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SURVEY

Outcome After Reconstruction of the Proximal Humerus for Tumor Resection: A Systematic Review

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Abstract

Background Tumors of the appendicular skeleton commonly affect the proximal humerus, but there is no consensus regarding the best reconstructive technique after proximal humerus resection for tumors of the shoulder.

Questions/purposes We wished to perform a systematic review to determine which surgical reconstruction offers the (1) best functional outcome as measured by the Musculoskeletal Tumor Society (MSTS) score, (2) longest construct survival, and (3) lowest complication rate after proximal humerus resection for malignant or aggressive benign tumors of the shoulder.

Methods We searched the literature up to June 1, 2013, from MEDLINE, EMBASE, and the Cochrane Library. Only studies reporting results in English, Dutch, or German and with followups of 80% or more of the patients at a minimum of 2 years were included. Twenty-nine studies with 693 patients met our criteria, seven studies (24%) were level of evidence III and the remainder were level IV. Studies reported on reconstruction with prostheses (n = 17), osteoarticular allografts (n = 10), and allograft-prosthesis composites (n = 11). Owing to substantial heterogeneity and bias, we narratively report our results.

Results Functional scores in prosthesis studies ranged from 61% to 77% (10 studies, 141 patients), from 50% to 78% (eight studies, 84 patients) in osteoarticular graft studies, and from 57% to 91% (10 studies, 141 patients) in allograft-prosthesis composite studies. Implant survival ranged from 0.38 to 1.0 in the prosthesis group (341 patients), 0.33 to 1.0 in the osteoarticular allograft group (143 patients), and 0.33 to 1.0 in allograft-prosthesis group (132 patients). Overall complications per patient varied between 0.045 and 0.85 in the prosthesis group, 0 and 1.5 in the osteoarticular graft group, and 0.19 and 0.79 in the prosthesis-composite graft group. We observed a higher fracture rate for osteoarticular allografts, but other specific complication rates were similar.

Conclusions Owing to the limitations of our systematic review, we found that allograft-prosthesis composites and prostheses seem to have similar functional outcome and survival rates, and both seem to avoid fractures that are observed with osteoarticular allografts. Further collaboration in the field of surgical oncology, using randomized controlled trials, is required to establish the superiority of any particular treatment.

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Introduction

The proximal humerus is the second most common site of all osseous sarcomas and the third most common site for osteosarcoma. Although osteosarcomas and Ewing's sarcomas occur characteristically in teenagers and young adults, chondrosarcomas occur in older individuals [18]. Reconstruction of the shoulder after resection of a malignant or a benign locally aggressive primary bone tumor of the proximal humerus poses the challenging problem of associated bone loss. In addition, an adequate tumor margin implies partial resection of the deltoid musculature and joint capsule and occasionally the rotator cuff, axillary nerve, glenoid, or the scapula.

There is no consensus regarding the best reconstructive technique after proximal humerus resection. Principal treatment approaches in use today include arthroplasty prostheses, osteoarticular allografts, and allograft-prosthesis composites [38, 58]. Moreover, several autologous grafts (fibula, scapular crest, or clavicle [5, 8, 47]) have been described. Because autologous grafts often are used in conjunction with a shoulder arthrodesis, prostheses, osteoarticular allografts, and allograft-prosthesis composites are the only reconstructions allowing for a mobile glenohumeral joint. Although all of these approaches are in use, and there are some situations where only one approach might be appropriate for a particular patient, there are many scenarios in which all are potential options. However, because there are no prospective or randomized trials, it is difficult to know which approach is best in terms of functional outcome, implant survivorship, or complications.

This review aims to identify which surgical reconstruction (1) offers the best functional outcome measured by the Musculoskeletal Tumor Society (MSTS) score [20], and (2) has the longest survival rate, and (3) lowest complication rate after proximal humerus resection for tumors of the shoulder.

Materials and Methods

Article Selection

On June 1, 2013, we searched PUBMED, EMBASE, and the Cochrane Library using the search string for title and abstract: (humerus OR shoulder OR "upper limb" OR "upper extremity") AND (neoplasm* OR tumor* OR tumour* OR malign* OR sarcoma* OR cancer*) AND (prosthe* OR autograft OR allograft OR fusion OR flail joint OR Tikhoff linberg OR arthrodesis OR clavicula pro humero OR graft OR forequarter amputation).

This search yielded 524 results from PubMed, 548 from EMBASE, and three from the Cochrane Library. Two reviewers (SAL-C, TT) independently examined the citation information for each result from the databases for relevant studies; subsequently, two independent reviewers screened the full texts (TT, SPFTN); they also scanned the reference lists of the included articles for additional studies that met the inclusion criteria (Fig. 1). Inclusion criteria were determined as follows: functional outcome after proximal humerus resection for any malignant or benign locally aggressive tumor, a minimum 2-year followup, and English, Dutch, or German language publication. We excluded cohorts with less than three patients and case reports, preclinical studies, meeting abstracts, indiscernible proximal humerus patient cohorts, inadequate outcome reporting, studies with more than 20% of patients lost to followup, and salvage procedures. In case of overlapping patient cohorts [36, 48, 51, 52], we included the study reporting on the largest cohort [36, 52]. In one of three studies [23, 37, 43], after correspondence with the author, we included the smaller cohort with a more comprehensive functional outcome [23].

Two independent reviewers (TT, SPFTN) critically appraised the included studies using predetermined criteria, and data were extracted with standardized sheets. Discordant judgments were resolved by consensus discussion between the two reviewers. Critical appraisal criteria included disclosure, selection of patients, outcome reporting and assessment, baseline display, and postoperative care. These criteria are based on the relevant literature [14, 28, 38, 49, 58]. Our review is registered with PROSPERO (registration number CRD42013005626) [54, 55].

