Musculoskeletal Tumor Society

# MANAGEMENT OF METASTATIC HUMERAL DISEASE

## Clinical Practice Guideline

*Adopted by:*
The Musculoskeletal Tumor Society Executive Committee
April 12, 2023

## Disclaimer

This clinical practice guideline (CPG) was developed by the clinical practice guideline development group composed of volunteer physicians based on a formal systematic review of the available scientific and clinical information and accepted approaches to treatment and/or diagnosis. This clinical practice guideline is not intended to be a fixed protocol, as some patients may require more or less treatment or different means of diagnosis. Clinical patients may not necessarily be the same as those found in a clinical trial. Patient care and treatment should always be based on a clinician's independent medical judgment, given the individual patient's specific clinical circumstances.

### Disclosure Requirement

In accordance with Musculoskeletal Tumor Society (MSTS) and American Academy of Orthopedic Surgeons (AAOS) policy, all individuals whose names appear as authors or contributors to the clinical practice guideline filed a disclosure statement as part of the submission process. All panel members provided full disclosure of potential conflicts of interest prior to voting on the recommendations contained within this clinical practice guideline.


### Funding Source

This clinical practice guideline was funded exclusively by the Musculoskeletal Tumor Society who received no funding from outside commercial sources to support the development of this document.


### FDA Clearance

Some drugs or medical devices referenced or described in this clinical practice guideline may not have been cleared by the Food and Drug Administration (FDA) or may have been cleared for a specific use only. The FDA has stated that it is the responsibility of the physician to determine the FDA clearance status of each drug or device he or she wishes to use in clinical practice.




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## SUMMARY OF ACTION STATEMENTS

### 1. Plating/Internal Fixation, Intramedullary Fixation, and/or Photodynamic Polymer

**When treating pathologic diaphyseal humerus fractures, clinicians can consider either the use of plating/internal fixation, intramedullary fixation, and/or photodynamic polymer, as there does not appear to be a significant difference in clinical outcomes or reoperation rate between these constructs based on limited available evidence.**

- Combined Strength of Recommendation = **Limited**

### 2. En Bloc Resection, Curettage, Internal Fixation, Or Intramedullary Nailing

**No studies met inclusion criteria comparing survivorship or other oncologic outcomes between en bloc resection, curettage, internal fixation, or intramedullary nailing. Based on the lack of evidence, no recommendations can be made for or against en bloc resection pertaining to metastatic disease of the humerus.**

- Combined Strength of Recommendation = **N/A**

### 3. Patient Selection for Nonsurgical Techniques Versus Surgical Techniques

**No studies met inclusion criteria to compare nonoperative vs operative treatment in the setting of metastatic disease of the humerus. Based on the lack of definitive evidence, no recommendations can be made for or against patient selection or indication for nonoperative vs. operative treatment pertaining to metastatic disease of the humerus.**

- Combined Strength of Recommendation = **N/A**

### 4. Cementation Vs No Cementation

**In patients undergoing surgical fixation of the humerus for metastatic bone disease, clinicians may consider cement augmentation. Two low quality studies meeting inclusion criteria suggested the addition of cement to surgical fixation of pathologic fractures of the humerus may provide short-term improvements in pain relief and functional mobility, however no difference in surgical complications were observed.**

- Combined Strength of Recommendation = **Limited**

## 5. Reconstruction Approach

**In patients undergoing arthroplasty to reconstruct the proximal humerus for metastatic bone disease, clinicians may consider reverse total shoulder arthroplasty over conventional shoulder arthroplasty and hemiarthroplasty in order to decrease shoulder instability and improve range-of-motion.**

- Combined Strength of Recommendation = **Limited**

## 6. Prognostic Markers

**Based on low levels of evidence, clinicians should consider the following potential negative socioeconomic prognostic markers when caring for patients with metastatic malignancy of the humerus:**

- **Age > 60 years**
- **Have Medicaid insurance compared to commercial insurance**
- **Black race compared to white race**
- **Lower income status**
- **Lower initial performance status**
- **Male sex**
- **Rapidly growing tumor histologies versus slow growing**

- Combined Strength of Recommendation = **Limited**

## 7. VTE Prophylaxis

**There is no available evidence to make an Action Statement on VTE prophylaxis for metastatic bone disease of the humerus. In the absence of direct evidence, we refer clinicians to the ASCO, ASH, and ICM-VTE guidelines which indicate that oncology patients are at a higher risk for VTE, and prophylaxis should be considered during the peri-operative period.**

- Combined Strength of Recommendation = **N/A**

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# INTRODUCTION

## Overview

This clinical practice guideline for the surgical management of metastatic humeral disease is based on a systematic review of published studies surrounding the management of metastatic disease, multiple myeloma, and lymphoma limited to the humerus. In addition to providing practice recommendations, this guideline also highlights both limitations in the literature and consequent areas that should be the focus of future research collaborations.

This guideline is intended to be used by all qualified and appropriately trained physicians and surgeons involved in the surgical management of metastatic disease of the humerus. It is also intended to serve as an information resource for decision makers, researchers, and developers of practice guidelines.

## Goals and Rationale

The purpose of this clinical practice guideline is to help improve treatment based on the current best evidence available. Practicing evidence-based medicine (EBM) demands that physicians use the best available evidence in their clinical decision making. The systematic review detailed herein was conducted between January 2022 and August 2022. These guidelines demonstrate where there is good evidence, where evidence is lacking, and what topics future research must target in order to improve the management of bony metastatic humeral disease burden. AAOS staff and the physician work group systematically reviewed the available literature and subsequently wrote the following recommendations using a rigorous, standardized process. Musculoskeletal oncology care in the setting of metastatic disease is provided in many different settings by many different providers. We created this guideline as an educational tool to guide qualified physicians through a series of treatment decisions in an effort to improve the quality and efficiency of care. Providers that may be impacted by the guideline include both surgical and non-surgical specialists. This guideline should not be construed as including all proper methods of care or excluding methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment must be made in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution.

## Intended Users

This guideline is intended to be used by orthopaedic surgeons and physicians managing metastatic bony disease of the humerus. While a fellowship-trained orthopaedic oncologist is considered a target audience for these guidelines, the rising burden of skeletal related events (SREs) due to metastatic disease means that management of metastatic bony disease will be increasingly shared burden amongst a variety of providers. This guideline addresses prognostic implications, peri-operative management, and operative vs. non-operative decision making that can help guide decision making for general/non-oncology orthopaedic specialty trained surgeons. Insurance payers, governmental bodies, and health-policy decision-makers may also find this guideline useful as both a foundation of evolving standard of evidence regarding management, as well as opportunities for future funded research surrounding management of humerus metastatic disease burden. Adult primary care physicians, medical oncologists, radiation oncologists, geriatricians, palliative medicine specialists, hospice providers, hospital based adult medicine specialists, physical therapists, occupational therapists, nurse practitioners, physician assistants, emergency physicians, and other healthcare professionals who routinely see this type of

patient in various practice settings may also benefit from this guideline.

Management of metastatic disease in the bony humerus is based on the assumption that decisions are predicated on communication between the patient and/or the patient's qualified heath care advocate and their physician regarding available treatments and procedures applicable to the individual patient. Once the patient and or their advocate have been informed of available therapies and have discussed these options with his/her physician, an informed decision can be made. Clinician input that balances their experience with conservative management and the clinician's surgical experience and skill set increases the probability of identifying patients who will benefit from specific treatment options. Because of the prognostic implications of metastatic (Stage 4) cancer, the decision-making process should weigh the goals of improved function and pain versus the recovery required and potential complications from a chosen intervention. Shared decision making with a multi-disciplinary team of surgeon providers, cancer providers, and ancillary rehabilitation specialists creates the best opportunity in determining the correct treatment for each patient.

## Patient Population

This document addresses the management of metastatic disease of the humerus. Multiple myeloma and lymphoma skeletal involvement can be considered as equivalent to metastatic malignancy. This guideline is not intended to address management of primary sarcomas involving the skeletal anatomy of the humerus or aggressive benign tumors of the humerus. This guideline also does not address metastatic disease of the peri-scapular location around the glenohumeral joint outside of the humerus. While all age groups were considered, the adult population was the primary focus given the predilection for metastatic disease of the skeleton in non-pediatric age groups.

## Burden of Disease, Incidence & Prevalence

The incidence of Metastatic Bone Disease (MBD) in the United States continues to climb, with estimates that 22 million Americans will have an active cancer diagnosis by 2030. Behind the lungs and liver, bone is the 3rd most commonly affected organ by metastatic cancer. As the incidence of cancer rises, so does the incidence of MBD – and subsequently skeletal related events (SREs). SREs can present in the form of impending or realized pathologic fracture, hypercalcemia, severe bone pain from malignancy, or spinal cord compression. It is estimated that there are now between 600,000 to 800,000 SREs in the United States annually. Additionally, the presentation of one SRE commonly is a harbinger for additional SREs that can occur in increasing frequency. Up to 1 in 5 patients can present with an SRE at the first initial presentation of bony involvement, and autopsy reports have suggested that up to 70% of patients with cancer history have involvement of the skeleton.[1] Additionally, the presence of a SRE has been correlated with worse survival.[2]

The economic burden of cancer care in the United States in 2030 is estimated to approach $246 billion.[3] Nearly one-fifth of this cost is attributed to the treatment of MBD.[1] Current spending on MBD per patient in the United States is approximately $18,000 per year, with overall cost expenditures over a lifetime of cancer treatment more than double in patients with MBD as compared to those without MBD.[1] Financial and Societal costs to be considered include:

1. Direct medical cost

2. Long-term medical and end-of-life cost

3. Balancing pain relief and functional improvement anticipated, the required recovery anticipated, and overall anticipated prognosis.

4. Time off work, disability payments, and family members assisting in care utilizing resources and Family Medical Leave Act (FMLA) assistance

It is also important to note that, with rare exceptions of oligometastatic disease in the setting of breast, thyroid, or renal cancer, the diagnosis of MBD involvement portends an incurable diagnosis. Therefore, the possibility of multiple interventions in a patient over their remaining lifetime of treatment is very real.

The most common sites for MBD involvement are the spine, pelvis, ribs, and proximal femur. Approximately 20% of MBD occurs in the upper extremity, with half of that occurring in the humerus. Additionally, metastatic disease in the humerus accounts for 16-39% of all impending or completed pathologic fractures in long bones.[4] This can dramatically affect the ability to perform activities of daily living (ADLs) and necessary feeding or personal hygiene activity.

## Etiology

Metastatic disease is the result of a primary malignancy arising from a distant organ (breast, colon, prostate, lung, skin, etc.) that spreads to a distant site, such as the skeletal system. This may present incidentally during routine cancer staging/surveillance or in the setting of worsening symptoms. Multiple Myeloma presents as a primary malignancy of the bone marrow and affects the entire skeletal system. Lymphoma can primarily arise in the bone or, more commonly, arise in the lymphatic system (spleen, lymph nodes, etc.) and concurrently involve the bone.

Several steps are involved in the development of metastatic disease. First, tumor cell intravasation needs to occur. This is typically mediated by the E Cadherin cell adhesion molecule on tumor cells. Then, the tumor cells within the blood or lymphatic system must avoid immune surveillance. Next, target tissue localization occurs, and the tumor cells attach to target organ endothelium via Integrin cell adhesion molecules that are expressed on tumor cells. The tumor cells then must extravasate into the target tissue and induce angiogenesis via Vasculoendothelial Growth Factor (VEGF). Finally, genomic instability must be present to allow for unchecked growth and decreased apoptosis.

These tumors, when localized to bone, can then induce osteolysis via upregulation of Receptor Activator of Nuclear Factor Kappa-B Ligand (RANK-L) or blastic disease via Endothelin I. Additionally, bone pain in the setting of BMD may occur from frank bony destruction by tumor grown or tumor-mediated release of cytokines, substance P, or pro-inflammatory molecules, such as the Tumor Necrosis Factor (TNF) superfamily.

## Risk Factors

Risk factors for development of a pathologic fracture of the humerus in the setting of multiple myeloma, lymphoma, or metastatic cancer include, but are not limited to, advanced stages of disease, poor disease control with systemic hormonal or chemotherapy agents, tumor size, faster tumor growth rate, lytic (as opposed to blastic disease), specific tumor location (i.e. tensile portion of the involved bone), continued pain following localized radiation therapy, nonuse of bone modifying drugs (ex. RANK-L inhibitors, bisphosphonates), female sex, advanced age, underlying

osteoporosis, patient noncompliance with medications or weightbearing restrictions, impaired balance, localized trauma, and inadequate home safety or supervision.

### Potential Benefits, Harms, and Contraindications

Most treatments are associated with some known risks, especially invasive and operative treatments. Even conservative non-operative management is not without potential risks to the patient. Contraindications vary widely based on the treatment administered, the performance status of the patient, expected prognosis, and medical comorbidities. A particular concern when managing impending or realized pathologic fractures in the humerus is the potential for the overall fracture treatment to result in increased patient mortality or decreased level of mobility and independence (compared to status prior to the presence of humeral disease). Additional factors may affect the choice of treatment including, but not limited to: associated injuries, mass-effect of the presenting tumor, or disease burden the patient may present with, the individual's age and medical co-morbidities, specific patient characteristics including low bone mass and presence of adjacent joint tumor involvement or pre-existing osteoarthritis, performance status of the patient, patient and family desires and expectations, dominant vs. nondominant extremity, overall prognosis and current or expected response to systemic treatment, radiosensitivity of the specific tumor pathology, or barriers to appropriate follow-up, rehabilitation, and compliance of the patient.

Clinician input based on previous experience increases the probability of identifying patients who will likely benefit from specific treatment options. The individual patient and/or their decision surrogate dynamic will also influence treatment decisions. Therefore, discussion of available treatments and procedures applicable to the individual patient rely on mutual communication between the patient and/or decision surrogate and physician, weighing the potential risks and benefits for that patient. Once the patient and/or their decision surrogate have been informed of available therapies and have discussed these options with the patient's physician via a thorough PARQ conference, an informed decision can be made.

### Future Research

Consideration for future research is provided for each recommendation within this document. In general, we found little high-quality evidence regarding surgical management of humerus metastatic disease. This is not surprising given the rarity of the diseases that orthopedic oncologists treat, and the paucity of data reported for musculoskeletal oncology pathologies as specific as humeral metastatic disease. Historically, single center case series have been the mainstay for orthopedic oncology clinical research and literature, with very few comparative or randomized studies available. The goal for any CPG is to provide evidence-based recommendations, but also importantly to drive future research that will help answer these questions more definitively and improve care and outcomes for the patients involved.[5]

## METHODS

The methods used to perform this systematic review were employed to minimize bias and enhance transparency in the selection, appraisal, and analysis of the available evidence. These processes are vital to the development of reliable, transparent, and accurate clinical recommendations. To view the full MSTS clinical practice guideline methodology please visit http://msts.org/index.php/education/evidence-based-medicine

This clinical practice guideline evaluates the management of metastatic humeral disease. The MSTS approach incorporates practicing physicians (clinical experts) and methodologists who are free of potential conflicts of interest relevant to the topic under study, as recommended by clinical practice guideline development experts.

This clinical practice guideline was prepared by the MSTS Metastatic Humeral Disease Guideline physician development group (clinical experts) with the assistance of the AAOS Clinical Quality and Value (CQV) Department (methodologists). To develop this clinical practice guideline, the clinical practice guideline development group held an introductory meeting on January 15th, 2022, to establish the scope of the clinical practice guideline. As physician experts, the clinical practice guideline development group defined the scope of the clinical practice guideline by creating PICO Questions (i.e., population, intervention, comparison, and outcome) that directed the literature search. The AAOS Medical Librarian created and executed the search (see Appendix III for search strategy).

## Literature Searches

The systematic review begins with a comprehensive search of the literature. Articles we consider must be published prior to the start date of the search in a minimum of three electronic databases; PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials. The medical librarian conducts the search using key terms determined from the guideline development group's PICO questions. The initial literature search was conducted Feb 3rd, 2022, and a final literature search as conducted on May 9th, 2022.
A methodologist reviewed/included primary literature and evaluated all recalled, full-text articles for possible inclusion based on the study selection criteria and summarized the evidence for the guideline development group of who assisted with reconciling possible errors and omissions.
A study attrition diagram is provided in the appendix of each document that details the numbers of identified abstracts, recalled and selected studies, and excluded studies that were evaluated in the CPG. The search strategies used to identify the abstracts is also included in the appendix of the CPG document.

## Defining the Strength of Recommendation

Judging the quality of evidence is only a steppingstone towards arriving at the strength of a CPG recommendation. The strength of recommendation also takes into account the quality, quantity, and the trade-off between the benefits and harms of a treatment, the magnitude of a treatment's effect, and whether data exists on critical outcomes.
Strength of recommendation expresses the degree of confidence one can have in a recommendation. As such, the strength expresses how possible it is that a recommendation will be overturned by future evidence. It is very difficult for future evidence to overturn a recommendation that is based on many high quality randomized controlled trials that show a large effect. It is much more feasible that future evidence could overturn recommendations derived from a few small retrospective comparative studies. Consequently, statements based on the former kind of evidence are given a "strong" strength of recommendation and statements based on the latter kind of evidence are given a "limited" strength. In the event there is no supporting evidence, the strength is unassigned (Table I). The recommendations can be further downgraded or upgraded based on the consensus of the GDG, utilizing the GRADE Evidence to Decision framework criteria. Physician workgroup members utilized an EtD form with numerical scores associated with the individual items. The scores were

summed and predetermined score thresholds were used to suggest whether a recommendation should be upgraded or downgraded (Table II).

## Voting on the Action Statements

The action statements and their strength were voted on by the guideline development group members before and after the final meeting. If disagreement between the guideline development group occurred during the meeting, there was further discussion to see whether the disagreement(s) could be resolved. Approval and adoption of action statements during the development of clinical practice guidelines requires, at minimum, a supermajority (i.e. two-thirds or 67%). GDGs may choose to continue revising a recommendation even if supermajority is reached to refine the statement with the aim of achieving consensus of the entire GDG. All approvals and scores are recorded in the final guideline document to ensure transparency to the end user.

## Peer and Public Review Period

Following the final meeting, the CPG draft undergoes a 3-week review period for additional input from external content experts. Written comments are provided on the structured review form. All reviewers are required to disclose their conflicts of interest.

To guide who participates, the CPG work group identifies specialty societies at the introductory meeting. Organizations, not individuals, are specified. The specialty societies are solicited for nominations of individual reviewers approximately six weeks before the final meeting. The review period is announced as it approaches, and others interested can volunteer to review the draft. The chairs of the guideline work group review the draft of the guideline prior to dissemination.

Some specialty societies (both orthopaedic and non-orthopaedic) ask their evidence-based practice (EBP) committee or equivalent to provide review of the guideline. The organization is responsible for coordinating the distribution of our materials and consolidating their comments onto one form. The chair of the external EBP committees provides disclosure of their conflicts of interest (COI) and manages the potential conflicts of their members.

The MSTS asks for comments to be assembled into a single response form by the specialty society and for the individual submitting the review to provide disclosure of potentially conflicting interests. The review stage gives external stakeholders an opportunity to provide evidence-based direction for modifications that they believe have been overlooked. Since the draft is subject to revisions until its approval by the MSTS Executive Committee as the final step in the guideline development process, confidentiality of all working drafts is essential.

The CPG is also provided to members of the MSTS Executive Committee, relevant external medical organizations, and the broader MSTS membership for review. Based on these bodies, over 200 commentators should have the opportunity to provide input into each CPG.

The chairs of the guideline work group and the methodologists draft the initial responses to comments that address methodology and the chair and co-chair, also organize initial responses to questions concerning clinical practice and techniques. All comments received and the initial drafts of the responses are also reviewed by all members of the guideline development group. All proposed changes to recommendation language as a result of the review period must be based on the evidence and must be approved by the GDG. Final revisions are summarized in a report that is provided alongside the guideline document throughout the remainder of the approval processes and final publication.

The MSTS believes in the importance of demonstrating responsiveness to input received during the review process and welcomes the critiques of external specialty societies. Following final approval of the guideline, all individual responses are posted on our website http:/www.MSTS.org/guidelines with a point-by-point reply to each non-editorial comment. Reviewers who wish to remain anonymous notify the MSTS to have their names de-identified; their comments, our responses, and their COI disclosures are still posted.

## The MSTS Approval Process

This final CPG draft must be approved by the MSTS Committee on Guidelines and Evidence Based Medicine and the MSTS Executive Committee. These decision-making bodies are described in the Appendix of each guideline. Their charge is to approve or reject its publication by majority vote, not suggest modifications to the content of the documents.

## Revision Plans

CPGs represent a cross-sectional view of current treatment and may become outdated as new evidence becomes available. They will be revised in accordance with new evidence, changing practice, rapidly emerging treatment options, and new technology. Additionally, they will be updated or withdrawn in five years.

## CPG Dissemination Plans

The primary purpose of CPGs is to provide interested readers with full documentation about not only our recommendations, but also about how we arrived at those recommendations.
To view all MSTS published CPG recommendations, please visit http://www.MSTS.org/guidelines.

Shorter versions of the CPGs are available in other venues. Publication of most CPGs is announced by an MSTS press release, articles authored by the CPG work group and published in the appropriate journals. Other dissemination efforts outside of the MSTS will include submitting the CPGs to the ECRI Guidelines Trust, Guidelines International Network Library, and distributing the guideline at other medical specialty societies' meetings.

