower than the study by Rovere *et al.* [16] which had an average MSTTS score of 81.65%.

The difference in results between the MSTTS scores in the studies conducted by Guo *et al.* [15] and Rovere *et al.* [16] may be due to the difference in the follow up periods. Also, it may be due to the difference in the patients' general condition, co-morbidities, aggressiveness of the metastatic lesion and whether it was multiple or solitary. In Rovere *et al.* [16] it was mentioned that an anterograde static locked undreamed intramedullary nail was used as a pillar for the cement used, however, in Guo *et al.* [15] the exact technique of the application of the Cement Spacer was not mentioned.

It was noted that in the study of Guo *et al.* [15] 30% of the patients were able to obtain 90° of shoulder

abduction with physiotherapy and most patients had painless distal limb function. However, in the study conducted by Rovere *et al.* [16] the MSTTS score averaged 80 and 84% at 12 and 72 months, respectively. At 12 months follow-up, there was significant pain reduction and the patient had the capability of carrying out daily activities but with absolute inability to carry heavy objects. However, at 72 months follow-up, it was noted that there was excellent recovery of limb function with no difficulty in carrying out actions of everyday living. Also, in the same study conducted by Rovere *et al.* [16] the endprosthesis group showed an average MSTTS score of 60 and 70.7% at 12 and 72 months of follow-up, respectively. At the 12 months follow-up, there was medium difficulty in conducting everyday activities with great difficulty in conducting heavy activities. However, at the 72 months follow-up, there was mild difficulty in daily activities as there was still difficulty conducting activities needing medium to large strength.

In comparing the different complications that occurred following cement spacer or endprosthesis application, it was found that no complications and in particular, no infection was identified in the papers that studied patients with cement spacer. This may be attributed according to Guo and colleagues to the usage of antibiotic impregnated cement when applying the cement spacer. However, in studies of the endprosthesis, it was noted that local recurrence was the most common complication followed by infection, dislocation and neurological injury. This may be due to the possibility of the surgeons' trail to limit the resection to try to preserve a functional axillary nerve and deltoid as well as the possibility of preserving the rotator cuff. However limitations do exist when comparing the complications, as some papers like Rovere and colleagues mentioned the presence of neurological complications and infections but the exact number of cases attributed to either cement spacer or endprosthesis could not be separated and identified.

When comparing the tumor characteristics of the studied patients, it was found that renal cell carcinoma was the most prevalent in the endprosthesis group. The most prevalent primary tumor site in the cement spacer group was breast cancer, followed by Lung carcinoma then renal cell carcinoma. However it may be due to a selection bias that the renal cell carcinoma was the most prevalent in the endprosthesis group, as the study of Casadei *et al.* [14] only studied metastatic lesions to the proximal humerus due to renal cell carcinoma which accounted for 29 out of the 78 patients. Whether the metastatic lesion to the proximal humerus was solitary or multiple could not be analyzed as the relative

information could not be isolated and most papers did not include it in their studies.

Conclusion

This systematic review suggests that cement spacer technique is not inferior to endoprosthetic replacement of the proximal humerus on cases of metastases. Therefore, we suggest that determining of whether to use an end prosthesis or a cement spacer depends on categorizing the patients into two groups. Endoprosthetic replacement will be an appropriate choice for patients with preserved deltoid and axillary nerve function following resection; solitary and non-aggressive metastatic lesion; long-life expectancy with minimal co-morbidities. We believe that cement spacer is a more appropriate choice in patients with nonfunctioning deltoid or axillary nerve following resection; multiple and aggressive metastatic lesions; short life expectancy with many co-morbidities, and poor socioeconomic status.

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Availability of data and material (data transparency)

The authors confirm that all data and materials as well as software application or custom code support their published claims and comply with field standards.

Authors' contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by all authors. The first draft of the manuscript was written by Dr Ayman El Masry and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval

This meta-analysis and systematic review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent for publication

Patients signed informed consent regarding publishing their data and photographs.

The authors state that the manuscript has been read and approved by all the authors and that the requirements for authorship as stated earlier in this document have been met and that each author believes that the manuscript represents honest work.

Conflicts of interest

The authors declare they have no conflict of interest in preparing this paper.

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