## INTERPRETING THE STRENGTH OF EVIDENCE

### Table I. Level of Evidence Descriptions

| Combined Strength of Recommendation | Aggregate Strength of Evidence | Description of Evidence Quality |
|---|---|---|
| **Strong** | Strong or Moderate | Evidence from two or more "High" quality studies with consistent findings for recommending for or against the intervention. Or Rec is upgrade from Moderate using the EtD framework. |
| **Moderate** | Strong, Moderate or Limited | Evidence from two or more "Moderate" quality studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. Or Rec is upgraded or downgraded from Limited or Strong using the EtD framework. |
| **Limited** | Limited or Moderate | Evidence from two or more "Low" quality studies with consistent findings or evidence from a single "Moderate" quality study recommending for or against the intervention. Or Rec is downgraded from Strong or Moderate using the EtD Framework. |
| **N/A** | No Evidence | There is no supporting evidence, or higher quality evidence was downgraded due to major concerns addressed in the EtD framework. In the absence of reliable evidence, the guideline work group is making a recommendation based on their clinical opinion. |

### Evidence to Decision Framework

The Evidence to Decision Framework (EtDF) utilized by the MSTS is a novel scoring rubric developed by the Guidelines and Evidence Based Medicine (GEBM) Committee. Some form of EtDF is used in any clinical practice guideline to leverage clinical experience with the quality of the literature to determine recommendation strength. The MSTS GEBM developed the scoring system as a means to quantify the quality of the literature more objectively, such that any recommendations would be more consistent, transparent, and reproducible across panelists. It is a series of categories with weighted numeric scaling that incorporates aggregate methodological critique and perceptions of importance, risks, benefits, consistency with other literature on the subject, and cost of the intervention studied to answer a particular PICO question (see Appendix VI). The scoring is used to determine where the strength of recommendation should ultimately fall.

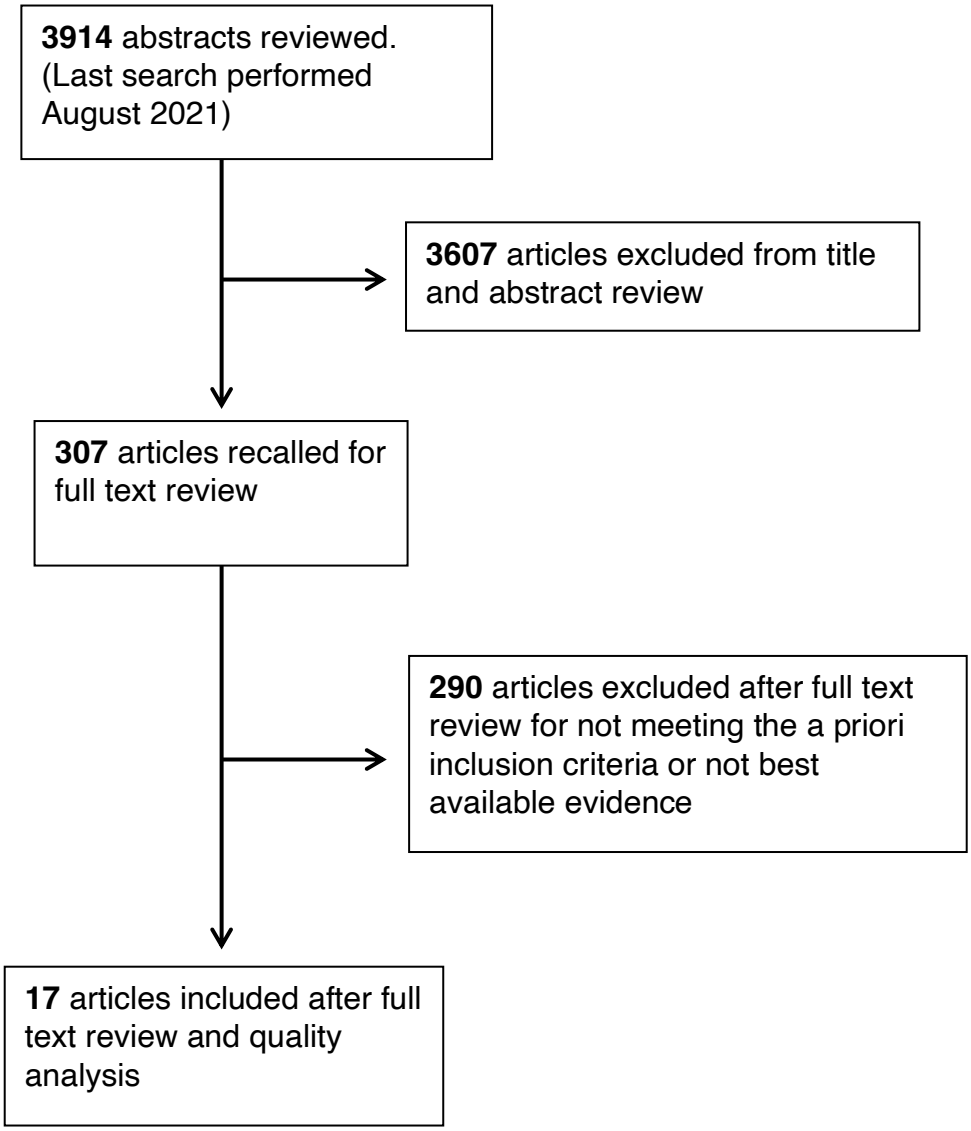
The study methodology and design incorporated into the level of evidence (ex. I-V) is first used to initially determine the strength of recommendation. Then, the EtDF scoring rubric is used to determine if that alone is enough to determine the strength of recommendation or if the risk-to-benefit profile, effect on the patients or society, or overall cost of implementing the intervention is so importantly skewed that the strength of the recommendation should be increased or decreased as appropriate (see Table II below). An example of this would be downgrading a recommendation based on Level I evidence that showed a benefit to an intervention, but had a

tremendous amount of treatment crossover, protocol deviations, and patient attrition with an intervention so expensive it would be largely unattainable for most institutions. So, while it might be level I evidence in favor of a specific intervention, there are too many variables, issues, and implementation pragmatics that make it a low overall recommendation that ultimately needs further research.

Table II. Evidence to Decision Framework Score Thresholds

| Upgrade/Downgrade Thresholds | EtDF Score |
|---|---|
| Increase recommendation strength +2 | 38-42 |
| Increase recommendation strength +1 | 31-37 |
| No change in recommendation strength | 18-30 |
| Decrease recommendation strength -1 | 13-17 |
| Decrease recommendation strength -2 | 3-12 |

## STUDY ATTRITION FLOWCHART



# ACTION STATEMENTS

## 1. Plating/Internal Fixation, Intramedullary Fixation, and/or Photodynamic Polymer

**When treating pathologic diaphyseal humerus fractures, clinicians can consider either the use of plating/internal fixation, intramedullary fixation, and/or photodynamic polymer, as there does not appear to be a significant difference in clinical outcomes or reoperation rate between these constructs based on limited available evidence.**

**Strength of Recommendation**

- Aggregate Evidence = **Limited** (3 Low quality Studies)
- EtD Framework Score = **21**
- Combined Strength of Recommendation = **Limited**

**Rationale**

Three lower quality studies were included and examined for this portion of the clinical practice guideline. These studies were retrospective and included low numbers of patients. Further, these studies included varied outcomes measured in terms of surgical complications and clinical function.

When treating pathologic diaphyseal humerus fractures in the setting of metastatic disease, the available evidence does not appear to show a significant difference in clinical outcomes (pain relief, upper extremity function, complication rates) between these constructs. However, with the low numbers available there was noted an increased failure rate with photodynamic polymer fixation compared to intramedullary nail fixation. Despite this potential difference, there does not appear to be a significant difference in reoperation rate between plating/internal fixation, intramedullary fixation, and photodynamic polymer.

Based on the low-level evidence of the articles analyzed, any of the constructs, including intramedullary nailing, photodynamic polymer, or plating/internal fixation, constitutes a reasonable and safe option when treating realized or impending pathologic diaphyseal humerus fractures. However, caution is advised regarding the use of photodynamic polymer fixation until further evidence is available due to the potential higher failure rates with this construct.

Further research is needed to better elucidate any potentially undetected outcome difference among the various constructs. The best study design to help determine this would be a collaborative, multicenter, randomized controlled trial.

**Included Evidence:**


1. Dijkstra, S., Stapert, J., Boxma, H., Wiggers, T. Treatment of pathological fractures of the humeral shaft due to bone metastases: a comparison of intramedullary locking nail and plate osteosynthesis with adjunctive bone cement. *European Journal of Surgical Oncology* 1996; 6: 621-6
2. Hoellwarth, J. S., Weiss, K., Goodman, M., Heyl, A., Hankins, M. L., McGough, R., 3rd Evaluating the reoperation rate and hardware durability of three stabilizing implants for 105 malignant pathologic humerus fractures. *Injury* 2020; 4: 947-954
3. Sarahrudi, K., Wolf, H., Funovics, P., Pajenda, G., Hausmann, J. T., Vecsei, V. Surgical treatment of pathological fractures of the shaft of the humerus. *Journal of Trauma-Injury Infection & Critical Care* 2009; 3: 789-94

930 **Evidence to Decision Framework Scoring**

| Criteria | Detailed considerations | Judgements (points) | Score |
|---|---|---|---|
| What is the baseline quality/strength of the evidence? See above. | Baseline strength of recommendation is listed above | No evidence (0)<br>Low (3)<br>Moderate (4)<br>High (5) | 3 |
| What is the value and importance of the outcomes to clinical practice? | Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)? | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | 3 |
| What is the magnitude of the desired effect? | | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | 3 |
| What is the magnitude of undesirable effects/complications? | | High (0)<br>Moderate (1)<br>Low (2)<br>None (3) | 2 |
| Do the benefits outweigh the risks? | Do the benefits clearly outweigh the risks or is there a balance of benefits and harms? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (3)<br>Yes (5) | 2 |
| What amount of resources are required to produce the desired effect? | What is the estimated equipment need, space, time, and ability of any institution to provide these needs? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (5) | 2 |
| What is the cost to produce the desired effect? | What is the estimated monetary cost? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (4) | 1 |
| Is the intervention/outcomes acceptable to key stakeholders? | -Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes?<br>-Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)?<br>-Would intervention effect people's autonomy? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | 1 |
| Is the intervention feasible to implement? | -Is intervention sustainable?<br>-Any barriers limiting the feasibility of implementing recommendation? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | 4 |
| **Total Score** | | | **21** |

931
932

## 2. En Bloc Resection, Curettage, Internal Fixation, or Intramedullary Nailing

**No studies met inclusion criteria comparing survivorship or other oncologic outcomes between en bloc resection, curettage, internal fixation, or intramedullary nailing. Based on the lack of evidence, no recommendations can be made for or against en bloc resection pertaining to metastatic disease of the humerus.**

**Strength of Recommendation**

- Aggregate Evidence = **N/A (**No Included Literature)
- EtD Framework Score = **15** (strength cannot be designated lower than N/A)
- Combined Strength of Recommendation = **N/A**

**Rationale**

No studies met inclusion criteria to compare en bloc resection and internal fixation in terms of disease control or clinical outcomes. Based on the lack of definitive evidence, no recommendations can be made for or against specific surgical treatments for metastatic disease of the humerus. While supporting literature is lacking, it is appropriate for the surgeon to consider en bloc resection based on the clinical circumstances and/or the reconstructive needs of the patient. The histologic subtype of metastatic bone disease, oligometastatic disease state, condition of the adjacent joint, available bone stock, and other patient-centric factors may indicate resection as an appropriate treatment.

Future studies should compare internal fixation versus intramedullary nailing versus en bloc resection for functional outcomes, failure and/or reoperation rates, pain relief, and oncologic outcomes. Comparisons between histologic primaries and number of bony metastases should be considered in these studies.

**Included Evidence:**

No evidence met inclusion criteria

965 **Evidence to Decision Framework Scoring**

| Criteria | Detailed considerations | Judgements (points) | Score |
|---|---|---|---|
| What is the baseline quality/strength of the evidence? See above. | Baseline strength of recommendation is listed above | No evidence (0)<br>Low (3)<br>Moderate (4)<br>High (5) | 0 |
| What is the value and importance of the outcomes to clinical practice? | Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)? | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | 0 |
| What is the magnitude of the desired effect? | | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | 2 |
| What is the magnitude of undesirable effects/complications? | | High (0)<br>Moderate (1)<br>Low (2)<br>None (3) | 2 |
| Do the benefits outweigh the risks? | Do the benefits clearly outweigh the risks or is there a balance of benefits and harms? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (3)<br>Yes (5) | 2 |
| What amount of resources are required to produce the desired effect? | What is the estimated equipment need, space, time, and ability of any institution to provide these needs? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (5) | 2 |
| What is the cost to produce the desired effect? | What is the estimated monetary cost? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (4) | 2 |
| Is the intervention/outcomes acceptable to key stakeholders? | -Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes?<br>-Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)?<br>-Would intervention effect people's autonomy? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | 1 |
| Is the intervention feasible to implement? | -Is intervention sustainable?<br>-Any barriers limiting the feasibility of implementing recommendation? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | 4 |
| **Total Score** | | | **15** |

966
967

## 3. Patient Selection for Nonoperative Techniques Versus Operative Techniques

**No studies met inclusion criteria to compare nonoperative vs operative treatment in the setting of metastatic disease of the humerus. Based on the lack of definitive evidence, no recommendations can be made for or against patient selection or indication for nonoperative vs. operative treatment pertaining to metastatic disease of the humerus.**

**Strength of Recommendation**

- Aggregate Evidence = **N/A** (No Included Literature)
- EtD Framework Score = **26**
- Combined Strength of Recommendation = **N/A**

**Rationale**

While specific literature is lacking, the group recommends that both nonoperative treatment and operative treatment can be considered based on the clinical circumstances of the patient, active comorbidities, metastatic disease burden and prognosis, location of the lesion, histologic subtype, presence of displacement or angulation, expected responsiveness to radiation and/or chemotherapy, and patient goals and expectations.

Future research such as prospective cohort studies could help elucidate the clinical scenarios in which patients can be treated successfully with nonoperative management for metastatic disease of the humerus.

**Included Evidence:**

No evidence met inclusion criteria

997 **Evidence to Decision Framework Scoring**

| Criteria | Detailed considerations | Judgements (points) | Score |
|---|---|---|---|
| What is the baseline quality/strength of the evidence? See above. | Baseline strength of recommendation is listed above | No evidence (0)<br>Low (3)<br>Moderate (4)<br>High (5) | 0 |
| What is the value and importance of the outcomes to clinical practice? | Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)? | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | 0 |
| What is the magnitude of the desired effect? | | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | 2 |
| What is the magnitude of undesirable effects/complications? | | High (0)<br>Moderate (1)<br>Low (2)<br>None (3) | 3 |
| Do the benefits outweigh the risks? | Do the benefits clearly outweigh the risks or is there a balance of benefits and harms? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (3)<br>Yes (5) | 3 |
| What amount of resources are required to produce the desired effect? | What is the estimated equipment need, space, time, and ability of any institution to provide these needs? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (5) | 5 |
| What is the cost to produce the desired effect? | What is the estimated monetary cost? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (4) | 4 |
| Is the intervention/outcomes acceptable to key stakeholders? | -Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes?<br>-Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)?<br>-Would intervention effect people's autonomy? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | 4 |
| Is the intervention feasible to implement? | -Is intervention sustainable?<br>-Any barriers limiting the feasibility of implementing recommendation? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | 5 |
| **Total Score** | | | **26** |

998
999

## 4. Cementation Vs No Cementation

**In patients undergoing surgical fixation of the humerus for metastatic bone disease, clinicians may consider cement augmentation. One low quality study meeting inclusion criterion suggested the addition of cement to surgical fixation of pathologic fractures of the humerus may provide short-term improvements in pain relief and functional mobility, however no difference in surgical complications were observed when compared to fixation alone.**

**Strength of Recommendation**

- Aggregate Evidence = **Limited** (2 Low quality Study)
- EtD Framework Score (from below) = **23**
- Combined Strength of Recommendation = **Limited**

**Rationale**

A single small, retrospective comparison study demonstrated improved postoperative pain relief and functional outcomes at 1 and 6 weeks postoperatively with the addition of cement to intramedullary nailing of pathologic humeral shaft fractures. These results were compared to a historical cohort of uncemented intramedullary nails. There was no difference in perioperative complications, and no difference in pain or functional outcomes at 6 months postoperatively. Two other studies included in the review were also retrospective studies, one of which included 39 patients and the other 208 patients. These both appeared to include lesions at the proximal, diaphyseal, and distal humerus. In the larger study (excluding endoprosthetic reconstruction), plate fixation (as compared to intramedullary fixation), had a higher failure rate. The other included study did not note a difference between these constructs.

Future studies should compare cemented and cementless constructs for fixation of pathologic humerus fractures, and evaluate pain, location of the lesion, functional outcomes, and mechanical failure rates of each construct.

**Included Evidence:**


1. Laitinen, M., Nieminen, J., Pakarinen, T. K. Treatment of pathological humerus shaft fractures with intramedullary nails with or without cement fixation. *Archives of Orthopaedic & Trauma Surgery* 2011; 4: 503-8
2. Sarahudi K., Wolf H., Funovics H., Pajenda G., Hausman J., Vecsei V. Surgical treatment of pathological fractures of the shaft of the humerus. J Trauma. 2009 Mar; 66(3):789-94.

**Additional References:**

1. Wedin R., Hansen B., Laitinen M., Trovik C., Zaikova O., Bergh P., Kalen A., Schwarz-Lausten G., von Steyern G., Walloe A., Keller J., Weiss R. Complications and survival after surgical treatment of 214 metastatic lesions of the humerus. *J Shoulder Elbow Surg*. 2012. Aug;21(8):1049-55.

**Evidence to Decision Framework Scoring**

| Criteria | Detailed considerations | Judgements (points) | Score |
|---|---|---|---|
| What is the baseline quality/strength of the evidence? See above. | Baseline strength of recommendation is listed above | No evidence (0)<br>Low (3)<br>Moderate (4)<br>High (5) | 3 |
| What is the value and importance of the outcomes to clinical practice? | Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)? | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | 2 |
| What is the magnitude of the desired effect? | | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | 2 |
| What is the magnitude of undesirable effects/complications? | | High (0)<br>Moderate (1)<br>Low (2)<br>None (3) | 2 |
| Do the benefits outweigh the risks? | Do the benefits clearly outweigh the risks or is there a balance of benefits and harms? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (3)<br>Yes (5) | 3 |
| What amount of resources are required to produce the desired effect? | What is the estimated equipment need, space, time, and ability of any institution to provide these needs? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (5) | 2 |
| What is the cost to produce the desired effect? | What is the estimated monetary cost? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (4) | 3 |
| Is the intervention/outcomes acceptable to key stakeholders? | -Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes?<br>-Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)?<br>-Would intervention effect people's autonomy? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | 1 |
| Is the intervention feasible to implement? | -Is intervention sustainable?<br>-Any barriers limiting the feasibility of implementing recommendation? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | 5 |
| **Total Score** | | | **23** |

1046
1047

## 5. Reconstruction Approach

**In patients undergoing arthroplasty to reconstruct the proximal humerus for metastatic bone disease, clinicians may consider reverse total shoulder arthroplasty over conventional shoulder arthroplasty and hemiarthroplasty in order to decrease shoulder instability and improve range-of-motion.**

**Strength of Recommendation**

- Aggregate Evidence = **Limited** (2 Low quality Studies)
- EtD Framework Score = **25**
- Combined Strength of Recommendation = **Limited**

**Rationale**

Two retrospective comparative studies demonstrate a decreased rate of dislocation/subluxation, improved shoulder range-of-motion, and decreased reoperation rates with reverse total shoulder arthroplasty compared to hemiarthroplasty. One study demonstrated decreased local tumor recurrence in the reverse arthroplasty group as well. Careful consideration of anatomy involved in resection and harboring metastatic disease (glenoid, deltoid insertion/muscle, axillary nerve) as well as patient-centric factors should be used to guide appropriate selection of technique.

Future research should involve cohort or randomized studies between hemiarthroplasty and reverse total shoulder arthroplasty in comparable patient populations to evaluate range-of-motion, instability, reoperation rates, and pain between the two reconstructive techniques.

**Included Evidence:**


1. Houdek, M. T., Bukowski, B. R., Athey, A. G., Elhassan, B. T., Barlow, J. D., Morrey, M. E., Rose, P. S., Wagner, E. R., Sanchez-Sotelo, J. Comparison of reconstructive techniques following oncologic intraarticular resection of proximal humerus. *Journal of Surgical Oncology* 2021; 1: 133-140
2. Grosel, T. W., Plummer, D. R., Everhart, J. S., Kirven, J. C., Ziegler, C. L., Mayerson, J. L., Scharschmidt, T. J., Barlow, J. D. Reverse total shoulder arthroplasty provides stability and better function than hemiarthroplasty following resection of proximal humerus tumors. *Journal of Shoulder & Elbow Surgery* 2019; 11: 2147-2152

1087 **Evidence to Decision Framework Scoring**

| Criteria | Detailed considerations | Judgements (points) | Score |
|---|---|---|---|
| What is the baseline quality/strength of the evidence? See above. | Baseline strength of recommendation is listed above | No evidence (0)<br>Low (3)<br>Moderate (4)<br>High (5) | 3 |
| What is the value and importance of the outcomes to clinical practice? | Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)? | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | 3 |
| What is the magnitude of the desired effect? | | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | 3 |
| What is the magnitude of undesirable effects/complications? | | High (0)<br>Moderate (1)<br>Low (2)<br>None (3) | 2 |
| Do the benefits outweigh the risks? | Do the benefits clearly outweigh the risks or is there a balance of benefits and harms? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (3)<br>Yes (5) | 3 |
| What amount of resources are required to produce the desired effect? | What is the estimated equipment need, space, time, and ability of any institution to provide these needs? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (5) | 3 |
| What is the cost to produce the desired effect? | What is the estimated monetary cost? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (4) | 2 |
| Is the intervention/outcomes acceptable to key stakeholders? | -Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes?<br>-Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)?<br>-Would intervention effect people's autonomy? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | 1 |
| Is the intervention feasible to implement? | -Is intervention sustainable?<br>-Any barriers limiting the feasibility of implementing recommendation? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | 5 |
| **Total Score** | | | **25** |

1088

## 6. Prognostic Markers

**Based on low levels of evidence, clinicians should consider the following potential negative socioeconomic prognostic markers when caring for patients with metastatic malignancy of the humerus:**

- **Age > 60 years**
- **Have Medicaid insurance compared to commercial insurance**
- **Black race compared to white race**
- **Lower income status**
- **Lower initial performance status**
- **Male sex**
- **Rapidly growing tumor histologies versus slow growing**

**Strength of Recommendation**

- Aggregate Evidence = **Limited** (11 Low quality Studies)
- EtD Framework Score = **21**
- Combined Strength of Recommendation = **Limited**

**Rationale**

There is a lack of data examining the socioeconomic impact of race, gender, and insurance status on the outcome of patients with non-primary malignancies. Current data is limited to small series of patients and a low-quality of evidence. Similar to studies in other types of cancers, lack of insurance or having Medicaid, lower household income and black race were associated with a poor outcome. The studies reviewed showed rapidly growing histologies to be most often lung, gastrointestinal, and renal. The slower growing histologies were most often breast, prostate and thyroid. There were no studies describing the type of lesion (lytic vs blastic) as a predictor. There is likely no way to improve the quality of evidence for these studies as it would be near impossible to maintain equipoise while performing a prospective randomized study on this topic, however future studies on the use of prospectively collected data from multicenter or international collaborations may shed insight into the impact of these socioeconomic factors.

**Included Evidence:**


1. Herget, G., Saravi, B., Schwarzkopf, E., Wigand, M., Sudkamp, N., Schmal, H., Uhl, M., Lang, G. Clinicopathologic characteristics, metastasis-free survival, and skeletal-related events in 628 patients with skeletal metastases in a tertiary orthopedic and trauma center. *World Journal of Surgical Oncology* 2021; 1: 62
2. Huang, Z., Du, Y., Zhang, X., Liu, H., Liu, S., Xu, T. Clear cell renal cell carcinoma bone metastasis: What should be considered in prognostic evaluation. *European Journal of Surgical Oncology* 2019; 7: 1246-1252
3. Hung, B., Pennington, Z., Hersh, A. M., Schilling, A., Ehresman, J., Patel, J., Antar, A., Porras, J. L., Elsamadicy, A. A., Sciubba, D. M. Impact of race on nonroutine discharge, length of stay, and postoperative complications after surgery for spinal metastases. *Journal of Neurosurgery Spine* 2021; 0: 1-8
4. Rades, D., Haus, R., Janssen, S., Schild, S. E. An easy-to-use scoring system to estimate the survival of patients irradiated for bone metastases from lung cancer. *Translational Lung Cancer Research* 2020; 4: 1067-1073
5. Rades, D., Haus, R., Janssen, S., Schild, S. E. Interval Between Cancer Diagnosis and Radiotherapy - An Independent Prognostic Factor of Survival in Patients Irradiated for Bone Metastases from Kidney Cancer. *In Vivo* 2020; 2: 767-770
6. Rades, D., Haus, R., Schild, S. E., Janssen, S. Prognostic factors and a new scoring system for survival of patients irradiated for bone metastases. *BMC Cancer* 2019; 1: 1156
7. Scott, E., Klement, M. R., Brigman, B. E., Eward, W. C. Beyond Mirels: Factors Influencing Surgical Outcome of Metastasis to the Extremities in the Modern Era. *Journal of Surgical Orthopaedic Advances* 2018; 3: 178-186
8. Vos, M., Ho, V. K. Y., Oosten, A. W., Verhoef, C., Sleijfer, S. Minimal Increase in Survival Throughout the Years in Patients with Soft Tissue Sarcoma with Synchronous Metastases: Results of a Population-Based Study. *Oncologist* 2019; 7: e526-e535
9. Wisanuyotin, T., Sirichativapee, W., Sumnanoont, C., Paholpak, P., Laupattarakasem, P., Sukhonthamarn, K., Kosuwon, W. Prognostic and risk factors in patients with metastatic bone disease of an upper extremity. *Journal of Bone Oncology* 2018; 0: 71-75
10. Wong, E., Chow, E., Zhang, L., Bedard, G., Lam, K., Fairchild, A., Vassiliou, V., Alm El-Din, M. A., Jesus-Garcia, R., Kumar, A., Forges, F., Tseng, L. M., Hou, M. F., Chie, W. C., Bottomley, A. Factors influencing health related quality of life in cancer patients with bone metastases. *Journal of Palliative Medicine* 2013; 8: 915-21
11. Yanamandra, U., Sharma, R., Shankar, S., Yadav, S., Kapoor, R., Pramanik, S., Ahuja, A., Kumar, R., Sharma, S., Das, S., Chatterjee, T., Somasundaram, V., Verma, T., Mishra, K., Singh, J., Sharma, A., Nair, V. Survival Outcomes of Newly Diagnosed Multiple Myeloma at a Tertiary Care Center in North India (IMAGe: 001A Study). *JCO Global Oncology* 2021; 0: 704-715

1163 **Evidence to Decision Framework Scoring**

| Criteria | Detailed considerations | Judgements (points) | Score |
|---|---|---|---|
| What is the baseline quality/strength of the evidence? See above. | Baseline strength of recommendation is listed above | No evidence (0)<br>Low (3)<br>Moderate (4)<br>High (5) | 3 |
| What is the value and importance of the outcomes to clinical practice? | Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)? | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | 5 |
| What is the magnitude of the desired effect? | | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | 5 |
| What is the magnitude of undesirable effects/complications? | | High (0)<br>Moderate (1)<br>Low (2)<br>None (3) | 0 |
| Do the benefits outweigh the risks? | Do the benefits clearly outweigh the risks or is there a balance of benefits and harms? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (3)<br>Yes (5) | 5 |
| What amount of resources are required to produce the desired effect? | What is the estimated equipment need, space, time, and ability of any institution to provide these needs? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (5) | 1 |
| What is the cost to produce the desired effect? | What is the estimated monetary cost? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (4) | 1 |
| Is the intervention/outcomes acceptable to key stakeholders? | -Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes?<br>-Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)?<br>-Would intervention effect people's autonomy? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | 1 |
| Is the intervention feasible to implement? | -Is intervention sustainable?<br>-Any barriers limiting the feasibility of implementing recommendation? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | 1 |
| **Total Score** | | | **21** |

1164
1165

## 7. VTE prophylaxis

**No studies met inclusion criteria to make a specific recommendation on VTE prophylaxis for metastatic bone disease of the humerus. In the absence of direct evidence, we refer clinicians to the ASCO, ASH, and ICM-VTE guidelines which indicate that oncology patients are at a higher risk for VTE, and prophylaxis should be considered during the peri-operative period.**

**Strength of Recommendation**

- Aggregate Evidence = **N/A** (No Included Literature)
- EtD Framework Score = **19**
- Combined Strength of Recommendation = **N/A**

**Rationale**

Both the American Society of Clinical Oncology and the American Society of Hematology (ASCO and ASH) guidelines recommend that patients with cancer without a history of VTE undergoing a major surgical procedure should be offered pharmacologic prophylaxis with either unfractionated heparin or low molecular weight heparin (LMWH), unless contraindicated because of active bleeding or high bleeding risk. The highest risk period for patients is in the perioperative setting in which they are hospitalized and immobilized.

Recommendations from the International Consensus Meeting – Venous Thromboembolism (ICM-VTE) for Shoulder and Elbow state that VTE prophylaxis should be considered in patients undergoing osteosynthesis who are also at high risk of VTE, and those undergoing surgery under general anesthesia that lasts over 90 minutes. Regarding shoulder arthroplasty, in patients without substantial risk factors for VTE, they do not recommend LMWH or direct oral anticoagulants (DOAC). However, they do not comment on those with substantial risk factors for VTE.

The ICM-VTE for Oncology states that all patients with bone metastases undergoing major surgical intervention should be offered pharmacologic thromboprophylaxis unless contraindicated. They state that larger studies are needed to determine optimal pharmacologic thromboprophylaxis between low molecular weight heparin, direct oral anticoagulants, vitamin K antagonists, and aspirin. These would include large, prospective, randomized studies conducted in collaboration with hematology and medical oncology specialists.

**Included Evidence:**

No evidence met inclusion criteria

1204 **Evidence to Decision Framework Scoring**

| Criteria | Detailed considerations | Judgements (points) | Score |
|---|---|---|---|
| What is the baseline quality/strength of the evidence? See above. | Baseline strength of recommendation is listed above | No evidence (0)<br>Low (3)<br>Moderate (4)<br>High (5) | 0 |
| What is the value and importance of the outcomes to clinical practice? | Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)? | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | 3 |
| What is the magnitude of the desired effect? | | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | 3 |
| What is the magnitude of undesirable effects/complications? | | High (0)<br>Moderate (1)<br>Low (2)<br>None (3) | 1 |
| Do the benefits outweigh the risks? | Do the benefits clearly outweigh the risks or is there a balance of benefits and harms? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (3)<br>Yes (5) | 3 |
| What amount of resources are required to produce the desired effect? | What is the estimated equipment need, space, time, and ability of any institution to provide these needs? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (5) | 2 |
| What is the cost to produce the desired effect? | What is the estimated monetary cost? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (4) | 3 |
| Is the intervention/outcomes acceptable to key stakeholders? | -Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes?<br>-Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)?<br>-Would intervention effect people's autonomy? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | 0 |
| Is the intervention feasible to implement? | -Is intervention sustainable?<br>-Any barriers limiting the feasibility of implementing recommendation? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | 4 |
| **Total Score** | | | **19** |

1205
1206

# APPENDICES

## Appendix I: References

### Introduction References


1. DiCaprio MR, Murtaza H, Palmer B, Evangelist M. Narrative review of the epidemiology, economic burden, and societal impact of metastatic bone disease. *Annals of Joint*. 2022;7(0). doi:10.21037/aoj-20-97

2. Saad F, Lipton A, Cook R, Chen YM, Smith M, Coleman R. Pathologic fractures correlate with reduced survival in patients with malignant bone disease. *Cancer*. 2007;110(8):1860-1867. doi:10.1002/cncr.22991

3. Mariotto AB, Enewold L, Zhao J, Zeruto CA, Yabroff KR. Medical Care Costs Associated with Cancer Survivorship in the United States. *Cancer Epidemiology, Biomarkers & Prevention*. 2020;29(7):1304-1312. doi:10.1158/1055-9965.EPI-19-1534

4. Voskuil RT, Mayerson JL, Scharschmidt TJ. Management of Metastatic Disease of the Upper Extremity. *JAAOS - Journal of the American Academy of Orthopaedic Surgeons*. 2021;29(3):e116. doi:10.5435/JAAOS-D-20-00819

5. Jiang, Tracey A. Martin, Lin Ye, Andrew J. Sanders, Jane Lane, Wen G. “Cancer Invasion and Metastasis: Molecular and Cellular Perspective - Madame Curie Bioscience Database - NCBI Bookshelf.” *National Center for Biotechnology Information*, edited by Rahul Jandial, Landes Bioscienc, 2013, https://www.ncbi.nlm.nih.gov/books/NBK164700/.


### Included Literature References


1. Dijkstra, S., Stapert, J., Boxma, H., Wiggers, T. Treatment of pathological fractures of the humeral shaft due to bone metastases: a comparison of intramedullary locking nail and plate osteosynthesis with adjunctive bone cement. *European Journal of Surgical Oncology* 1996; 6: 621-6

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## Appendix II: PICO Questions and Inclusion Criteria Used to Define Literature Search

### PICO Questions

1. In patients undergoing surgical fixation of the humerus for metastatic bone disease, does plating/internal fixation, intramedullary fixation, and/or photodynamic polymer reduce local disease progression, revision rates, reoperations, time to union, pain, QoL and other relevant patient-reported outcomes?
2. In patients with metastatic bones disease undergoing surgical intervention of the humerus, is en bloc resection associated with better disease control/defined outcomes than curettage (intralesional resection), internal fixation, and/or intramedullary nailing?
3. In patients with metastatic disease of the humerus and a pathologic/impending/displaced humerus fracture (excluding osteoporotic fracture, fragility fracture) who have not undergone surgery, which patients are best served utilizing nonsurgical techniques versus surgical techniques?
4. In patients undergoing surgical fixation of the humerus for metastatic bone disease, does cementation vs no cementation reduce local disease progression, revision rates, reoperations, time to union, pain, QoL and other relevant patient-reported outcomes?
5. For patients with metastatic bone disease undergoing arthroplasty to reconstruct the proximal humerus for metastatic humeral bone disease, which reconstruction approach (conventional vs. reverse) is preferred in terms of resulting in better/improved patient-reported outcomes?
6. In patients with metastatic malignancies, disease, myeloma etc, which factors affect patient outcomes (disease burden, histology, socioeconomic, insurance status, race, sex, gender, medical co-morbidities, health literacy, etc.)?
7. In patients with metastatic bone disease undergoing surgical intervention, does type of VTE prophylaxis and/or use (vs. no use) of VTE prophylaxis affect postoperative complications?

### Inclusion Criteria

#### Standard Criteria for all CPGs

1. Article must be a full article report of a clinical study.
2. Medical records review, meeting abstracts, historical articles, editorials, letters, and commentaries are excluded. Bibliographies of meta-analyses and systematic reviews will be examined to ensure inclusion of all relevant literature.
3. Confounded studies (i.e. studies that give patients the treatment of interest AND another treatment) are excluded.
4. Composite measures or outcomes are excluded even if they are patient-oriented.
5. Study must appear in a peer-reviewed publication
6. Study must be of humans
7. Study must be published in English
8. Study results must be quantitatively presented
9. Study must not be an in vitro study
10. Study must not be a biomechanical study
11. Study must not have been performed on cadavers

12. Surrogate outcomes are evaluated only when no patient-oriented outcomes are available.

**Project Dependent Criteria**

A priori article inclusion criteria are constructed for all CPGs. These criteria are our "rules of evidence" and articles that did not meet them are, for the purposes of this guideline, not evidence.

The following criteria may be adjusted by the GDG prior to beginning the systematic literature review, depending on the topic under study:

1. Study must be published in or after <**1990**>
2. Study should have < **5** > or more patients per group
3. For surgical treatment a minimum of: **no minimum**
4. For nonoperative treatment a minimum of: **no minimum**

**Patient population definitions**:

- Study must be of adults with Metastatic Disease of the Humerus (include myeloma, lymphoma, metastatic sarcoma)
  - Adults>= 18
  - Excluding osteoporotic and fragility Fxs; Excluding any pathologic Fxs related to genetics or other bone metabolism diseases, metastatic disease of other bones)
  - Mixed populations acceptable?: yes
- Authors must report specific stratifications of number of patient type (location of disease, indication for Tx, diagnosis)

**Agreement Threshold for Voting on Final Recommendations:**

- Supermajority (three-fourths; 75%)

***Best Available Evidence***

When examining primary studies, we will analyze the best available evidence regardless of study design. We will first consider randomized controlled trials identified by the search strategy. In the absence of two or more RCTs, we will sequentially search for prospective controlled trials, prospective comparative studies, retrospective comparative studies, and prospective case-series studies. Only studies of the highest level of available evidence are included, assuming that there were 2 or more studies of that higher level. For example, if there are two Level II studies that address the recommendation, Level III and IV studies are not included

## Appendix III: Quality Appraisal

KEY:

High Risk of Bias = ○

Unclear Risk of Bias = ◑

No/Minimal Risk of Bias = ●

| Study | Patient Spectrum | Participant Recruitment | Treatment recording | Confounding Variables | Outcome measurement bias | Incomplete Outcome Data | Adequate Reporting | Strength |
|---|---|---|---|---|---|---|---|---|
| Dijkstra, S., 1996 | ● | ● | ● | ● | ● | ● | ● | Low Quality |
| Grosel, T. W., 2019 | ● | ◑ | ○ | ◑ | ● | ● | ● | Low Quality |
| Herget, G., 2021 | ● | ○ | ○ | ○ | ● | ● | ● | Low Quality |
| Hoellwarth, J. S., 2020 | ● | ● | ● | ● | ● | ● | ● | Low Quality |
| Houdek, M. T., 2021 | ● | ◑ | ○ | ○ | ● | ● | ● | Low Quality |
| Huang, Z., 2019 | ● | ○ | ◑ | ○ | ● | ● | ● | Low Quality |
| Hung, B., 2021 | ● | ○ | ○ | ○ | ● | ● | ● | Low Quality |
| Laitinen, M., 2011 | ● | ○ | ○ | ○ | ● | ● | ● | Low Quality |
| Rades, D., 2019 | ● | ○ | ○ | ○ | ● | ● | ● | Low Quality |
| Rades, D., 2020 | ● | ○ | ○ | ○ | ● | ● | ● | Low Quality |
| Rades, D., 2020 | ● | ○ | ○ | ○ | ● | ● | ● | Low Quality |
| Raschka, T., 2022 | ● | ◑ | ○ | ○ | ● | ● | ● | Low Quality |
| Sarahrudi, K., 2009 | ● | ◑ | ○ | ○ | ◑ | ● | ● | Low Quality |
| Scott, E., 2018 | ● | ◑ | ○ | ○ | ● | ● | ● | Low Quality |

| Study | Patient Spectrum | Participant Recruitment | Treatment recording | Confounding Variables | Outcome measurement bias | Incomplete Outcome Data | Adequate Reporting | Strength |
|---|---|---|---|---|---|---|---|---|
| Vos, M., 2019 | ● | ◑ | ○ | ○ | ● | ● | ● | Low Quality |
| Wisanuyotin, T., 2018 | ● | ◑ | ○ | ◑ | ○ | ● | ● | Low Quality |
| Wong, E., 2013 | ● | ◑ | ○ | ◑ | ○ | ● | ● | Low Quality |

## Appendix IV: Literature Search Strategy

### Literature Search Methods

The medical librarian conducted a comprehensive search of MEDLINE, Embase, and the Cochrane Library based on key terms and concepts from the workgroup-defined PICO questions. Bibliographies of relevant systematic reviews were hand searched for additional references. All databases were last searched on May 9, 2022 with limits for English-language publications with publication dates from 1990 to present.

### PRISMA Diagram Data

Records identified through database searching: 5,449
Records after duplicates removed: 3,913
Additional records identified through other sources: 1
Records screened: 3,914

### Literature Search Strategies by Database

**Database**: Ovid MEDLINE® and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions ® 1946 to May 8, 2022
**Interface**: Ovid (http://ovidsp.ovid.com/autologin)
**Date Searched**: 5/9/2022

| Line | Search Strategy |
|---|---|
| **1** | English.lg. |
| **2** | (exp Animals/ NOT Humans/) OR exp Cadaver/ OR (animal? OR dog OR dogs OR sheepdog OR canine OR cats OR feline OR horse? OR equine OR mouse OR mice OR murine OR rat OR rats OR rabbit? OR sheep OR ovine OR porcine OR pig OR pigs OR rodent? OR monkey? OR hen OR hens OR veterinar* OR avian OR reindeer OR dolphin).ti. OR cadaver*.ti,ab. OR in-vitro.ti. OR ((comment OR editorial OR letter OR historical article) NOT clinical trial).pt. OR address.pt. OR news.pt. OR newspaper article.pt. OR pmcbook.af. OR case reports.pt. OR (case report? OR abstracts OR editorial OR reply OR comment? OR commentary OR letter).ti. |
| **3** | 1 NOT 2 |
| **4** | limit 3 to yr=1990-Current |
| **5** | exp Humerus/ OR Humeral-Fractures/ OR (humer* OR (long ADJ (bone? OR limb?))).ti,ab. |
| **6** | exp Neoplasms/sc OR exp Neoplasm-Metastasis/ OR (metasta* OR ((disseminat* OR spread*) ADJ2 (disease OR tumo?r* OR malignan* OR lesion?)) OR (lymphoma* NOT (primary ADJ4 lymphoma*)) OR myeloma* OR (tumo?r* ADJ3 lesion?) OR (pathologic* ADJ5 fracture?) OR (secondar* ADJ5 (tumo?r* OR neoplas* OR malignan* OR chondrosarcoma*)) OR (tumo?r* ADJ4 invad*)).ti,ab. |
| **7** | 4 AND 5 AND 6 |
| **8** | (exp Infant/ OR exp Child/ OR exp Adolescent/ OR (p?ediatric* OR child OR children OR childhood OR adolescen* OR juvenile? OR teen OR teens OR teenager? OR youth? OR infant*).ti.) NOT (exp Adult/ OR adult*.ti. OR (elderly OR geriatric? OR (older ADJ (adult? OR people OR person? OR women OR men OR patient?))).ti,ab. OR (mean-age ADJ3 18*).ab.) |
| **9** | 7 NOT 8 |

| | |
|---|---|
| **10** | exp Bone-and-Bones/ OR exp Bone-Neoplasms/ OR (bone? OR extremit* OR hip OR vertebra* OR spine OR spinal OR osteosarcoma* OR skelet*).ti,ab. |
| **11** | (10 AND 6 AND 4) NOT 8 |
| **12** | Venous-Thrombosis/ OR Thrombophlebitis/ OR Venous-Thromboembolism/ OR (dvt OR vte OR thrombos* OR thrombotic OR thromboembol* OR thrombophlebitis).ti,ab. |
| **13** | exp Anticoagulants/ OR (anticoagul* OR anti-coagul*).ti,ab. OR exp Fibrinolytic-Agents/ OR exp Thrombolytic-Therapy/ OR (antithromb* OR thrombolytic* OR thromboprophyla* OR chemoprophyla*).ti,ab. OR exp Platelet Aggregation Inhibitors/ OR (antiplatelet* OR anti-platelet*).ti,ab. OR exp Heparin/ OR (heparin* OR dalteparin OR Fragmin OR tinzaparin OR Innohep OR enoxaparin OR Lovenox).ti,ab. OR Clopidogrel/ OR (Plavix OR clopidogrel).ti,ab. OR Warfarin/ OR (Coumadin OR Jantoven OR warfarin*).ti,ab. OR exp Antithrombins/ OR Fondaparinux/ OR Dabigatran/ OR (Arixtra OR factor-Xa-inhibitor* OR rivaroxaban OR Xarelto OR apixaban OR Eliquis OR edoxaban OR Savaysa OR betrixaban OR Bevyxxa OR bivalirudin OR Angiomax OR lepirudin OR Refludan OR dabigatran OR Pradaxa OR desirudin OR Iprivask).ti,ab. OR exp Aspirin/ OR aspirin.ti,ab. |
| **14** | Stockings-Compression/ OR (compression ADJ (stocking? OR device?)).ti,ab. OR Intermittent-Pneumatic-Compression-Devices/ OR (foot AND pump?).ti,ab. OR ((pneumatic OR leg OR calf) ADJ compression).ti,ab. OR (mechanical ADJ3 prophyla*).ti,ab. |
| **15** | (11 AND 12 AND (13 OR 14)) |
| **16** | 9 OR 15 |
| **17** | Healthcare-Disparities/ OR Health-Status-Disparities/ OR exp Sociological-Factors/ OR exp Socioeconomic-Factors/ OR Race-Factors/ OR Sex-Factors/ OR exp Insurance-Coverage/ OR exp *Health-Facilities/ OR exp *Population/ OR exp Population-Groups/ OR ((race OR racial* OR sex OR sexual OR male OR female OR age OR gender OR transgender OR social OR socio* OR insurance OR insured OR uninsured OR ethnic* OR demographic* OR black OR disabilit* OR disabled OR handicap*) ADJ5 (difference? OR disparit* OR impact* OR outcome? OR effect? OR predict* OR factor? OR prognos* OR risk? OR correlat* OR related OR relationship? OR determinant*)).ti,ab. OR (exp Health-Facilities/ AND (facilit* OR center? OR hospital? OR clinic?).ti.) |
| **18** | exp Regression-Analysis/ OR exp Analysis-of-Variance/ OR (regression OR ((varia* OR univaria* OR multivaria* OR Cox) ADJ5 (analys* OR model* OR tests))).ti,ab. |
| **19** | 11 AND 17 AND 18 |
| **20** | 19 OR 16 |
| **21** | ((exp *Bone Diseases, Metabolic/ OR *Osteoporotic-Fractures/ OR exp *Metabolic-Diseases/) NOT exp *Neoplasm-Metastasis/) OR (osteoporo* OR diabet* OR ((fragility OR insufficiency OR low-energy) ADJ4 fracture?)).ti. |
| **22** | 20 NOT 21 |

**Database**: Embase

**Interface**: Elsevier (https://embase.com)
**Date Searched**: 5/9/2022

| Line | Search Strategy |
|---|---|
| **1** | [english]/lim |
| **2** | abstract-report/de OR book/de OR editorial/de OR editorial:it OR note/de OR note:it OR letter/de OR letter:it OR case-study/de OR case-report/de OR chapter:it OR conference-paper/exp OR conference-paper:it OR conference-abstract:it OR conference-review:it OR (abstracts OR editorial OR reply OR comment$ OR commentary OR letter):ti OR cadaver/de OR in-vitro-study/exp OR cadaver*:ti,ab OR in-vitro:ti OR animal-experiment/exp OR (animal$ OR dog OR dogs OR sheepdog OR canine OR cats OR feline OR horse$ OR equine OR mouse OR mice OR murine OR rat OR rats OR rabbit$ OR sheep OR ovine OR porcine OR pig OR pigs OR rodent$ OR monkey$ OR hen OR hens OR veterinar* OR avian OR reindeer OR dolphin):ti |
| **3** | (#1 NOT #2) AND [1990-3000]/py |
| **4** | humerus/exp OR humerus-fracture/exp OR long-bone/de OR (humer* OR (long NEXT/1 (bone$ OR limb$))):ti,ab |
| **5** | metastasis/exp OR (metasta* OR ((disseminat* OR spread*) NEAR/2 (disease OR tumo$r* OR malignan* OR lesion$)) OR myeloma* OR (lymphoma* NOT (primary NEAR/4 lymphoma*)) OR (tumo$r* NEAR/3 lesion$) OR (pathologic* NEXT/5 fracture$) OR (secondar* NEXT/5 (tumo$r* OR neoplas* OR malignan* OR chondrosarcoma*)) OR (tumo$r* NEAR/4 invad*)):ti,ab |
| **6** | #3 AND #4 AND #5 |
| **7** | (Juvenile/exp OR (p$ediatric* OR child OR children OR childhood OR adolescen* OR juvenile$ OR teen OR teens OR teenager$ OR youth$ OR infant*):ti) NOT (adult/exp OR adult*:ti OR (elderly OR geriatric$ OR (older NEXT/1 (adult$ OR people OR person$ OR women OR men OR patient$))):ti,ab OR (mean-age NEXT/3 18*):ab) |
| **8** | #6 NOT #7 |
| **9** | bone/exp or bone-tumor/exp OR (bone$ OR extremit* OR hip OR vertebra* OR spine OR spinal OR osteosarcoma* OR skelet*):ti,ab |
| **10** | (#9 AND #5 AND #3) NOT #7 |
| **11** | vein-thrombosis/exp OR thromboembolism/exp OR (dvt OR vte OR thrombos* OR thrombotic OR thromboembol* OR thrombophlebitis):ti,ab OR ((pulmonary OR lung$) AND (infarct* OR embol* OR clot*)):ti,ab |
| **12** | anticoagulant-agent/exp OR (anticoagul* OR anti-coagul*):ti,ab OR fibrinolytic-agent/exp OR fibrinolytic-therapy/exp OR chemoprophylaxis/de OR blood-clotting-inhibitor/exp OR antithrombocytic-agent/exp OR thrombocyte-aggregation-inhibition/de OR (antithromb* OR thrombolytic* OR thromboprophyla* OR chemoprophyla*):ti,ab OR (antiplatelet* OR anti-platelet*):ti,ab OR heparin/exp OR heparin-derivative/exp OR (heparin* OR dalteparin OR Fragmin OR tinzaparin OR Innohep OR enoxaparin OR Lovenox):ti,ab OR clopidogrel/exp OR (Plavix OR clopidogrel):ti,ab OR warfarin/exp OR (Coumadin OR Jantoven OR warfarin*):ti,ab OR dabigatran-etexilate/exp OR (Arixtra OR fondaparinux OR factor-Xa-inhibitor* OR rivaroxaban OR Xarelto OR apixaban OR Eliquis OR edoxaban OR Savaysa OR betrixaban OR Bevyxxa OR bivalirudin OR Angiomax OR lepirudin OR Refludan OR |

| | |
|---|---|
| | dabigatran OR Pradaxa OR desirudin OR desulfatohirudin OR Iprivask OR argatroban OR aspirin):ti,ab |
| **13** | compression-garment/exp OR (compression NEXT/1 (stocking$ OR device$)):ti,ab OR intermittent-pneumatic-compression-device/de OR (foot AND pump$):ti,ab OR ((pneumatic OR leg OR calf) NEXT/1 compression):ti,ab OR (mechanical NEXT/3 prophyla*):ti,ab |
| **14** | (#10 AND #11 AND (#12 OR #13)) |
| **15** | #8 OR #14 |
| **16** | health-care-disparity/de OR social-status/exp OR ethnic-or-racial-aspects/exp OR gender/exp OR sex-difference/exp OR sex/de OR population/exp OR demography/exp OR population-parameters/exp OR population-research/de OR population-group/exp OR health-insurance/exp OR ((race OR racial* OR sex OR sexual OR male OR female OR age OR gender OR transgender OR social OR socio* OR insurance OR insured OR uninsured OR ethnic* OR demographic* OR black OR disabilit* OR disabled or handicap*) NEAR/5 (difference$ OR disparit* OR impact* OR outcome$ OR effect$ OR predict* OR factor$ OR prognos* OR risk$ OR correlat* OR related OR relationship$ OR determinant*)):ti,ab OR (health-care-facilities-and-services/exp AND (facilit* OR center$ OR hospital$ OR clinic$):ti) |
| **17** | regression-analysis/exp OR analysis-of-variance/de OR (regression OR ((varia* OR univaria* OR multivaria* OR Cox) NEAR/5 (analys* OR model* OR tests))):ti,ab |
| **18** | #10 AND #16 AND #17 |
| **19** | #18 OR #15 |
| **20** | ((metabolic-bone-disease/exp/mj OR fragility-fracture/mj OR metabolic-disorder/exp/mj) NOT metastasis/exp/mj) OR (osteoporo* OR diabet* OR ((fragility OR insufficiency OR low-energy) NEAR/4 fracture$)):ti |
| **21** | #19 NOT #20 |

**Database**: Cochrane Library
**Interface**: Wiley (https://www.cochranelibrary.com/central)
**Date Searched**: 5/9/2022

| Line | Search Strategy |
|---|---|
| **1** | (humer* OR (long NEXT/1 (bone? OR limb?))):ti,ab |
| **2** | (metasta* OR ((disseminat* OR spread*) NEAR/2 (disease OR tumo?r* OR malignan* OR lesion?)) OR (lymphoma* NOT (primary NEAR/4 lymphoma*)) OR myeloma* OR (tumo?r* NEAR/3 lesion?) OR (pathologic* NEXT/5 fracture?) OR (secondar* NEXT/5 (tumo?r* OR neoplas* OR malignan* OR chondrosarcoma*)) OR (tumo?r* NEAR/4 invad*)):ti,ab |
| **3** | #1 AND #2 |
| **4** | (bone? or extremit* or hip or vertebra* or spine or spinal OR osteosarcoma* OR skelet*):ti,ab |

| | |
|---|---|
| **5** | #4 AND #2 |
| **6** | (dvt OR vte OR thrombos* OR thrombotic OR thromboembol* OR thrombophlebitis OR ((pulmonary OR lung?) AND (infarct* OR embol* OR clot*))):ti,ab |
| **7** | (anticoagul* OR "anti coagul*"):ti,ab OR (antithromb* OR thrombolytic* OR thromboprophyla* OR chemoprophyla*):ti,ab OR (antiplatelet* OR (anti NEXT/1 platelet*)):ti,ab OR (heparin* OR dalteparin OR Fragmin OR tinzaparin OR Innohep OR enoxaparin OR Lovenox):ti,ab OR (Plavix OR clopidogrel):ti,ab OR (Coumadin OR Jantoven OR warfarin*):ti,ab OR (Arixtra OR fondaparinux OR (factor NEXT/1 Xa NEXT/1 inhibitor*) OR rivaroxaban OR Xarelto OR apixaban OR Eliquis OR edoxaban OR Savaysa OR betrixaban OR Bevyxxa OR bivalirudin OR Angiomax OR lepirudin OR Refludan OR dabigatran OR Pradaxa OR desirudin OR desulfatohirudin OR Iprivask OR argatroban OR aspirin):ti,ab |
| **8** | (compression NEXT/1 (stocking? OR device?)):ti,ab OR (foot AND pump?):ti,ab OR ((pneumatic OR leg OR calf) NEXT/1 compression):ti,ab OR (mechanical NEXT/3 prophyla*):ti,ab |
| **9** | #5 AND #6 AND (#7 OR #8) |
| **10** | #3 OR #9 |
| **11** | ((race OR racial* OR sex OR sexual OR male OR female OR age OR gender OR transgender OR social OR socio* OR insurance OR insured OR uninsured OR ethnic* OR demographic* OR black OR disabilit* OR disabled OR handicap*) NEAR/5 (difference? OR disparit* OR impact* OR outcome? OR effect? OR predict* OR factor? OR prognos* OR risk? OR correlat* OR related OR relationship? OR determinant*)):ti,ab OR ([mh "Health Facilities"] AND (facilit* OR center? OR hospital? OR clinic?):ti) |
| **12** | (regression OR ((varia* OR univaria* OR multivaria* OR Cox) NEAR/5 (analys* OR model* OR tests))):ti,ab |
| **13** | #5 AND #11 AND #12 |
| **14** | #10 OR #13 |
| **15** | "conference abstract":pt OR (abstracts OR editorial OR reply OR comment? OR commentary OR letter):ti OR cadaver*:ti,ab OR "in vitro":ti OR (animal? OR dog OR dogs OR sheepdog OR canine OR cats OR feline OR horse? OR equine OR mouse OR mice OR murine OR rat OR rats OR rabbit? OR sheep OR ovine OR porcine OR pig OR pigs OR rodent? OR monkey? OR hen OR hens OR veterinar* OR avian OR reindeer OR dolphin):ti |
| **16** | ([mh Infant] OR [mh Child] OR [mh Adolescent] OR (pediatric* OR paediatric* OR child OR children OR childhood OR adolescen* OR juvenile? OR teen OR teens OR teenager? OR youth? OR infant*):ti) NOT ([mh Adult] OR adult*:ti OR (elderly OR geriatric? OR (older NEXT/1 (adult? OR people OR person? OR women OR men OR patient?))):ti,ab OR (mean-age NEXT/3 18*):ab) |
| **17** | (osteoporo* OR diabet* OR ((fragility OR insufficiency OR "low energy") NEAR/4 fracture?)):ti |
| **18** | #14 NOT (#15 OR #16 OR #17) *with Publication Year from 1990 to 2022, in Trials* |
| **19** | #14 NOT (#15 OR #16 OR #17) *with Cochrane Library publication date from Jan 1990 to Feb 2022, in Cochrane Reviews* |
| **20** | #18 OR #19 |

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## Appendix V: Excluded literature not meeting inclusion criteria

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Prevalence and countermeasures for venous thromboembolic diseases associated with spinal surgery: A follow-up study of an institutional protocol in 209 patients | Akeda, K.; Matsunaga, H.; Imanishi, T.; Hasegawa, M.; Sakakibara, T.; Kasai, Y.; Sudo, A. | 2014 | patient population, only 21 pts had metastatic bone disease |
| Extra-articular shoulder resections: outcomes of 54 patients | Angelini, A.; Mavrogenis, A. F.; Trovarelli, G.; Pala, E.; Arbelaez, P.; Casanova, J.; Berizzi, A.; Ruggieri, P. | 2017 | irrelevant topic; no metastatic bone disease |
| Risk factors of distant metastasis after surgery among different breast cancer subtypes: a hospital-based study in Indonesia | Anwar, S. L.; Avanti, W. S.; Nugroho, A. C.; Choridah, L.; Dwianingsih, E. K.; Harahap, W. A.; Aryandono, T.; Wulaningsih, W. | 2020 | irrelevant topic; risk of metastatic disease |
| What Factors Are Associated with Local Metastatic Lesion Progression After Intramedullary Nail Stabilization? | Arpornsuksant, P.; Morris, C. D.; Forsberg, J. A.; Levin, A. S. | 2021 | irrelevant comparison; no treatment comparison; pts <18 years old |
| Complications of Percutaneous Bone Tumor Cryoablation: A 10-year Experience | Auloge, P.; Cazzato, R. L.; Rousseau, C.; Caudrelier, J.; Koch, G.; Rao, P.; Chiang, J. B.; Garnon, J.; Gangi, A. | 2019 | irrelevant topic; no humerus |
| Predictors of short-term mortality in critically ill patients with solid malignancies | Azoulay, E.; Moreau, D.; Alberti, C.; Leleu, G.; Adrie, C.; Barboteu, M.; Cottu, P.; Levy, V.; Le Gall, J. R.; Schlemmer, B. | 2000 | Irrelevant topic; Non-metastatic cancer |
| Comparison of outcomes of 2 surgical treatments for proximal humerus giant cell tumors: a multicenter retrospective study | Bai, W. Z.; Guo, S. B.; Zhao, W.; Yu, X. C.; Xu, M.; Zheng, K.; Hu, Y. C.; Wang, F.; Zhang, G. C. | 2019 | irrelevant topic; no metastatic bone disease |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Demographics, Pattern of Care, and Outcome Analysis of Malignant Melanomas - Experience From a Tertiary Cancer Centre in India | Bajpai, J.; Abraham, G.; Saklani, A. P.; Agarwal, A.; Das, S.; Chatterjee, A.; Kapoor, A.; Eaga, P.; Mondal, P. K.; Chandrasekharan, A.; Bhargava, P. G.; Srinivas, S.; Turkar, S.; Rekhi, B.; Khanna, N.; Janu, A. K.; Bal, M.; Ostwal, V. S.; Ramaswamy, A.; Rohila, J.; Desouza, A. L.; Guha, A.; Kumar, R.; Menon, N. S.; Rath, S.; Patil, V. M.; Noronha, V. M.; Joshi, A. P.; Laskar, S.; Rangarajan, V.; Prabhash, K.; Gupta, S.; Banavali, S. | 2021 | irrelevant comparison; metastatic vs non-metastatic |
| Pathological fractures; a consideration with metachondromatosis and differential diagnoses. Osteochondromatosis and Gauchers disease | Banks, R. J. | 2002 | irrelevant topic; Goucher's disease |
| Treatment of pathological fractures of the humerus with a locked intramedullary nail | Bauze, A. J.; Clayer, M. T. | 2003 | no comparison group |
| Prognostic factors affecting survival of patients with pathologic humerus shaft fractures treated with intramedullary nailing without tumor removal | Bayram, S.; Ozmen, E.; Birisik, F.; Kiral, D.; Salduz, A.; Ersen, A. | 2019 | no comparison group |
| Treatment of venous thromboembolism in cancer patients: The dark side of the moon | Becattini, C.; Di Nisio, M.; Franco, L.; Lee, A.; Agnelli, G.; Mandala, M. | 2021 | Irrelevant topic; Review article |
| Risk factors for same-admission mortality after pathologic fracture secondary to metastatic cancer | Behnke, N. K.; Baker, D. K.; Xu, S.; Niemeier, T. E.; Watson, S. L.; Ponce, B. A. | 2017 | irrelevant topic; spinal metastases |
| Humeral Nail: Comparison of the Antegrade and Retrograde Application | Bencic, I.; Cengic, T.; Prenc, J.; Bulatovic, N.; Matejcic, A. | 2016 | irrelevant comparison; fracture type, not treatment type |
| Inferior vena cava filters prevent pulmonary emboli in patients with metastatic pathologic fractures of the lower extremity | Benevenia, J.; Bibbo, C.; Patel, D. V.; Grossman, M. G.; Bahramipour, P. F.; Pappas, P. J. | 2004 | irrelevant topic; vena cava filters |
| Outcomes of a Modular Intercalary Endoprosthesis as Treatment for Segmental Defects of the Femur, Tibia, and Humerus | Benevenia, J.; Kirchner, R.; Patterson, F.; Beebe, K.; Wirtz, D. C.; Rivero, S.; Palma, M.; Friedrich, M. J. | 2016 | not all pts have metastatic bone disease |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Supplemental Bone Grafting in Giant Cell Tumor of the Extremity Reduces Nononcologic Complications | Benevenia, J.; Rivero, S. M.; Moore, J.; Ippolito, J. A.; Siegerman, D. A.; Beebe, K. S.; Patterson, F. R. | 2017 | irrelevant topic; no humerus/metastatic bone disease |
| Economic burden of skeletal-related events in patients with multiple myeloma: analysis of US commercial claims database | Bhowmik, D.; Hines, D. M.; Intorcia, M.; Wade, R. L. | 2018 | irrelevant topic; skeletal-related events vs non-skeletal-related events |
| Function after resection of humeral metastases: analysis of 59 consecutive patients | Bickels, J.; Kollender, Y.; Wittig, J. C.; Meller, I.; Malawer, M. M. | 2005 | irrelevant comparison: endoprosthesis vs cemented nailing |
| Focal anatomic resurfacing implantation for bilateral humeral and femoral heads' avascular necrosis in a patient with Hodgkin's lymphoma and literature review | Bilge, O.; Doral, M. N.; Miniaci, A. | 2015 | Case Report |
| Incidence of venous thrombosis in a large cohort of 66,329 cancer patients: results of a record linkage study | Blom, J. W.; Vanderschoot, J. P.; Oostindier, M. J.; Osanto, S.; van der Meer, F. J.; Rosendaal, F. R. | 2006 | risk factors, not postop |
| Pathologic fracture and healthcare resource utilisation: A retrospective study in eight European countries | Body, J. J.; Acklin, Y. P.; Gunther, O.; Hechmati, G.; Pereira, J.; Maniadakis, N.; Terpos, E.; Finek, J.; von Moos, R.; Talbot, S.; Sleeboom, H. | 2016 | irrelevant outcomes |
| Young age and autologous stem cell transplantation are associated with improved survival in newly diagnosed multiple myeloma | Bove, V.; Garrido, D.; Riva, E. | 2021 | irrelevant comparison |
| Humeral stress shielding following cemented endoprosthetic reconstruction: An under-reported complication? | Braig, Z. V.; Tagliero, A. J.; Rose, P. S.; Elhassan, B. T.; Barlow, J. D.; Wagner, E. R.; Sanchez-Sotelo, J.; Houdek, M. T. | 2021 | irrelevant topic; stress shielding |
| Gender, anthropometric factors and risk of colorectal cancer with particular reference to tumour location and TNM stage: a cohort study | Brandstedt, J.; Wangefjord, S.; Nodin, B.; Gaber, A.; Manjer, J.; Jirstrom, K. | 2012 | irrelevant topic; colorectal cancer |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Analysis of predictors of pain response in patients with bone metastasis undergoing palliative radiotherapy: Does age matter? | Cacicedo, J.; Gomez-Iturriaga, A.; Navarro, A.; Morillo, V.; Willisch, P.; Lopez-Guerra, J. L.; Illescas, A.; Casquero, F.; Del Hoyo, O.; Ciervide, R.; Martinez-Indart, L.; Bilbao, P.; Rades, D. | 2018 | irrelevant topic; palliative care |
| Reconstruction by allograft-prosthetic composite reverse shoulder arthroplasty after proximal humerus tumor resection: clinical and radiographic assessment at a minimum 2 years' follow-up | Callamand, G.; Barret, H.; Saint-Genez, F.; Bonnevialle, P.; Mansat, P.; Bonnevialle, N. | 2021 | No comparison group |
| Prosthetic joint replacement for long bone metastases: Analysis of 154 cases | Camnasio, F.; Scotti, C.; Peretti, G. M.; Fontana, F.; Fraschini, G. | 2008 | Irrelevant topic; patient population not all humerus |
| Prognostic factors for survival in patients with metastatic lung adenocarcinoma: An analysis of the SEER database | Campos-Balea, B.; de Castro Carpeno, J.; Massuti, B.; Vicente-Baz, D.; Perez Parente, D.; Ruiz-Gracia, P.; Crama, L.; Cobo Dols, M. | 2020 | irrelevant topic; SEER database used |
| New concepts in the surgical treatment of actual and impending pathological fractures in metastatic disease | Cappellari, A.; Trovarelli, G.; Crimi, A.; Pala, E.; Angelini, A.; Berizzi, A.; Ruggieri, P. | 2020 | irrelevant comparison; plate vs prosthesis |
| Humeral metastasis of renal cancer: Surgical options and review of literature | Casadei, R.; Drago, G.; Di Pressa, F.; Donati, D. | 2018 | no comparison group |
| Metastatic renal cell carcinoma: Patterns and predictors of metastases-A contemporary population-based series | Chandrasekar, T.; Klaassen, Z.; Goldberg, H.; Kulkarni, G. S.; Hamilton, R. J.; Fleshner, N. E. | 2017 | Irrelevant topic; predictors of metastatic disease |
| Comparison of the use of the humerus intramedullary nail and dynamic compression plate for the management of diaphyseal fractures of the humerus. A randomised controlled study | Changulani, M.; Jain, U. K.; Keswani, T. | 2007 | irrelevant topic; no tumors |
| Prognosis-Based Shoulder Hemiarthroplasty After Resection of Proximal Humeral Malignancy | Chen, C. M.; Wu, P. K.; Tsai, S. W.; Chen, C. F.; Chen, W. M. | 2017 | Irrelevant topic; patient population, some <18 years old |
| Ante-grade intramedullary nailing for the treatment of humeral shaft metastatic bone tumor | Chen, J. L.; Yeh, T. T.; Pan, R. Y.; Wu, C. C. | 2014 | case series |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Prognostic factors and survival according to tumor subtype in newly diagnosed breast cancer with liver metastases: A competing risk analysis | Chen, Q. F.; Huang, T.; Shen, L.; Wu, P.; Huang, Z. L.; Li, W. | 2019 | irrelevant topic; SEER database used |
| Risk factors for bone metastasis from renal cell cancer | Chen, X. Y.; Lan, M.; Zhou, Y.; Chen, W. Z.; Hu, D.; Liu, J. M.; Huang, S. H.; Liu, Z. L.; Zhang, Z. H. | 2017 | irrelevant topic; bone metastasis vs no bone metastasis |
| Risk factors and prognostic predictors for Cervical Cancer patients with lung metastasis | Chen, X.; Chen, L.; Zhu, H.; Tao, J. | 2020 | irrelevant topic; SEER database used |
| Role of BMI and age in predicting pathologic vertebral fractures in newly diagnosed multiple myeloma patients: A retrospective cohort study | Chen, Y. L.; Liu, Y. C.; Wu, C. H.; Yeh, C. M.; Chiu, H. I.; Lee, G. Y.; Lee, Y. T.; Hsu, P.; Lin, T. W.; Gau, J. P.; Hsiao, L. T.; Chiou, T. J.; Liu, J. H.; Liu, C. J. | 2018 | irrelevant topic; spinal metastases |
| Reconstruction of the Shoulder and Humerus in Metastatic Bone Disease | Cheng, E. Y.; Ogilvie, C. M. | 2019 | review |
| Long bone fractures: treatment patterns and factors contributing to use of intramedullary nailing | Chitnis, A.; Ray, B.; Sparks, C.; Grebenyuk, Y.; Vanderkarr, M.; Holy, C. E. | 2020 | irrelevant comparison; metastatic cancer vs not |
| Intramedullary Nailing for Pathological Fractures of the Proximal Humerus | Choi, E. S.; Han, I.; Cho, H. S.; Park, I. W.; Park, J. W.; Kim, H. S. | 2016 | irrelevant comparison; only compares nailing to other study results |
| Skeletal Complications and Mortality in Thyroid Cancer: A Population-Based Study | Choksi, P.; Papaleontiou, M.; Guo, C.; Worden, F.; Banerjee, M.; Haymart, M. | 2017 | irrelevant topic; SEER database used |
| Gender differences in pain and patient reported outcomes: a secondary analysis of the NCIC CTG SC. 23 randomized trial | Chow, S.; Ding, K.; Wan, B. A.; Brundage, M.; Meyer, R. M.; Nabid, A.; Chabot, P.; Coulombe, G.; Ahmed, S.; Kuk, J.; Dar, A. R.; Mahmud, A.; Fairchild, A.; Wilson, C. F.; Wu, J. S. Y.; Dennis, K.; DeAngelis, C.; Wong, R. K. S.; Zhu, L.; Chow, E. | 2017 | irrelevant topic; vertebrae and hip/pelvis radiotherapy |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Patient Reported Outcomes After Radiation Therapy for Bone Metastases as a Function of Age: A Secondary Analysis of the NCIC CTG SC-Twenty-Three Randomized Trial | Chow, S.; Ding, K.; Wan, B. A.; Brundage, M.; Meyer, R. M.; Nabid, A.; Chabot, P.; Coulombe, G.; Ahmed, S.; Kuk, J.; Dar, A. R.; Mahmud, A.; Fairchild, A.; Wilson, C. F.; Wu, J. S. Y.; Dennis, K.; DeAngelis, C.; Wong, R. K. S.; Zhu, L.; Chow, E. | 2018 | Irrelevant topic; out-comes of radiotherapy as a function of age |
| Analysis of 90-Day Readmissions After Total Shoulder Arthroplasty | Chung, A. S.; Makovicka, J. L.; Hydrick, T.; Scott, K. L.; Arvind, V.; Hattrup, S. J. | 2019 | irrelevant topic; readmissions |
| Hospitalization of hospice patients with cancer | Cintron, A.; Hamel, M. B.; Davis, R. B.; Burns, R. B.; Phillips, R. S.; McCarthy, E. P. | 2003 | Irrelevant topic; patient population, primary lung or colorectal cancer |
| Surgical treatment in bone metastases in the appendicular skeleton | Clara-Altamirano, M. A.; Garcia-Ortega, D. Y.; Martinez-Said, H.; Caro-Sanchez, C. H. S.; Herrera-Gomez, A.; Cuellar-Hubbe, M. | 2018 | irrelevant comparison; 8 subjects with humerus tumor, no comparison treatment |
| Intramedullary Nail Fixation for the Treatment of Pathologic Humeral Shaft Fractures | Colello, M. J.; Hunter, M. D.; Tanner, S. L.; Porter, S. E. | 2020 | irrelevant topic; reamed vs unreamed nails |
| The invisible nail: a technique report of treatment of a pathological humerus fracture with a radiolucent intramedullary nail | Collis, P. N.; Clegg, T. E.; Seligson, D. | 2011 | review |
| Constrained or unconstrained shoulder replacement for musculoskeletal tumor resections? | Cundy, W. J.; McArthur, M. S.; Dickinson, I. C.; Rowell, P. D.; Sommerville, S. M. M. | 2020 | irrelevant topic; constrained vs unconstrained |
| Predictors of overall survival in non-small-cell lung cancer patients with metastatic spinal cord compression treated with short-course radiotherapy | da Silva, G. T.; da Costa, T. G. P.; De Bessa, C. M.; Zamboni, M. M.; Bergmann, A.; Thuler, L. C. S. | 2021 | irrelevant topic; radiotherapy |
| Risk of venous thromboembolism in bone and soft-tissue sarcoma patients undergoing surgical intervention: a report from prior to the initiation of SCIP measures | Damron, T. A.; Wardak, Z.; Glodny, B.; Grant, W. | 2011 | risk factors, not postop |
| The impact of insurance status on outcomes after surgery for spinal metastases | Dasenbrock, H. H.; Wolinsky, J. P.; Sciubba, D. M.; Witham, T. F.; Gokaslan, Z. L.; Bydon, A. | 2012 | irrelevant topic; spinal metastases |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Risk of venous thromboembolism after shoulder arthroplasty in the Medicare population | Day, J. S.; Ramsey, M. L.; Lau, E.; Williams, G. R. | 2015 | irrelevant topic; 0.5% pts had metastatic tumors |
| Retrospective, multicenter, observational study of 112 surgically treated cases of humerus metastasis | de Geyer, A.; Bourgoin, A.; Rousseau, C.; Ropars, M.; Bonnevialle, N.; Bouthors, C.; Descamps, J.; Niglis, L.; Sailhan, F.; Bonnevialle, P.; SoFcot, | 2020 | no comparison group |
| Racial disparities in clinical presentation, type of intervention, and in-hospital outcomes of patients with metastatic spine disease: An analysis of 145,809 admissions in the United States | De la Garza Ramos, R.; Benton, J. A.; Gelfand, Y.; Echt, M.; Flores Rodriguez, J. V.; Yanamadala, V.; Yassari, R. | 2020 | irrelevant topic; spinal metastases |
| Racial Disparities in Perioperative Morbidity Following Oncological Spine Surgery | De la Garza Ramos, R.; Choi, J. H.; Naidu, I.; Benton, J. A.; Echt, M.; Yanamadala, V.; Passias, P. G.; Shin, J. H.; Altschul, D. J.; Goodwin, C. R.; Sciubba, D. M.; Yassari, R. | 2021 | irrelevant topic; spinal metastases |
| Timing of Prophylactic Anticoagulation and Its Effect on Thromboembolic Events After Surgery for Metastatic Tumors of the Spine | De la Garza Ramos, R.; Longo, M.; Gelfand, Y.; Echt, M.; Kinon, M. D.; Yassari, R. | 2019 | Irrelevant topic; case series |
| Operative treatment of humeral shaft fractures. Comparison of plating and intramedullary nailing | Denies, E.; Nijs, S.; Sermon, A.; Broos, P. | 2010 | irrelevant topic; no metastatic bone disease/tumor |
| Chondroblastoma: Is intralesional curettage with the use of adjuvants a sufficient way of therapy? | Deventer, N.; Deventer, N.; Gosheger, G.; de Vaal, M.; Budny, T.; Laufer, A.; Heitkoetter, B.; Luebben, T. | 2021 | review |
| Risk factors of regional lymph node (RLN) metastasis among patients with bone sarcoma and survival of patients with RLN-positive bone sarcoma | Dong, Y.; Wu, W.; Kang, H.; Xiong, W.; Ye, D.; Fang, Z.; Guan, H.; Liao, H.; Li, F. | 2021 | irrelevant topic; SEER database used |
| Prognostic factors for survival in patients with high-grade osteosarcoma using the Surveillance, Epidemiology, and End Results (SEER) Program database | Duchman, K. R.; Gao, Y.; Miller, B. J. | 2015 | irrelevant topic; SEER database used |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Functional and Oncological Outcome After Treatment of Chondroblastoma With Intralesional Curettage | Ebeid, W. A.; Hasan, B. Z.; Badr, I. T.; Mesregah, M. K. | 2019 | no comparison group |
| Present day controversies and consensus in curettage for giant cell tumor of bone | Errani, C.; Tsukamoto, S.; Ciani, G.; Donati, D. M. | 2019 | Irrelevant topic; Giant cell tumor of bone |
| Survival Analysis of 3 Different Age Groups and Prognostic Factors among 402 Patients with Skeletal High-Grade Osteosarcoma. Real World Data from a Single Tertiary Sarcoma Center | Evenhuis, R. E.; Acem, I.; Rueten-Budde, A. J.; Karis, D. S. A.; Fiocco, M.; Dorleijn, D. M. J.; Speetjens, F. M.; Anninga, J.; Gelderblom, H.; van de Sande, M. A. J. | 2021 | combined age group populations include <18 |
| Risk factors and nomogram for newly diagnosis of bone metastasis in bladder cancer: A SEER-based study | Fan, Z.; Huang, Z.; Hu, C.; Tong, Y.; Zhao, C. | 2020 | irrelevant topic; SEER database used |
| Bone Metastasis in Renal Cell Carcinoma Patients: Risk and Prognostic Factors and Nomograms | Fan, Z.; Huang, Z.; Huang, X. | 2021 | irrelevant topic; SEER database used |
| Intramedullary nailing of humeral shaft fractures. A retrospective study of 126 cases | Flinkkila, T.; Hyvonen, P.; Lakovaara, M.; Linden, T.; Ristiniemi, J.; Hamalainen, M. | 1999 | no comparison treatment |
| Pathological fractures of the humeral shaft | Flinkkila, T.; Hyvonen, P.; Leppilahti, J.; Hamalainen, M. | 1998 | no comparison group |
| Pathologic fractures due to metastatic disease. A retrospective study of 160 surgically treated fractures | Fourneau, I.; Broos, P. | 1998 | Irrelevant topic; patient population not all humerus |
| An expandable nailing system for the management of pathological humerus fractures | Franck, W. M.; Olivieri, M.; Jannasch, O.; Hennig, F. F. | 2002 | irrelevant topic; no comparison group |
| Salvage of the upper extremity in cases of tumorous destruction of the proximal humerus | Fuhrmann, R. A.; Roth, A.; Venbrocks, R. A. | 2000 | No comparison group |
| Modular prosthetic reconstruction of major bone defects of the distal end of the humerus | Funovics, P. T.; Schuh, R.; Adams, S. B., Jr.; Sabeti-Aschraf, M.; Dominkus, M.; Kotz, R. I. | 2011 | irrelevant topic; tumor group vs reconstruction group |
| Thirty-day Outcomes After Surgery for Metastatic Bone Disease of the Extremities: An Analysis of the NSQIP Database | Gallaway, K. E.; Ahn, J.; Callan, A. K. | 2020 | no comparison group |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Complications and functional outcomes of reconstruction with an osteoarticular allograft after intra-articular resection of the proximal aspect of the humerus | Getty, P. J.; Peabody, T. D. | 1999 | case series |
| Metastatic Esophageal Carcinoma: Prognostic Factors and Survival | Ghazy, H. F.; El-Hadaad, H. A.; Wahba, H. A.; Abbas, R.; Abbas, O. A. | 2021 | irrelevant topic; esophageal cancer |
| Impact of Asian ethnicity on outcome in metastatic EGFR-mutant non-small cell lung cancer | Gibson, A. J. W.; D'Silva, A.; Elegbede, A. A.; Tudor, R. A.; Dean, M. L.; Bebb, D. G.; Hao, D. | 2019 | irrelevant topic; 56% bone metastasis |
| Humeral Shaft Fracture Fixation: Incidence Rates and Complications as Reported by American Board of Orthopaedic Surgery Part II Candidates | Gottschalk, M. B.; Carpenter, W.; Hiza, E.; Reisman, W.; Roberson, J. | 2016 | irrelevant topic; no tumor/metastatic bone disease |
| The outcome of locking plate fixation for the treatment of periarticular metastases | Gregory, J. J.; Ockendon, M.; Cribb, G. L.; Cool, P. W.; Williams, D. H. | 2011 | case series |
| Body composition predictors of mortality in patients undergoing surgery for long bone metastases | Groot, O. Q.; Bongers, M. E. R.; Buckless, C. G.; Twining, P. K.; Kapoor, N. D.; Janssen, S. J.; Schwab, J. H.; Torriani, M.; Bredella, M. A. | 2022 | irrelevant topic; biomarkers |
| Clinical Outcome Differences in the Treatment of Impending Versus Completed Pathological Long-Bone Fractures | Groot, O. Q.; Lans, A.; Twining, P. K.; Bongers, M. E. R.; Kapoor, N. D.; Verlaan, J. J.; Newman, E. T.; Raskin, K. A.; Lozano-Calderon, S. A.; Janssen, S. J.; Schwab, J. H. | 2021 | irrelevant topic; no humerus |
| High Risk of Venous Thromboembolism After Surgery for Long Bone Metastases: A Retrospective Study of 682 Patients | Groot, O. Q.; Ogink, P. T.; Janssen, S. J.; Paulino Pereira, N. R.; Lozano-Calderon, S.; Raskin, K.; Hornicek, F.; Schwab, J. H. | 2018 | all outcomes are combined |
| High Risk of Symptomatic Venous Thromboembolism After Surgery for Spine Metastatic Bone Lesions: A Retrospective Study | Groot, O. Q.; Ogink, P. T.; Paulino Pereira, N. R.; Ferrone, M. L.; Harris, M. B.; Lozano-Calderon, S. A.; Schoenfeld, A. J.; Schwab, J. H. | 2019 | all post op data is combined |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Quality of life of patients with proximal humerus metastasis treated with cement spacer | Guo, W.; Gao, X.; Wang, D.; Wang, T.; Tang, L.; Wang, Y.; Liu, B. | 2019 | irrelevant comparison; surgical vs nonsurgical group |
| Prognostic Significance of Young Age and Non-Bone Metastasis at Diagnosis in Patients with Metastatic Prostate Cancer: a SEER Population-Based Data Analysis | Guo, Y.; Mao, S.; Zhang, A.; Wang, R.; Zhang, Z.; Zhang, J.; Wang, L.; Zhang, W.; Wu, Y.; Ye, L.; Yang, B.; Yao, X. | 2019 | irrelevant topic; SEER database used |
| Curettage with cement augmentation of large bone defects in giant cell tumors with pathological fractures in lower-extremity long bones | Gupta, S. P.; Garg, G. | 2016 | case series |
| Results of the treatment of bone metastases with modular prosthetic replacement--analysis of 67 patients | Guzik, G. | 2016 | <5 patients per group |
| Prevalence and risk factors of preoperative venous thromboembolism in patients with malignant musculoskeletal tumors: an analysis based on D-dimer screening and imaging | Hayashida, K.; Kawabata, Y.; Saito, K.; Fujita, S.; Choe, H.; Kato, I.; Takeyama, M.; Inaba, Y. | 2022 | irrelevant comparison |
| Clinical Characteristics and Survival Outcomes in Neuroblastoma With Bone Metastasis Based on SEER Database Analysis | He, B.; Mao, J.; Huang, L. | 2021 | irrelevant topic; SEER database used |
| Megaprosthetic replacement of the distal humerus: still a challenge in limb salvage | Henrichs, M. P.; Liem, D.; Gosheger, G.; Streitbuerger, A.; Nottrott, M.; Andreou, D.; Hardes, J. | 2019 | case series |
| Effect of socioeconomic status as measured by education level on survival in breast cancer clinical trials | Herndon, J. E., 2nd; Kornblith, A. B.; Holland, J. C.; Paskett, E. D. | 2013 | irrelevant topic; breast cancer |
| Prognostic factors following pathological fractures | Hill, T.; D'Alessandro, P.; Murray, K.; Yates, P. | 2015 | irrelevant topic; <50% humerus |
| Shoulder and elbow function following Marchetti-Vicenzi humeral nail fixation | Hossain, S.; Roy, N.; Ayeko, C.; Elsworth, C. F.; Jacobs, L. G. | 2003 | no comparison group |
| The Personalized Shoulder Reconstruction Assisted by 3D Printing Technology After Resection of the Proximal Humerus Tumours | Hu, H.; Liu, W.; Zeng, Q.; Wang, S.; Zhang, Z.; Liu, J.; Zhang, Y.; Shao, Z.; Wang, B. | 2019 | case series |

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|---|---|---|---|
| Risk factors, prognostic factors, and nomograms for bone metastasis in patients with newly diagnosed infiltrating duct carcinoma of the breast: a population-based study | Huang, Z.; Hu, C.; Liu, K.; Yuan, L.; Li, Y.; Zhao, C.; Hu, C. | 2020 | irrelevant topic; SEER database used |
| Surgical fixation of pathologic fractures: an evaluation of evolving treatment methods | Hunt, K. J.; Gollogly, S.; Randall, R. L. | 2006 | case series |
| Risk of skeletal related events among elderly prostate cancer patients by site of metastasis at diagnosis | Hussain, A.; Aly, A.; Daniel Mullins, C.; Qian, Y.; Arellano, J.; Onukwugha, E. | 2016 | irrelevant topic; SEER database used |
| Treatment of pathological fractures of the humerus with Ender nails | Hyder, N.; Wray, C. C. | 1993 | no comparison group |
| Immediate family support is important to discharge home for cancer patient with bone metastasis after rehabilitation: A retrospective study | Ikeguchi, R.; Nankaku, M.; Yamawaki, R.; Tanaka, H.; Hamada, R.; Kawano, T.; Murao, M.; Kitamura, G.; Sato, T.; Nishikawa, T.; Noguchi, T.; Kuriyama, S.; Sakamoto, A.; Matsuda, S. | 2021 | irrelevant topic; rehabilitation outcomes |
| Intramedullary interlocking nailing for humeral fractures: experiences with the Russell-Taylor humeral nail | Ikpeme, J. O. | 1994 | no comparison group |
| Locked intramedullary nailing of humeral shaft fractures. Implant design, surgical technique, and clinical results | Ingman, A. M.; Waters, D. A. | 1994 | population did not have metastatic bone disease |
| Resection of the proximal humerus for metastases and replacement with RPS prosthesis | Ippolito, V.; Saccalani, M.; Ianni, L.; Spaggiari, L.; Cavina, F.; Modonesi, F.; Bonetti, L.; Sartori, G. | 2003 | no comparison group |
| Management of metastatic humeral fractures: Variations according to orthopedic subspecialty, tumor characteristics | Janssen, S. J.; Bramer, J. A. M.; Guitton, T. G.; Hornicek, F. J.; Schwab, J. H. | 2018 | irrelevant outcomes; tumor characteristics and ortho surgeon specialties |
| Complications after surgery for metastatic humeral lesions | Janssen, S. J.; van Dijke, M.; Lozano-Calderon, S. A.; Ready, J. E.; Raskin, K. A.; Ferrone, M. L.; Hornicek, F. J.; Schwab, J. H. | 2016 | case series |

| Article Title | Authors | Year | Reason for Exclusion |
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| Factors associated with improved outcomes following decompressive surgery for prostate cancer metastatic to the spine | Ju, D. G.; Zadnik, P. L.; Groves, M. L.; Hwang, L.; Kaloostian, P. E.; Wolinksy, J. P.; Witham, T. F.; Bydon, A.; Gokaslan, Z. L.; Sciubba, D. M. | 2013 | Irrelevant topic; outcomes based on surgery |
| Reverse shoulder replacement after resection of the proximal humerus for bone tumours | Kaa, A. K.; Jorgensen, P. H.; Sojbjerg, J. O.; Johannsen, H. V. | 2013 | case series |
| Revision rate of reconstructions in surgically treated diaphyseal metastases of bone | Kask, G.; Nieminen, J.; Parry, M. C.; van Iterson, V.; Pakarinen, T. K.; Ratasvuori, M.; Laitinen, M. K. | 2019 | humerus data combined with other body parts |
| Statistical analysis of prognostic factors for survival in patients with spinal metastasis | Kataoka, M.; Kunisada, T.; Tanaka, M.; Takeda, K.; Itani, S.; Sugimoto, Y.; Misawa, H.; Senda, M.; Nakahara, S.; Ozaki, T. | 2012 | irrelevant topic; treatment options |
| Characteristics and Prognostic Factors of Bone Metastasis in Patients With Colorectal Cancer | Kawamura, H.; Yamaguchi, T.; Yano, Y.; Hozumi, T.; Takaki, Y.; Matsumoto, H.; Nakano, D.; Takahashi, K. | 2018 | Irrelevant outcomes |
| Does surgical technique influence the burden of lung metastases in patients with pathologic long bone fractures? | Kendal, J. K.; Heard, B. J.; Abbott, A. G.; Moorman, S. W.; Saini, R.; Puloski, S. K. T.; Monument, M. J. | 2022 | irrelevant topic; lung metastases |
| Assessment of whole body MRI and sestamibi technetium-99m bone marrow scan in prediction of multiple myeloma disease progression and outcome: a prospective comparative study | Khalafallah, A. A.; Snarski, A.; Heng, R.; Hughes, R.; Renu, S.; Arm, J.; Dutchke, R.; Robertson, I. K.; To, L. B. | 2013 | irrelevant topic; imaging |
| Minimally invasive surgery of humeral metastasis using flexible nails and cement in high-risk patients with advanced cancer | Kim, J. H.; Kang, H. G.; Kim, J. R.; Lin, P. P.; Kim, H. S. | 2011 | case series |
| Outcomes after extensive manual curettage and limited burring for atypical cartilaginous tumour of long bone | Kim, W.; Lee, J. S.; Chung, H. W. | 2018 | no comparison group |
| Closed intramedullary nailing with percutaneous cement augmentation for long bone metastases | Kim, Y. I.; Kang, H. G.; Kim, J. H.; Kim, S. K.; Lin, P. P.; Kim, H. S. | 2016 | irrelevant topic; femur and humerus data combined |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Results with the isoelastic shoulder prosthesis in primary and secondary tumors of the proximal humerus | Klestil, T.; Kerber, W.; Sterzinger, W.; Krismer, M. | 1993 | No comparison group |
| Outcomes of critically ill cancer patients in a university hospital setting | Kress, J. P.; Christenson, J.; Pohlman, A. S.; Linkin, D. R.; Hall, J. B. | 1999 | irrelevant topic; critically ill cancer patients |
| Early Experience in Pathologic Humerus Fracture Treated With the Photodynamic Bone Stabilization System Shows Limitations Related to Patient Selection | Krumme, J.; MacConnell, A.; Wallace, M.; Aboulafia, A.; Jelinek, J.; Adams, B.; Henshaw, R. | 2021 | no comparison group |
| Closed retrograde nailing of pathological humeral fractures | Kumta, S. M.; Quintos, A. D.; Griffith, J. F.; Chow, L. T.; Wong, K. C. | 2002 | no comparison group |
| Proximal humeral reconstruction using nail cement spacer in primary and metastatic tumours of proximal humerus | Kundu, Z. S.; Gogna, P.; Gupta, V.; Kamboj, P.; Singla, R.; Sangwan, S. S. | 2013 | case series |
| Clinical significance of trabecular bone score for prediction of pathologic fracture risk in patients with multiple myeloma | Lee, E. M.; Kim, B. | 2018 | irrelevant topic; fracture vs no fracture |
| Cement Intercalary Reconstruction After Bone Tumor Resection | Lesensky, J.; Mavrogenis, A. F. | 2021 | case series |
| Precise resection and biological reconstruction for patients with bone sarcomas in the proximal humerus | Li, J.; Wang, Z.; Guo, Z.; Wu, Y.; Chen, G.; Pei, G. | 2012 | case series |
| Prognostic factors and survival according to tumour subtype in women presenting with breast cancer bone metastases at initial diagnosis: a SEER-based study | Li, X.; Zhang, X.; Liu, J.; Shen, Y. | 2020 | irrelevant topic; SEER database used |
| Bone defect reconstruction with autologous bone inactivated with liquid nitrogen after resection of primary limb malignant tumors: An observational study | Li, Y.; Yang, Y.; Huang, Z.; Shan, H.; Xu, H.; Niu, X. | 2020 | case series |
| Systematic Pan-Cancer Population-Based Analysis Reveals the Incidence and Prognosis of Lung Metastases at Diagnosis | Liang, X.; Cheng, Y.; Zhou, W.; Ni, J.; Li, Y.; Feng, G. | 2021 | irrelevant topic; SEER database used |
| Treatment of humeral shaft fractures by retrograde locked nailing | Lin, J.; Hou, S. M.; Hang, Y. S.; Chao, E. Y. | 1997 | irrelevant topic; no metastatic bone disease |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Osteosynthesis of pathologic fractures and prophylactic internal fixation of metastases in long bones | Linclau, L.; Dokter, G. | 1992 | no treatment or comparison group |
| Treatment and outcome of malignant bone tumors of the proximal humerus: biological versus endoprosthetic reconstruction | Liu, T.; Zhang, Q.; Guo, X.; Zhang, X.; Li, Z.; Li, X. | 2014 | case series |
| Comparison of percutaneous long bone cementoplasty with or without embedding a cement-filled catheter for painful long bone metastases with impending fracture | Liu, X. W.; Jin, P.; Liu, K.; Chen, H.; Li, L.; Li, M.; Tang, H.; Sun, G. | 2017 | irrelevant topic; cement filled catheter |
| Reverse shoulder endoprosthesis for pathologic lesions of the proximal humerus: a minimum 3-year follow-up | Maclean, S.; Malik, S. S.; Evans, S.; Gregory, J.; Jeys, L. | 2017 | case series |
| Pathologic fracture of the distal humerus due to a textiloma | Maier, M.; Bratschitsch, G.; Friesenbichler, J.; Bodo, K.; Leithner, A.; Holzer, L. A. | 2016 | case report |
| What Is the Value of Undergoing Surgery for Spinal Metastases at Dedicated Cancer Centers? | Malik, A. T.; Khan, S. N.; Voskuil, R. T.; Alexander, J. H.; Drain, J. P.; Scharschmidt, T. J. | 2021 | irrelevant topic; spinal metastases |
| Minimally invasive plate osteosynthesis with locking plate for metastatic humeral fractures | Matsumura, T.; Saito, T.; Akiyama, T.; Takeshita, K. | 2021 | case series |
| Custom endoprosthetic reconstruction for malignant bone disease in the humeral diaphysis | McGrath, A.; Sewell, M. D.; Hanna, S. A.; Pollock, R. C.; Skinner, J. A.; Cannon, S. R.; Briggs, T. W. | 2011 | case series |
| Impact of symptomatic skeletal events on health-care resource utilization and quality of life among patients with castration-resistant prostate cancer and bone metastases | McKay, R.; Haider, B.; Duh, M. S.; Valderrama, A.; Nakabayashi, M.; Fiorillo, M.; Ristovska, L.; Wen, L.; Kantoff, P. | 2017 | irrelevant topic; symptomatic skeletal events |
| Operative treatment of humeral shaft fractures. The Leuven experience | Meekers, F. S.; Broos, P. L. | 2002 | irrelevant topic; no tumor/metastatic bone disease |
| Aspirin for Prophylaxis Against Venous Thromboembolism After Orthopaedic Oncologic Surgery | Mendez, G. M.; Patel, Y. M.; Ricketti, D. A.; Gaughan, J. P.; Lackman, R. D.; Kim, T. W. B. | 2017 | no comparison group |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Risk factors for metastatic disease at presentation with osteosarcoma: an analysis of the SEER database | Miller, B. J.; Cram, P.; Lynch, C. F.; Buckwalter, J. A. | 2013 | irrelevant topic; SEER database used |
| Socioeconomic measures influence survival in osteosarcoma: an analysis of the National Cancer Data Base | Miller, B. J.; Gao, Y.; Duchman, K. R. | 2017 | Irrelevant topic; patient population, half under 18yo |
| Does surgery or radiation provide the best overall survival in Ewing's sarcoma? A review of the National Cancer Data Base | Miller, B. J.; Gao, Y.; Duchman, K. R. | 2017 | Irrelevant topic; patient population |
| Deep vein thrombosis following the treatment of lower limb pathologic bone fractures - a comparative study | Mioc, M. L.; Prejbeanu, R.; Vermesan, D.; Haragus, H.; Niculescu, M.; Pop, D. L.; Balanescu, A. D.; Malita, D.; Deleanu, B. | 2018 | irrelevant topic; 64% metastatic |
| Is It Appropriate to Treat Sarcoma Metastases With Intramedullary Nailing? | Moon, B. S.; Dunbar, D. J.; Lin, P. P.; Satcher, R. L.; Bird, J. E.; Lewis, V. O. | 2017 | case series |
| Simultaneous nailing of skeletal metastases: is the mortality really that high? | Moon, B.; Lin, P.; Satcher, R.; Lewis, V. | 2011 | case series |
| Postoperative survival and ambulatory outcome in metastatic spinal tumors : prognostic factor analysis | Moon, K. Y.; Chung, C. K.; Jahng, T. A.; Kim, H. J.; Kim, C. H. | 2011 | irrelevant topic; post op survival |
| Treatment of Pathological Humerus-Shaft Tumoral Fractures with Rigid Static Interlocking Intramedullary Nail-22 Years of Experience | Moura, D. L.; Alves, F.; Fonseca, R.; Freitas, J.; Casanova, J. | 2019 | not in English |
| Evaluation of Intramedullary Methods with Polymethylmethacrylate for Fixation of Bone Lesions of the Extremities | Moura, M.; Sanches, D. P.; Pinto, A. F.; Milano, S. S.; Villela, M. M. | 2021 | not in English |
| Treatment of metastatic bone lesions in the upper extremity: indications for surgery | Muramatsu, K.; Ihara, K.; Iwanagaa, R.; Taguchi, T. | 2010 | case series |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Risk factors for recurrence after operation in patients with pT1a renal cell carcinoma: sub-analysis of the multi-institutional national database of the Japanese Urological Association | Nakajima, N.; Miyajima, A.; Shinohara, N.; Obara, W.; Kondo, T.; Kimura, G.; Kume, H.; Fujimoto, H.; Sugiyama, T.; Nonomura, N.; Hongo, F.; Fukumori, T.; Takahashi, M.; Kanayama, H. O.; Eto, M. | 2022 | irrelevant topic; renal cancer |
| Early Improvement in Pain and Functional Outcome but Not Quality of Life After Surgery for Metastatic Long Bone Disease | Nooh, A.; Goulding, K.; Isler, M. H.; Mottard, S.; Arteau, A.; Dion, N.; Turcotte, R. | 2018 | irrelevant topic; humerus data combined, treatment comparison cannot be extracted |
| Functional Outcomes and Complications After Oncologic Reconstruction of the Proximal Humerus | Nota, S.; Teunis, T.; Kortlever, J.; Ferrone, M.; Ready, J.; Gebhardt, M.; Raskin, K.; Hornicek, F.; Schwab, J.; Lozano Calderon, S. | 2018 | no comparison group |
| Minimally invasive treatment of pathological fractures of the humeral shaft | Ofluoglu, O.; Erol, B.; Ozgen, Z.; Yildiz, M. | 2009 | no comparison group |
| Allograft reconstruction of the humerus: Complications and revision surgery | Ogink, P. T.; Teunissen, F. R.; Massier, J. R.; Raskin, K. A.; Schwab, J. H.; Lozano-Calderon, S. A. | 2019 | no comparison group |
| Impact of hospital volume on postoperative complications and in-hospital mortality after musculoskeletal tumor surgery: analysis of a national administrative database | Ogura, K.; Yasunaga, H.; Horiguchi, H.; Ohe, K.; Shinoda, Y.; Tanaka, S.; Kawano, H. | 2013 | irrelevant topic; hospital volume |
| Enchondromas and atypical cartilaginous tumors at the proximal humerus treated with intralesional resection and bone cement filling with or without osteosynthesis: retrospective analysis of 42 cases with 6 years mean follow-up | Omlor, G. W.; Lohnherr, V.; Lange, J.; Gantz, S.; Merle, C.; Fellenberg, J.; Raiss, P.; Lehner, B. | 2018 | irrelevant topic; no metastatic bone disease |
| Prediction of Long Bone Fractures in Multiple Myeloma Patients in an Advanced Imaging World | Or, O.; Saiyed, R.; Marty, E.; Boyer, A.; Jahnwar, Y. S.; Niesvizky, R.; Lane, J. M. | 2021 | irrelevant topic; PET/CT imaging |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Surgical treatment of extra-articular distal-third diaphyseal fractures of the humerus using a modified posterior approach and an extra-articular plate | Paramo-Diaz, P.; Arroyo-Hernandez, M.; Rodriguez Vega, V.; Aroca-Peinado, M.; Leon-Baltasar, J. L.; Caba-Doussoux, P. | 2017 | no comparison group |
| Joint-preserving palliative surgery using self-locking screws of intramedullary nail and percutaneous cementoplasty for proximal humeral metastasis in the advanced cancer patients | Park, J. W.; Kim, Y. I.; Kang, H. G.; Kim, J. H.; Kim, H. S. | 2018 | case series |
| Preliminary results: use of multi-hole injection nails for intramedullary nailing with simultaneous bone cement injection in long-bone metastasis | Park, J. W.; Kim, Y. I.; Kang, H. G.; Kim, J. H.; Kim, H. S. | 2019 | case series |
| Aspirin and compression devices versus low-molecular-weight heparin and PCD for VTE prophylaxis in orthopedic oncology patients | Patel, A. R.; Crist, M. K.; Nemitz, J.; Mayerson, J. L. | 2010 | Irrelevant topic; patient population, not all metastatic and hip included |
| Effect of Pharmacologic Prophylaxis on Venous Thromboembolism After Radical Prostatectomy: The PREVENTER Randomized Clinical Trial | Patel, H. D.; Faisal, F. A.; Trock, B. J.; Joice, G. A.; Schwen, Z. R.; Pierorazio, P. M.; Johnson, M. H.; Bivalacqua, T. J.; Han, M.; Gorin, M. A.; Carter, H. B.; Partin, A. W.; Pavlovich, C. P.; Allaf, M. E. | 2020 | irrelevant comparison; <4% metastatic tumors |
| Drivers of Readmission and Reoperation After Surgery for Vertebral Column Metastases | Patel, J.; Pennington, Z.; Hersh, A. M.; Hung, B.; Schilling, A.; Antar, A.; Elsamadicy, A. A.; de la Garza Ramos, R.; Lubelski, D.; Larry Lo, S. F.; Sciubba, D. M. | 2021 | irrelevant topic; spinal metastases |
| Histologic Subtype, Tumor Grade, Tumor Size, and Race Can Accurately Predict the Probability of Synchronous Metastases in T2 Renal Cell Carcinoma | Pecoraro, A.; Palumbo, C.; Knipper, S.; Rosiello, G.; Luzzago, S.; Tian, Z.; Shariat, S. F.; Saad, F.; Lavallee, L.; Briganti, A.; Kapoor, A.; Fiori, C.; Porpiglia, F.; Karakiewicz, P. I. | 2020 | irrelevant topic; nephrectomy |
| Limb Sparing Resection for Tumors Involving the Distal Humerus and Reconstruction with a Modular Endoprosthesis | Peterson, J. R.; Villalobos, C. E.; Zamora, R.; Wittig, J. C. | 2015 | case series |
| Surgical treatment of pathologic fractures of humerus | Piccioli, A.; Maccauro, G.; Rossi, B.; Scaramuzzo, L.; Frenos, F.; Capanna, R. | 2010 | no comparison group |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Carbon-fiber reinforced intramedullary nailing in musculoskeletal tumor surgery: a national multicentric experience of the Italian Orthopaedic Society (SIOT) Bone Metastasis Study Group | Piccioli, A.; Piana, R.; Lisanti, M.; Di Martino, A.; Rossi, B.; Camnasio, F.; Gatti, M.; Maniscalco, P.; Gherlinzoni, F.; Spinelli, M. S.; Donati, D. M.; Biagini, R.; Capanna, R.; Denaro, V.; Italian Orthopaedic Society Bone Metastasis Study, Group | 2017 | no comparison group |
| Distally Unlocked Intramedullary Nailing With Cement Fixation for Impending and Actual Pathologic Humerus Fractures: A Retrospective Case Series | Pizzo, R. A.; Hoskins, T.; Patel, J. N.; Miller, J. M.; Goyette, D.; Mazzei, C.; Wittig, J. C. | 2020 | no comparison group |
| Internal fixation of proximal humerus fractures using the locking proximal humerus plate | Plecko, M.; Kraus, A. | 2005 | irrelevant topic; fracture types |
| Treatment of pathological humeral shaft fractures with intramedullary nailing. A retrospective study | Pretell, J.; Rodriguez, J.; Blanco, D.; Zafra, A.; Resines, C. | 2010 | case series |
| Insurance status as a mediator of clinical presentation, type of intervention, and short-term outcomes for patients with metastatic spine disease | Price, M. J.; De la Garza Ramos, R.; Dalton, T.; McCray, E.; Pennington, Z.; Erickson, M.; Walsh, K. M.; Yassari, R.; Sciubba, D. M.; Goodwin, A. N.; Goodwin, C. R. | 2022 | irrelevant topic; medicare/medicaid |
| Gender disparities in clinical presentation, treatment, and outcomes in metastatic spine disease | Price, M.; Goodwin, J. C.; De la Garza Ramos, R.; Baeta, C.; Dalton, T.; McCray, E.; Yassari, R.; Karikari, I.; Abd-El-Barr, M.; Goodwin, A. N.; Rory Goodwin, C. | 2021 | irrelevant topic; spinal metastases |
| Rapid-prototype endoprosthesis for palliative reconstruction of an upper extremity after resection of bone metastasis | Pruksakorn, D.; Chantarapanich, N.; Arpornchayanon, O.; Leerapun, T.; Sitthiseripratip, K.; Vatanapatimakul, N. | 2015 | case series |
| En bloc resection and intercalary prosthesis implantation for the treatment of humeral diaphyseal bone metastases | Pu, F.; Zhang, Z.; Wang, B.; Liu, J.; Shao, Z. | 2021 | case series |
| A study of 853 high grade osteosarcomas from a single institution-Are outcomes in Indian patients different? | Puri, A.; Byregowda, S.; Gulia, A.; Crasto, S.; Chinaswamy, G. | 2018 | Irrelevant topic; Non-metastatic cancer |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Bone metastasis in esophageal adenocarcinoma and squamous cell carcinoma: a SEER-based study | Qin, Y.; Mao, J.; Liang, X.; Wang, N.; Yuan, M.; Zhu, J.; Wu, D.; Wang, Q. | 2022 | irrelevant topic; bone metastasis vs no bone metastasis |
| Do Disparities in Wait Times to Operative Fixation for Pathologic Fractures of the Long Bones and 30-day Complications Exist Between Black and White Patients? A Study Using the NSQIP Database | Raad, M.; Puvanesarajah, V.; Wang, K. Y.; McDaniel, C. M.; Srikumaran, U.; Levin, A. S.; Morris, C. D. | 2022 | irrelevant topic; 13% had humerus fractures |
| Bone-Specific Metastasis Pattern of Advanced-Stage Lung Adenocarcinoma According to the Localization of the Primary Tumor | Radeczky, P.; Moldvay, J.; Fillinger, J.; Szeitz, B.; Ferencz, B.; Boettiger, K.; Rezeli, M.; Bogos, K.; Renyi-Vamos, F.; Hoetzenecker, K.; Hegedus, B.; Megyesfalvi, Z.; Dome, B. | 2021 | irrelevant topic; lung cancer |
| Risk factors for detectable metastatic disease at presentation in Ewing sarcoma - An analysis of the SEER registry | Ramkumar, D. B.; Ramkumar, N.; Miller, B. J.; Henderson, E. R. | 2018 | Irrelevant topic; patient population |
| Healing of Pathologic Humeral Fractures in Patients with Metastatic Disease: Consideration for Operative Fixation in Patients | Rao, S. S.; El Abiad, J. M.; Puvanesarajah, V.; Raad, M.; Morris, C. D.; Forsberg, J. A.; Levin, A. S. | 2020 | no comparison group |
| Do locking plates have a role in orthopaedic oncological reconstruction | Rastogi, S.; Kumar, A.; Khan, S. A. | 2010 | no comparison group |
| Venous thromboembolism after surgical treatment of non-spinal skeletal metastases - An underdiagnosed complication | Ratasvuori, M.; Lassila, R.; Laitinen, M. | 2016 | no outcomes of interest |
| Predictors of prognosis of synchronous brain metastases in small-cell lung cancer patients | Reddy, S. P.; Dowell, J. E.; Pan, E. | 2020 | irrelevant topic; SEER database used |
| Interlocking intramedullary nailing of pathological fractures of the shaft of the humerus | Redmond, B. J.; Biermann, J. S.; Blasier, R. B. | 1996 | no comparison group |
| Intramedullary Nailing Versus Plate Osteosynthesis for Humeral Shaft Metastatic Lesions | Ricard, M. M.; Stavropoulos, N. A.; Nooh, A.; Ste-Marie, N.; Goulding, K.; Turcotte, R. | 2021 | case series |
| Seidel intramedullary nailing of humeral diaphyseal fractures: a preliminary report | Riemer, B. L.; Butterfield, S. L.; D'Ambrosia, R.; Kellam, J. | 1991 | no comparison group |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Two freezing cycles ensure interface sterilization by cryosurgery during bone tumor resection | Robinson, D.; Halperin, N.; Nevo, Z. | 2001 | no comparison group |
| Retrograde nailing of humeral shaft fractures | Rommens, P. M.; Blum, J.; Runkel, M. | 1998 | no comparison group |
| Racial differences in the distribution of bladder cancer metastases: a population-based analysis | Rosiello, G.; Palumbo, C.; Deuker, M.; Stolzenbach, L. F.; Martin, T.; Tian, Z.; Gallina, A.; Montorsi, F.; Black, P.; Kassouf, W.; Shariat, S. F.; Saad, F.; Briganti, A.; Karakiewicz, P. I. | 2020 | irrelevant topic; bladder cancer |
| Prognosis of renal cell carcinoma with bone metastases: Experience from a large cancer centre | Ruatta, F.; Derosa, L.; Escudier, B.; Colomba, E.; Guida, A.; Baciarello, G.; Loriot, Y.; Fizazi, K.; Albiges, L. | 2019 | irrelevant topic; spinal metastases |
| Closed humeral shaft fractures treated by elastic intramedullary retrograde nail | Sala, F.; Chiodini, F.; Bau, D.; Ceriani, A.; Borromeo, U. M. | 2002 | no comparison group |
| Effect of metastatic site on emergency department disposition in men with metastatic prostate cancer | Sammon, J. D.; Kaczmarek, B. F.; Ravi, P.; Sun, M.; Roghmann, F.; Sukumar, S.; Ghani, K.; Sharma, P.; Karakiewicz, P. I.; Peabody, J. O.; Elder, J. S.; Menon, M.; Trinh, Q. D. | 2013 | Irrelevant topic; ED admission rates in prostate cancer |
| Treatment results of pathological fractures of the long bones: a retrospective analysis of 88 patients | Sarahrudi, K.; Hora, K.; Heinz, T.; Millington, S.; Vecsei, V. | 2006 | irrelevant topic; humerus data combined, treatment comparison cannot be extracted |
| Silver-coated endoprosthetic replacement of the proximal humerus in case of tumour-is there an increased risk of periprosthetic infection by using a trevira tube? | Schmolders, J.; Koob, S.; Schepers, P.; Kehrer, M.; Frey, S. P.; Wirtz, D. C.; Pennekamp, P. H.; Strauss, A. C. | 2017 | irrelevant comparison: tube vs no tube |
| Predictors of 30- and 90-Day Survival Following Surgical Intervention for Spinal Metastases: A Prognostic Study Conducted at Four Academic Centers | Schoenfeld, A. J.; Leonard, D. A.; Saadat, E.; Bono, C. M.; Harris, M. B.; Ferrone, M. L. | 2016 | Irrelevant topic; Surgical intervention and survival rates |
| Racial disparities in the development of breast cancer metastases among older women: a multilevel study | Schootman, M.; Jeffe, D. B.; Gillanders, W. E.; Aft, R. | 2009 | Irrelevant topic; risk of developing metastases, incorrect patient population |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Metastatic lesions of the humerus treated with the isoelastic diaphysis prosthesis | Schurmann, M.; Gradl, G.; Andress, H. J.; Kauschke, T.; Hertlein, H.; Lob, G. | 2000 | no comparison group |
| Surgical management and outcome of skeletal metastatic disease of the humerus | Schwabe, P.; Ruppert, M.; Tsitsilonis, S.; Melcher, I.; Schaser, K. D.; Mardian, S. | 2014 | case series |
| Comparison of Latino and non-Latino patients with Ewing sarcoma | Sharib, J.; Horvai, A.; Gray Hazard, F. K.; Daldrup-Link, H.; Goldsby, R.; Marina, N.; DuBois, S. G. | 2014 | Irrelevant topic; patient population |
| Comparative analysis of the surgical treatment results for multiple myeloma bone disease of the spine and the long bone/soft tissue | Shen, J.; Du, X.; Zhao, L.; Luo, H.; Xu, Z. | 2018 | Irrelevant topic; MM surgical interventions, spine vs. long bones |
| Models for Predicting Early Death in Patients With Stage IV Esophageal Cancer: A Surveillance, Epidemiology, and End Results-Based Cohort Study | Shi, M.; Zhai, G. Q. | 2022 | irrelevant topic; esophageal cancer |
| Reconstructing humerus defects after tumor resection using an intramedullary cortical allograft strut | Shih, H. N.; Shih, L. Y.; Cheng, C. Y.; Hsu, K. Y.; Chang, C. H. | 2002 | no comparison group; describes surgical methods |
| Pathological fractures of the proximal humerus treated with a proximal humeral locking plate and bone cement | Siegel, H. J.; Lopez-Ben, R.; Mann, J. P.; Ponce, B. A. | 2010 | no comparison group |
| Ninety day mortality and its predictors after primary shoulder arthroplasty: an analysis of 4,019 patients from 1976-2008 | Singh, J. A.; Sperling, J. W.; Cofield, R. H. | 2011 | no comparison group |
| The preoperative machine learning algorithm for extremity metastatic disease can predict 90-day and 1-year survival: An external validation study | Skalitzky, M. K.; Gulbrandsen, T. R.; Groot, O. Q.; Karhade, A. V.; Verlaan, J. J.; Schwab, J. H.; Miller, B. J. | 2022 | irrelevant topic; validation vs development |
| Epidemiology of musculoskeletal tumors in Shiraz, south of Iran | Solooki, S.; Vosoughi, A. R.; Masoomi, V. | 2011 | patient population; <18 |
| Impact of the homogeneous and heterogeneous risk factors on the incidence and survival outcome of bone metastasis in NSCLC patients | Song, Q.; Shang, J.; Zhang, C.; Zhang, L.; Wu, X. | 2019 | irrelevant topic; SEER database used |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Extent of Surgery Does Not Influence 30-Day Mortality in Surgery for Metastatic Bone Disease: An Observational Study of a Historical Cohort | Sorensen, M. S.; Hindso, K.; Hovgaard, T. B.; Petersen, M. M. | 2016 | Irrelevant topic; surgery influence on mortality |
| Risk factors for infections in newly diagnosed Multiple Myeloma patients: A Danish retrospective nationwide cohort study | Sorrig, R.; Klausen, T. W.; Salomo, M.; Vangsted, A.; Gimsing, P. | 2019 | Irrelevant topic; risk factors for infection in newly diagnosed MM |
| No recurrences in selected patients after curettage with cryotherapy for grade I chondrosarcomas | Souna, B. S.; Belot, N.; Duval, H.; Langlais, F.; Thomazeau, H. | 2010 | no comparison group |
| Locked intramedullary nailing of symptomatic metastases in the humerus | Spencer, S. J.; Holt, G.; Clarke, J. V.; Mohammed, A.; Leach, W. J.; Roberts, J. L. | 2010 | no comparison group |
| Long-term survival of proximal humerus allografts for reconstruction following resection of malignant bone tumours | Squire, G.; Grundy, T. J.; Ferran, N. A.; Harper, W. M.; Ashford, R. U. | 2013 | case series |
| Prognostic factors for patients with skeletal metastases from carcinoma of the breast | Stevenson, J. D.; McNair, M.; Cribb, G. L.; Cool, W. P. | 2016 | Irrelevant outcomes |
| Improvement of the shoulder function after large segment resection of the proximal humerus with the use of an inverse tumour prosthesis | Streitbuerger, A.; Henrichs, M.; Gosheger, G.; Ahrens, H.; Nottrott, M.; Guder, W.; Dieckmann, R.; Hardes, J. | 2015 | case series |
| Risk factors for surgical site infection after posterior fixation surgery and intraoperative radiotherapy for spinal metastases | Sugita, S.; Hozumi, T.; Yamakawa, K.; Goto, T.; Kondo, T. | 2016 | Irrelevant topic; risk factors for surgical site infection |
| Frequency and Prognosis of Pulmonary Metastases in Newly Diagnosed Gastric Cancer | Sun, Z.; Liu, H.; Yu, J.; Huang, W.; Han, Z.; Lin, T.; Chen, H.; Zhao, M.; Hu, Y.; Jiang, Y.; Li, G. | 2019 | Irrelevant topic; patient population |
| Liver Metastases in Newly Diagnosed Gastric Cancer: A Population-Based Study from SEER | Sun, Z.; Zheng, H.; Yu, J.; Huang, W.; Li, T.; Chen, H.; Hu, Y.; Zhao, M.; Liu, H.; Jiang, Y.; Li, G. | 2019 | Irrelevant topic; patient population |
| Complications using the Seidel intramedullary humeral nail: outcome in 31 patients | Svend-Hansen, H.; Skettrup, M.; Rathcke, M. W. | 1998 | no comparison group |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Cancer's impact on employment and earnings--a population-based study from Norway | Syse, A.; Tretli, S.; Kravdal, O. | 2008 | Irrelevant topic; cancer survivors and working life |
| Bone Diaphysis Metastases, the Ways and Results of Surgical Treatment Saving the Joints | Szczerba, P.; Guzik, G.; Bohatyrewicz, A.; Kotrych, D. | 2019 | irrelevant topic; <50% humerus |
| Assessment of the risk factors for impending fractures following radiotherapy for long bone metastases using CT scan-based virtual simulation: a retrospective study | Tatar, Z.; Soubrier, M.; Dillies, A. F.; Verrelle, P.; Boisgard, S.; Lapeyre, M. | 2014 | irrelevant topic; <50% humerus |
| The treatment of primary and metastatic renal cell carcinoma (RCC) with image-guided stereotactic body radiation therapy (SBRT) | Teh, B.; Bloch, C.; Galli-Guevara, M.; Doh, L.; Richardson, S.; Chiang, S.; Yeh, P.; Gonzalez, M.; Lunn, W.; Marco, R.; Jac, J.; Paulino, A.; Lu, H.; Butler, E.; Amato, R. | 2007 | irrelevant topic; radiation therapy |
| Segmental limb reconstruction after tumor resection | Temple, H. T.; Kuklo, T. R.; Lehman, R. A., Jr.; Heekin, R. D.; Berrey, B. H. | 2000 | no comparison group |
| Prognostic variables for survival and skeletal complications in patients with multiple myeloma osteolytic bone disease | Terpos, E.; Berenson, J.; Cook, R. J.; Lipton, A.; Coleman, R. E. | 2010 | Irrelevant topic; patients on zoledronic acid with pamidronate |
| Outcome of surgical management of bony metastases to the humerus and shoulder girdle: a retrospective analysis of 93 patients | Thai, D. M.; Kitagawa, Y.; Choong, P. F. | 2006 | no comparison group |
| Interlocking nailing of humeral shaft fractures | Thomsen, N. O.; Mikkelsen, J. B.; Svendsen, R. N.; Skovgaard, N.; Jensen, C. H.; Jorgensen, U. | 1998 | case report |
| Treatment of pathologic fractures of the humerus with Seidel nailing | Tome, J.; Carsi, B.; Garcia-Fernandez, C.; Marco, F.; Lopez-Duran Stern, L. | 1998 | no comparison group |
| Novel nomogram to predict risk of bone metastasis in newly diagnosed thyroid carcinoma: a population-based study | Tong, Y.; Hu, C.; Huang, Z.; Fan, Z.; Zhu, L.; Song, Y. | 2020 | Irrelevant topic; nomogram development/validation |
| Treatment of pathologic fracture of the humerus | Vail, T. P.; Harrelson, J. M. | 1991 | no comparison group |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Proximal humerus reconstruction after tumour resection: biological versus endoprosthetic reconstruction | van de Sande, M. A.; Dijkstra, P. D.; Taminiau, A. H. | 2011 | no comparison group |
| The Seidel locking humeral nail: the Nottingham experience | Varley, G. W. | 1995 | no comparison group |
| Management of Metastatic Disease of the Upper Extremity | Voskuil, R. T.; Mayerson, J. L.; Scharschmidt, T. J. | 2021 | review |
| The homogeneous and heterogeneous risk factors for occurrence and prognosis in lung cancer patients with bone metastasis | Wang, B.; Chen, L.; Huang, C.; Lin, J.; Pan, X.; Shao, Z.; Hu, S.; Zhang, X.; Wang, X. | 2019 | Irrelevant topic; patient population, not all metastatic |
| Survival and prognostic factors in Chinese patients with osteosarcoma: 13-year experience in 365 patients treated at a single institution | Wang, W.; Yang, J.; Wang, Y.; Wang, D.; Han, G.; Jia, J.; Xu, M.; Bi, W. | 2017 | Irrelevant topic; not all metastatic |
| Prognostic Factors Associated With Bone Lymphoma Primarily Presenting in the Spine | Wang, Y.; Li, J.; Wei, R.; Liu, C.; Nataraj, A.; Yan, J. | 2019 | irrelevant topic; no metastatic bone disease |
| Functional outcomes and complications of reconstruction of the proximal humerus after intra-articular tumor resection | Wang, Z.; Guo, Z.; Li, J.; Li, X. D.; Sang, H. X. | 2010 | irrelevant comparison: prosthesis and resection |
| Complications and survival after surgical treatment of 214 metastatic lesions of the humerus | Wedin, R.; Hansen, B. H.; Laitinen, M.; Trovik, C.; Zaikova, O.; Bergh, P.; Kalen, A.; Schwarz-Lausten, G.; Vult von Steyern, F.; Walloe, A.; Keller, J.; Weiss, R. J. | 2012 | case series |
| Fixation of pathological humeral fractures by the cemented plate technique | Weiss, K. R.; Bhumbra, R.; Biau, D. J.; Griffin, A. M.; Deheshi, B.; Wunder, J. S.; Ferguson, P. C. | 2011 | no comparison group |
| Race does not predict the development of metastases in men with nonmetastatic castration-resistant prostate cancer | Whitney, C. A.; Howard, L. E.; Amling, C. L.; Aronson, W. J.; Cooperberg, M. R.; Kane, C. J.; Terris, M. K.; Freedland, S. J. | 2016 | Irrelevant topic; impact of race on development of metastases in non-met cancer |
| Survival analysis after intramedullary stabilization for metastatic disease of the femur: prognostic value of common laboratory parameters | Willoughby, J. E.; Baker, J. F. | 2021 | Irrelevant topic; patient population |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Stabilisation of pathological humerus fractures using cement augmented plating: A case series | Wilson, W. T.; Pickup, A. R.; Findlay, H.; Gupta, S.; Mahendra, A. | 2021 | no comparison group |
| Ethnic and racial differences in patients with Ewing sarcoma | Worch, J.; Matthay, K. K.; Neuhaus, J.; Goldsby, R.; DuBois, S. G. | 2010 | Irrelevant topic; patient population |
| Venous thromboembolism in patients with acute leukemia, lymphoma, and multiple myeloma | Wun, T.; White, R. H. | 2010 | review |
| Racial disparities in bone metastasis patterns and targeted screening and treatment strategies in newly diagnosed lung cancer patients | Xu, G.; Cui, P.; Zhang, C.; Lin, F.; Xu, Y.; Guo, X.; Cai, J.; Baklaushev, V. P.; Peltzer, K.; Chekhonin, V. P.; Wang, X.; Wang, G. | 2020 | irrelevant topic; SEER database used |
| Analysis of definitive chemo-radiotherapy for esophageal cancer with supra-clavicular node metastasis based on CT in a single institutional retrospective study: a propensity score matching analysis | Xu, H. Y.; Wu, S. X.; Luo, H. S.; Chen, C. Y.; Lin, L. X.; Huang, H. C. | 2018 | Irrelevant topic; patient population |
| Predictors for survival in patients with bone metastasis of small cell lung cancer: A population-based study | Xue, M.; Chen, G.; Chen, X.; Hu, J. | 2021 | irrelevant topic; SEER database used |
| Deep-vein thrombosis after resection of musculoskeletal tumours of the lower limb | Yamaguchi, T.; Matsumine, A.; Niimi, R.; Nakamura, T.; Matsubara, T.; Asanuma, K.; Hasegawa, M.; Sudo, A. | 2013 | irrelevant topic; <4% metastatic tumors |
| Survival Outcomes of Newly Diagnosed Multiple Myeloma at a Tertiary Care Center in North India (IMAGe: 001A Study) | Yanamandra, U.; Sharma, R.; Shankar, S.; Yadav, S.; Kapoor, R.; Pramanik, S.; Ahuja, A.; Kumar, R.; Sharma, S.; Das, S.; Chatterjee, T.; Somasundaram, V.; Verma, T.; Mishra, K.; Singh, J.; Sharma, A.; Nair, V. | 2021 | irrelevant outcomes |
| Analysis of prognostic factors relating to postoperative survival in spinal metastases | Yang, S. B.; Cho, W.; Chang, U. K. | 2012 | irrelevant topic; spinal metastases |
| Risk factors and survival outcomes of laryngeal squamous cell carcinoma patients with lung metastasis: A population-based study | Yang, W.; Mei, X.; Zhou, Y.; Su, R.; Lei, W.; Zheng, S.; Zhu, R.; Guo, L.; Tao, Y.; Su, Y.; Li, J.; Ding, C.; Zou, S.; Li, X.; Hu, H. | 2021 | irrelevant topic; SEER database used |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Mid- to long-term effects of two different biological reconstruction techniques for the treatment of humerus osteosarcoma involving caput humeri | Yao, W.; Cai, Q.; Wang, J.; Hou, J. | 2020 | case series |
| Incidence, prognosis and nomograms of breast cancer with bone metastases at initial diagnosis: a large population-based study | Yao, Y. B.; Zheng, X. E.; Luo, X. B.; Wu, A. M. | 2021 | irrelevant topic; SEER database used |
| Metastatic bone disease. A study of the surgical treatment of 166 pathologic humeral and femoral fractures | Yazawa, Y.; Frassica, F. J.; Chao, E. Y.; Pritchard, D. J.; Sim, F. H.; Shives, T. C. | 1990 | irrelevant topic; no humerus |
| Risk and prognostic nomograms for hepatocellular carcinoma with newly-diagnosed pulmonary metastasis using SEER data | Ye, G.; Wang, L.; Hu, Z.; Liang, J.; Bian, Y.; Zhan, C.; Lin, Z. | 2019 | irrelevant topic; SEER database used |
| Management of humeral impending or pathological fractures with intramedullary nailing: reaming versus non reaming technique-a retrospective comparative study | Younis, M.; Barnhill, S. W.; Maguire, J.; Pretell-Mazzini, J. | 2020 | irrelevant topic; reamed vs unreamed nails |
| Incidence and risk factors for preoperative deep venous thrombosis in 314 consecutive patients undergoing surgery for spinal metastasis | Zacharia, B. E.; Kahn, S.; Bander, E. D.; Cederquist, G. Y.; Cope, W. P.; McLaughlin, L.; Hijazi, A.; Reiner, A. S.; Laufer, I.; Bilsky, M. | 2017 | risk factors, not postop |
| Correlation and Survival Analysis of Distant Metastasis Site and Prognosis in Patients With Hepatocellular Carcinoma | Zhan, H.; Zhao, X.; Lu, Z.; Yao, Y.; Zhang, X. | 2021 | irrelevant topic; SEER database used |
| Bone Metastases Pattern in Newly Diagnosed Metastatic Bladder Cancer: A Population-Based Study | Zhang, C.; Liu, L.; Tao, F.; Guo, X.; Feng, G.; Chen, F.; Xu, Y.; Li, L.; Han, X.; Baklaushev, V. P.; Bryukhovetskiy, A. S.; Wang, X.; Wang, G. | 2018 | Irrelevant outcomes |
| Evaluation of bone grafting for treatment of low-grade chondrosarcoma of long bones | Zhang, G.; Cheon, S.; Park, I. | 2021 | irrelevant topic; chondrosarcoma |
| Analysis of Homogeneous and Heterogeneous Factors for Bone Metastasis in Esophageal Cancer | Zhang, J.; Ma, W.; Wu, H.; Wang, J.; Lin, Y.; Wang, X.; Zhang, C. | 2019 | irrelevant topic; SEER database used |

| Article Title | Authors | Year | Reason for Exclusion |
|---|---|---|---|
| Population-based evaluation of the risk factors and prognosis among renal cell carcinoma patients with initially diagnosed lung metastases | Zhang, Z.; Liang, C.; Hou, B.; Zhou, L. | 2021 | irrelevant topic; SEER database used |
| Intercalary prosthetic reconstruction for pathologic diaphyseal humeral fractures due to metastatic tumors: outcomes and improvements | Zhao, J.; Yu, X. C.; Xu, M.; Zheng, K.; Hu, Y. C.; Wang, F.; Lun, D. X. | 2018 | <5 patients per group |
| Intercalary prosthetic replacement is a reliable solution for metastatic humeral shaft fractures: retrospective, observational study of a single center series | Zhao, Z.; Ye, Z.; Yan, T.; Tang, X.; Guo, W.; Yang, R. | 2021 | case series |
| Incidence, prognostic factors, and a nomogram of lung cancer with bone metastasis at initial diagnosis: a population-based study | Zheng, X. Q.; Huang, J. F.; Lin, J. L.; Chen, L.; Zhou, T. T.; Chen, D.; Lin, D. D.; Shen, J. F.; Wu, A. M. | 2019 | Irrelevant outcomes |
| The IlluminOss R photodynamic bone stabilization system for pathological osteolyses and fractures of the humerus: indications, advantages and limits in a series of 12 patients at 24 months of minimum follow-up | Zoccali, C.; Attala, D.; Pugliese, M.; di Uccio, A. S.; Baldi, J. | 2021 | case series |

## Appendix VI: MSTS GEBM EtDF Scoring Rubric

| Criteria | Detailed considerations | Judgements (points) | Score |
|---|---|---|---|
| What is the baseline quality/strength of the evidence? See above. | Baseline strength of recommendation is listed above | No evidence (0)<br>Low (3)<br>Moderate (4)<br>High (5) | |
| What is the value and importance of the outcomes to clinical practice? | Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)? | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | |
| What is the magnitude of the desired effect? | | None (0)<br>Low (2)<br>Moderate (3)<br>High (5) | |
| What is the magnitude of undesirable effects/complications? | | High (0)<br>Moderate (1)<br>Low (2)<br>None (3) | |
| Do the benefits outweigh the risks? | Do the benefits clearly outweigh the risks or is there a balance of benefits and harms? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (3)<br>Yes (5) | |
| What amount of resources are required to produce the desired effect? | What is the estimated equipment need, space, time, and ability of any institution to provide these needs? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (5) | |
| What is the cost to produce the desired effect? | What is the estimated monetary cost? | Prohibitive (0)<br>High (1)<br>Moderate (2)<br>Minimal (3)<br>None (4) | |
| Is the intervention/outcomes acceptable to key stakeholders? | -Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes?<br>-Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)?<br>-Would intervention effect people's autonomy? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | |
| Is the intervention feasible to implement? | -Is intervention sustainable?<br>-Any barriers limiting the feasibility of implementing recommendation? | No (0)<br>Probably No (1)<br>Uncertain (2)<br>Probably Yes (4)<br>Yes (5) | |
| **Total Score** | | | |

## Appendix VII: PICO Action Statement Final Voting

| PICO | Agreement % | Average Rating | Panelist 1 | Panelist 2 | Panelist 3 | Panelist 4 | Panelist 5 | Panelist 6 | Panelist 7 | Panelist 8 | Panelist 9 | Panelist 10 | Panelist 11 | Panelist 12 | Panelist 13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 70.0% | 3.8 | | 4 | 1 | 5 | 4 | 5 | 1 | 5 | | 5 | 3 | 5 | |
| 2 | 100.0% | 4.9 | 5 | 5 | 5 | 5 | | 5 | | 4 | 5 | 5 | | 5 | 5 |
| 3 | 90.0% | 4.7 | 5 | 4 | 3 | 5 | | 5 | | 5 | 5 | | 5 | 5 | 5 |
| 4 | 100.0% | 4.8 | 5 | | 4 | 5 | 5 | 5 | 5 | 5 | 5 | 4 | | 5 | |
| 5 | 100.0% | 4.6 | 5 | | | 5 | 5 | 5 | 4 | | 5 | 4 | 4 | 4 | 5 |
| 6 | 80.0% | 4.5 | | 5 | | 5 | 5 | 5 | 5 | 5 | 3 | 5 | 2 | | 5 |
| 7 | 88.9% | 4.7 | 5 | 5 | 3 | 5 | 4 | 5 | 5 | | | | 5 | | 5 |

**Supermajority = 67% agreement**

**Key:**

**1 = Strongly Disagree**
**2 = Disagree**
**3 = Neither Agree nor Disagree**
**4 = Agree**
**5 = Strongly Agree**

# Appendix VIII: Evidence Tables for PICO Questions

## PICO 1: Plating vs. Intramedullary Nailing vs Photodynamic Polymer for Midshaft Pathologic Humerus Fractures

| Reference Title | Quality | Outcome Details | Duration | Treatment 1 | Treatment 2 | Effect Measure | Result (95% CI) | Favored Treatment |
|---|---|---|---|---|---|---|---|---|
| Hoellwarth, 2020 | Low | Reoperations | 1 yrs | Photodynamic Bone Stabilization | Intramedullary Nail | Mean Difference | 0.04 (-0.10, 0.19) | NS |
| Hoellwarth, 2020 | Low | Reoperations | 2 yrs | Photodynamic Bone Stabilization | Intramedullary Nail | Mean Difference | 0.09 (-0.07, 0.27) | NS |
| Hoellwarth, 2020 | Low | Reoperations | 614 days | Photodynamic Bone Stabilization | Intramedullary Nail | Mean Difference | 0.08 (-0.09, 0.25) | NS |
| Hoellwarth, 2020 | Low | Broken Implants | 1 yrs | Photodynamic Bone Stabilization | Intramedullary Nail | Mean Difference | 0.10 (-0.03, 0.24) | Intramedullary Nail |
| Hoellwarth, 2020 | Low | Broken Implants | 2 yrs | Photodynamic Bone Stabilization | Intramedullary Nail | Mean Difference | 0.15 (-0.006, 0.32) | Intramedullary Nail |
| Hoellwarth, 2020 | Low | Broken Implants | 614 days | Photodynamic Bone Stabilization | Intramedullary Nail | Mean Difference | 0.15 (-0.00, 0.32) | Intramedullary Nail |
| Hoellwarth, 2020 | Low | Survival | 1 yrs | Photodynamic Bone Stabilization | Intramedullary Nail | Mean Difference | 0.02 (-0.18, 0.23) | NS |
| Hoellwarth, 2020 | Low | Survival | 2 yrs | Photodynamic Bone Stabilization | Intramedullary Nail | Mean Difference | 0.24 (-0.009, 0.49) | NS |
| Hoellwarth, 2020 | Low | Survival | 614 days | Photodynamic Bone Stabilization | Intramedullary Nail | Mean Difference | 0.15 (-0.08, 0.40) | NS |
| Hoellwarth, 2020 | Low | Reoperations | 1 yrs | Photodynamic Bone Stabilization | Cemented Plate Fixation | Mean Difference | 0.05 (-0.10, 0.22) | NS |
| Hoellwarth, 2020 | Low | Reoperations | 2 yrs | Photodynamic Bone Stabilization | Cemented Plate Fixation | Mean Difference | 0.06 (-0.14, 0.26) | NS |
| Hoellwarth, 2020 | Low | Reoperations | 614 days | Photodynamic Bone Stabilization | Cemented Plate Fixation | Mean Difference | 0.01 (-0.20, 0.23) | NS |
| Hoellwarth, 2020 | Low | Broken Implants | 1 yrs | Photodynamic Bone Stabilization | Cemented Plate Fixation | Mean Difference | 0.05 (-0.10, 0.22) | NS |
| Hoellwarth, 2020 | Low | Broken Implants | 2 yrs | Photodynamic Bone Stabilization | Cemented Plate Fixation | Mean Difference | 0.06 (-0.14, 0.26) | NS |
| Hoellwarth, 2020 | Low | Broken Implants | 614 days | Photodynamic Bone Stabilization | Cemented Plate Fixation | Mean Difference | 0.01 (-0.20, 0.23) | NS |
| Hoellwarth, 2020 | Low | Survival | 1 yrs | Photodynamic Bone Stabilization | Cemented Plate Fixation | Mean Difference | 0.02 (-0.23, 0.28) | NS |
| Hoellwarth, 2020 | Low | Survival | 2 yrs | Photodynamic Bone Stabilization | Cemented Plate Fixation | Mean Difference | 0.05 (-0.25, 0.36) | NS |
| Hoellwarth, 2020 | Low | Survival | 614 days | Photodynamic Bone Stabilization | Cemented Plate Fixation | Mean Difference | 0.04 (-0.26, 0.34) | NS |
| Hoellwarth, 2020 | Low | Reoperations | 1 yrs | Intramedullary Nail | Cemented Plate Fixation | Mean Difference | -0.01 (-0.12, 0.09) | NS |
| Hoellwarth, 2020 | Low | Reoperations | 2 yrs | Intramedullary Nail | Cemented Plate Fixation | Mean Difference | 0.03 (-0.10, 0.17) | NS |
| Hoellwarth, 2020 | Low | Reoperations | 614 days | Intramedullary Nail | Cemented Plate Fixation | Mean Difference | 0.06 (-0.09, 0.22) | NS |
| Hoellwarth, 2020 | Low | Broken Implants | 1 yrs | Intramedullary Nail | Cemented Plate Fixation | Mean Difference | 0.04 (-0.04, 0.13) | NS |
| Hoellwarth, 2020 | Low | Broken Implants | 2 yrs | Intramedullary Nail | Cemented Plate Fixation | Mean Difference | 0.09 (-0.03, 0.22) | NS |
| Hoellwarth, 2020 | Low | Broken Implants | 614 days | Intramedullary Nail | Cemented Plate Fixation | Mean Difference | 0.14 (-0.006, 0.29) | Intramedullary Nail |
| Hoellwarth, 2020 | Low | Survival | 1 yrs | Intramedullary Nail | Cemented Plate Fixation | Mean Difference | -0.007 (-0.21, 0.20) | NS |
| Hoellwarth, 2020 | Low | Survival | 2 yrs | Intramedullary Nail | Cemented Plate Fixation | Mean Difference | 0.18 (-0.05, 0.42) | NS |
| Hoellwarth, 2020 | Low | Survival | 614 days | Intramedullary Nail | Cemented Plate Fixation | Mean Difference | 0.11 (-0.11, 0.35) | NS |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sarahrudi, 2009 | Low | Radial Nerve Palsy | 2.1 mos | Open Reduction and Internal Plate Fixation | Intramedullary Fixation | Mean Difference | 0.19 (-0.02, 0.35) | Intramedullary Nail |
| Sarahrudi, 2009 | Low | Refracture | 2.1 mos | Open Reduction and Internal Plate Fixation | Intramedullary Fixation | Mean Difference | 0.04 (-0.04, 0.13) | NS |
| Sarahrudi, 2009 | Low | Implant Loosening | 2.1 mos | Open Reduction and Internal Plate Fixation | Intramedullary Fixation | Mean Difference | 0.04 (-0.04, 0.13) | NS |
| Sarahrudi, 2009 | Low | Instability | 2.1 mos | Open Reduction and Internal Plate Fixation | Intramedullary Fixation | Mean Difference | -0.1 (-0.23, 0.03) | NS |
| Sarahrudi, 2009 | Low | Local Tumor Progression | 2.1 mos | Open Reduction and Internal Plate Fixation | Intramedullary Fixation | Mean Difference | -0.05 (-0.14, 0.04) | NS |
| Dijkstra, 1996 | Low | Subjective Relief of Pain - Excellent | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | 0.19 (-0.10, 0.49) | NS |
| Dijkstra, 1996 | Low | Subjective Relief of Pain - Good | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | -0.2 (-0.56, 0.04) | NS |
| Dijkstra, 1996 | Low | Subjective Relief of Pain - Fair | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | 0.005 (-0.13, 0.14) | NS |
| Dijkstra, 1996 | Low | Subjective Relief of Pain - Poor | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | 0.05 (-0.05, 0.16) | NS |
| Dijkstra, 1996 | Low | Objective Relief of Pain - Excellent | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | -0.3 (-0.61, -0.05) | NS |
| Dijkstra, 1996 | Low | Objective Relief of Pain - Good | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | 0.31 (-0.009, 0.61) | NS |
| Dijkstra, 1996 | Low | Objective Relief of Pain - Fair | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | -0.08 (-0.31, 0.13) | NS |
| Dijkstra, 1996 | Low | Objective Relief of Pain - Poor | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | 0.11 (-0.03, 0.25) | NS |
| Dijkstra, 1996 | Low | Function - Excellent | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | -0.0 (-0.36, 0.26) | NS |
| Dijkstra, 1996 | Low | Function - Good | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | 0.04 (-0.26, 0.35) | NS |
| Dijkstra, 1996 | Low | Function - Fair | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | 0.005 (-0.13, 0.14) | NS |
| Dijkstra, 1996 | Low | Function - Poor | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | 0 (0, 0) | NS |
| Dijkstra, 1996 | Low | Wound Dehiscence | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | -0.05 (-0.14, 0.04) | NS |
| Dijkstra, 1996 | Low | Wound Haematoma | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | 0.005 (-0.13, 0.14) | NS |
| Dijkstra, 1996 | Low | Radial Nerve Paresis | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | -0.05 (-0.14, 0.04) | NS |
| Dijkstra, 1996 | Low | Rebleeding | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | -0.05 (-0.14, 0.04) | NS |
| Dijkstra, 1996 | Low | Primary Tumor | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | -0.03 (-0.25, 0.17) | NS |
| Dijkstra, 1996 | Low | Sepsis | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | 0.005 (-0.14, 0.04) | NS |
| Dijkstra, 1996 | Low | Cardiac | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | 0.05 (-0.05, 0.16) | NS |
| Dijkstra, 1996 | Low | Angulation | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | 0.005 (-0.13, 0.14) | NS |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Dijkstra, 1996 | Low | Rotation | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | 0.05 (-0.05, 0.16) | NS |
| Dijkstra, 1996 | Low | Refracture at the end of fixation device | 4 wks | Intramedullary Nail | ORIF Plate | Mean Difference | 0.05 (-0.05, 0.16) | NS |

## PICO 4: Role of Cement vs. No Cement

| Reference Title | Quality | Outcome Details | Duration | Treatment 1 | Treatment 2 | Effect Measure | Result (95% CI) | Favored Treatment |
|---|---|---|---|---|---|---|---|---|
| Laitinen, 2011 | Low | Pain Relief at Operated Site | 1 wks | Cemented Nails | Non-Cemented Nails | Mean Difference | -0.6 (-3.3, 2.1) | NS |
| Laitinen, 2011 | Low | Pain Relief at Operated Site | 6 mos | Cemented Nails | Non-Cemented Nails | Mean Difference | -0.93 (-2.4, 0.54) | NS |
| Laitinen, 2011 | Low | Pain Relief at Operated Site | 6 mos | Cemented Nails | Non-Cemented Nails | Mean Difference | -0.62 (-2.01, 0.77) | NS |
| Laitinen, 2011 | Low | Use of Analgesics | 1 wks | Cemented Nails | Non-Cemented Nails | Mean Difference | 0 (-3.8, 3.8) | NS |
| Laitinen, 2011 | Low | Use of Analgesics | 6 mos | Cemented Nails | Non-Cemented Nails | Mean Difference | -0.7 (-3.22, 1.8) | NS |
| Laitinen, 2011 | Low | Use of Analgesics | 6 mos | Cemented Nails | Non-Cemented Nails | Mean Difference | -0.4 (-2.9, 2.1) | NS |

## PICO 5: Shoulder Arthroplasty Reconstruction Options

| Reference Title | Quality | Outcome Details | Duration | Treatment 1 | Treatment 2 | Effect Measure | Result (95% CI) | Favored Treatment |
|---|---|---|---|---|---|---|---|---|
| Houdek, 2021 | Low | Subluxation (>25%) | 2 yrs | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | -0.3 (-0.54, -0.1) | Reverse Arthroplasty |
| Houdek, 2021 | Low | Allograft Resorption | 3 yrs | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | -0.002 (-0.20, 0.19) | NS |
| Houdek, 2021 | Low | Periprosthetic or Allograft Fracture | 4 yrs | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | -0.015 (-0.18, 0.14) | NS |
| Houdek, 2021 | Low | Infection | 5 yrs | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | 0.004 (-0.07, 0.08) | NS |
| Houdek, 2021 | Low | Reoperations | 6 yrs | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | -0.03 (-0.19, 0.12) | NS |
| Houdek, 2021 | Low | Revision Procedure | 7 yrs | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | -0.01 (-0.08, 0.05) | NS |
| Grosel, 2019 | Low | Revision Procedure | 8 yrs | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | 0.02 (-0.02, 0.07) | NS |
| Grosel, 2019 | Low | Death | 9 yrs | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | 0.71 (-0.56, 0.85) | Reverse Arthroplasty |
| Grosel, 2019 | Low | Local Recurrence | 10 yrs | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | 0.07 (-0.006, 0.16) | NS |
| Grosel, 2019 | Low | Infection | 11 yrs | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | 0.07 (-0.006, 0.16) | NS |
| Grosel, 2019 | Low | Dislocation and Subluxation Events | 12 yrs | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | 0.27 (-0.08, 0.45) | NS |
| Grosel, 2019 | Low | ROM; Forward Flexion | 13 yrs | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | -57 (-146.4, 32.4) | Reverse Arthroplasty |
| Grosel, 2019 | Low | American Shoulder and Elbow Surgeons Score | 14 yrs | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | 4 (-82.3, 90.3) | NS |
| Grosel, 2019 | Low | Simple Shoulder Test Score | 15 yrs | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | 1.4 (-3.09, 5.89) | NS |
| Grosel, 2019 | Low | VAS | NA | Hemiarthroplasty | Reverse Arthroplasty | Mean Difference | -0.1 (-3.5, 3.3) | NS |

## PICO 6: Equity/Disparities Present in the Treatment of Metastatic Bone Disease Patients

| Reference Title | Quality | Outcome Details | Duration | Treatment 1 | Treatment 2 | Effect Measure | Result (95% CI) | Favored Treatment |
|---|---|---|---|---|---|---|---|---|

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Hung, 2021 | Low | KPS Score <70 | White | Black | Mean Difference | -0.2 (-0.31, -0.0) | Black |
| Hung, 2021 | Low | Frankel Grade A-C | White | Black | Mean Difference | -0.05 (-0.13, 0.01) | NS |
| Hung, 2021 | Low | ASA Class >2 | White | Black | Mean Difference | 0.01 (-0.07, 0.10) | NS |
| Hung, 2021 | Low | Complications | White | Black | Mean Difference | -0.02 (-0.13, 0.08) | NS |
| tHung, 2021 | Low | Deceased | White | Black | Mean Difference | 0.00 (-0.02, 0.03) | NS |
| Hung, 2021 | Low | Length of Stay | White | Black | Mean Difference | -0.06 (-0.13, -0.002) | White |
| Hung, 2021 | Low | Prolonged Length of Stay | White | Black | Mean Difference | -0.06 (-0.16, 0.03) | NS |
| Herget, 2021 | Low | Age | <60 | >60 | Mean Difference | -0.04 (-0.10, 0.007) | NS |
| Herget, 2021 | Low | Sex | Female | Male | Mean Difference | 0.05 (-0.004, 0.10) | NS |
| Huang, 2019 | Low | Sex | Female | Male | Mean Difference | 0.60 (-0.49, 0.71) | Males |
| Rades, 2020 A | Low | Age | <65 | >66 | Mean Difference | 0.005 (-0.10, 0.11) | NS |
| Rades, 2020 A | Low | Sex | Female | Male | Mean Difference | -0.1 (-0.24, -0.02) | Males |
| Rades, 2020 B | Low | Age | <70 | >71 | Mean Difference | 0.03 (-0.22, 0.29) | NS |
| Rades, 2020 B | Low | Sex | Female | Male | Mean Difference | -0.4 (-0.67, -0.2) | Males |
| Rades, 2019 | Low | Age | <60 | 61-70 | Mean Difference | 0.002 (-0.05, 0.06) | NS |
| Rades, 2019 | Low | Age | <60 | >70 | Mean Difference | -0.1 (-0.17, -0.05) | >70 |
| Rades, 2019 | Low | Age | 61-70 | >70 | Mean Difference | -0.1 (-0.17, -0.05) | >70 |
| Rades, 2019 | Low | Sex | Female | Male | Mean Difference | 0.01 (-0.04, 0.08) | NS |
| Scott, 2018 | Low | Sex | Female | Male | Mean Difference | 0.21 (-0.06, 0.35) | Females |
| Vos, 2019 | Low | Sex | Female | Male | Mean Difference | -0.06 (-0.10, -0.02) | Males |
| Vos, 2019 | Low | Socioeconomic Status | High | Medium | Mean Difference | -0.1 (-0.13, -0.06) | Medium |
| Vos, 2019 | Low | Socioeconomic Status | High | Low | Mean Difference | -0.03 (-0.06, -0.001) | Low |
| Vos, 2019 | Low | Socioeconomic Status | Medium | Low | Mean Difference | 0.06 (-0.03, 0.10) | Medium |
| Wisanuyotin, 2018 | Low | Sex | Female | Male | Mean Difference | 0.05 (-0.07, 0.19) | NS |
| Wisanuyotin, 2018 | Low | Age | <60 | >60 | Mean Difference | -0.01 (-0.15, 0.11) | NS |
| Wong, 2013 | Low | Age | <60 | >60 | Mean Difference | 0.23 (-0.16, 0.30) | <60 |
| Wong, 2013 | Low | Sex | Female | Male | Mean Difference | 0.52 (-0.46, 0.57) | Females |
| Raschka, 2022 | Low | Age | <65 | >65 | Mean Difference | -0.1 (-0.30, -0.07) | NS |
| Raschka, 2022 | Low | Sex | Female | Male | Mean Difference | -0.04 (-0.16, 0.07) | NS |

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## Appendix IX: Guideline Development Group Disclosures

**Felasfa Wodajo, MD –** Onkos Surgical: Paid consultant

**Nate Mesko, MD –** Bone Support: Paid consultant

Musculoskeletal Tumor Society: Board or committee member

ONKOS Surgical: Paid consultant; Paid presenter or speaker

Stryker: Paid consultant; Paid presenter or speaker

**Nicholas Tedesco, DO –** Doctorpedia: Stock or stock Options

Journal of the American Osteopathic Academy of Orthopedics: Editorial board

Medscape: Publishing royalties, financial or material support

Musculoskeletal Tumor Society: Board or committee member

RomTech, Inc.: Stock or stock Options

**Cecilia Belzarena, MD –** Nothing to disclose.

**Alexander Christ, MD –** AAOS: Board or committee member

DJ Orthopaedics: Other financial or material support

Intellijoint Surgical: Paid consultant

Musculoskeletal Tumor Society: Board or committee member

Orthopaedic Research Society: Board or committee member

Smith & Nephew: Paid consultant

**Matthew Colman, MD –**Alphatec Spine: IP royalties; Paid consultant

AO Spine North America: Board or committee member; Research support

Cervical Spine Research Society: Board or committee member

CSRS: Research support

DePuy, A Johnson & Johnson Company: Paid presenter or speaker

K2M: Paid presenter or speaker

K2M/Stryker Spine: Paid consultant

LSRS: Board or committee member

Musculoskeletal Tumor Society: Board or committee member

North American Spine Society: Board or committee member

Orthofix: Paid consultant

Orthofix, Inc.: Paid presenter or speaker

Spinal Elements: IP royalties; Paid consultant

Xenix Medical: Paid consultant

**Yee-Cheen Doung, MD –** Musculoskeletal Tumor Society: Board or committee member

**Michelle Ghert, MD –** Journal of Orthopaedic Research: Editorial or governing board

Clinical Orthopaedics and Related Research: Editorial or governing board

Musculoskeletal Tumor Society: Board or committee member

Stryker: Paid consultant; Paid presenter or speaker

**Trey Gurich, MD –** Nothing to disclose.

**Matthew Houdek, MD –** Link Orthopaedics: Paid consultant

Mid-America Orthopaedic Association: Board or committee member

Musculoskeletal Tumor Society: Board or committee member

**Dipak Ramkumar, MD –** Nothing to disclose.

**Geoffrey Siegel, MD –** Annals of Medical Case Reports- Oncology: Editorial or governing board

**Steve Thorpe, MD –** AAOS: Board or committee member

Musculoskeletal Tumor Society: Board or committee member

**Matthew Wallace, MD –** Nothing to disclose.