Outcome Measurements

The following data were extracted from the selected articles: author, year of publication, institute, study type, construct included, number of patients, age, followup, patients lost to followup, nature of the tumor (benign or malignant), metastasis, implant survival, complications, and MSTS score. We considered the following reconstructive techniques: prostheses, osteoarticular allografts, allograft-prosthesis composites, fibula autografts, scapular crest flaps, clavicle pro humero reconstruction, flail joint, and amputation.

Functional Outcome

In case of missing MSTS score standard deviations or baseline characteristics, we contacted the corresponding authors; of the contacted authors of 19 studies [1, 6, 9, 12, 16, 17, 19, 25, 27, 31, 36, 43, 45, 47, 50, 56, 60–62], 13 replied [1, 6, 9, 16, 17, 27, 31, 36, 43, 45, 50, 56, 61] and seven were able to provide us with the requested additional data [6, 9, 17, 27, 36, 45, 56]. We regarded autoclaved autograft and allograft bone combined with a prosthesis as allograft-prosthesis composites. Osteoblastomas and giant cell tumors are scored

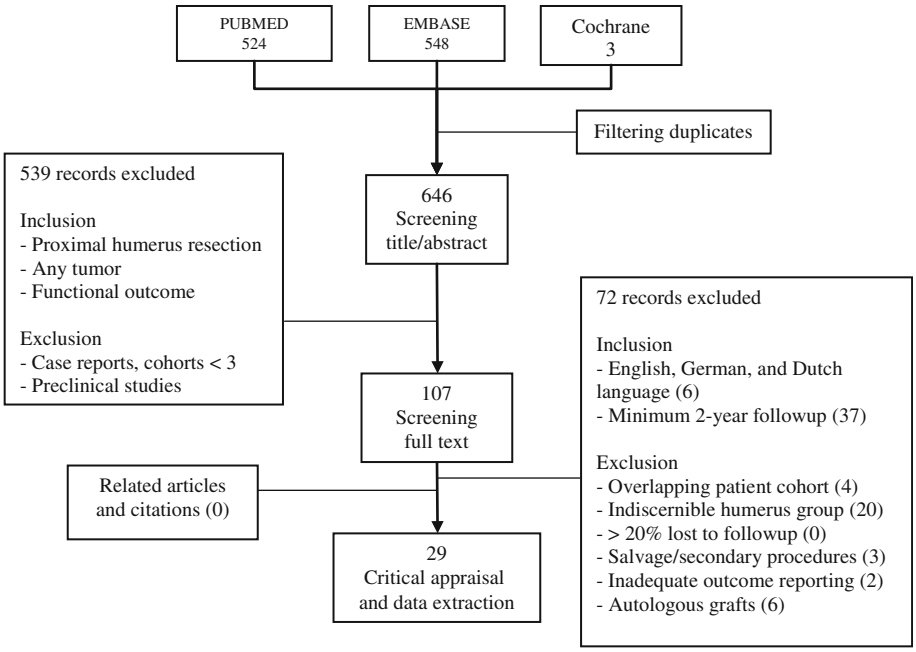

Fig. 1 The flowchart shows our literature search and selection of relevant articles. The last search was performed on June 1, 2013.

as benign locally aggressive tumors with their unpredictable behavior and rare incidences of metastasis [13, 26].

The mean MSTS score with its SD was extracted or, if appropriate, calculated from individual patient data. In two cases, scores were calculated differently: in one instance, we used the lowest possible MSTS score reflecting "poor", "good", and "excellent" outcomes as reported by the authors, possibly underestimating the functional results [30]. In another study we estimated the SD by computing the two and four missing values resulting in the largest SD [44].

Implant Survival

We considered total or partial removal of the reconstruction a failure. Kaplan-Meier implant survival rates were extracted at the 5-year end point.

Complications

We evaluated the following complications: deep infections, fracture, subluxation, dislocation, proximal migration, component loosening, nonunion, and permanent nerve deficit.

Study Characteristics

Articles on amputation either focused on patient survival or included multiple disorders other than proximal humerus malignancies. No article on clavicula pro humero satisfied our inclusion criteria. Scapular crest and fibula grafts used various proximal fixation methods: plate [5, 8, 60] or wire [34], wire and tendon [59], suture [36], or none at all [7, 21]. In addition, in three studies, it was reported that an allograft was used to strut the fibular grafts [7, 21, 60], and Kumar et al. [34] reported that in one instance, an additional scapular crest graft was used. Arthoplasty prostheses, osteoarticular allografts, and allograft-prosthesis composites are comparable in the sense that they allow for reconstructions of a mobile glenohumeral joint and have similar indications, therefore only those reconstructions were included in our final analysis.

Approximately ¼ of the studies were level III evidence and the remainder were level IV. Critical appraisal shows only 55% of the studies reported eligibility criteria, sources, and methods of selection of participants, possibly resulting in selection bias. As only 14% reported what complications would be collected before their actual data collection and only one study used objective, independent outcome reporting, outcome bias cannot be excluded (Fig. 2) (Appendix 1, Supplemental material is available with the online version of CORR). Asymmetry of the funnel plots seems to reflect the clinical and methodologic heterogeneity rather than publication bias (Fig. 3) [28].

Study Population

For this review, a total of 693 patients were included with a mean age per study ranging from 9 to 57 years. The percentage of primary malignancies varied between 23% and 100%, secondary malignancies from 0% to 77% (0% in 21 studies), and benign tumors from 0% to 75% (0% in 18 studies; Table 1).

Analysis

Because of heterogeneity and sensitivity to bias when not including randomized controlled trials we narratively reported our results. MSTS scores are reported as percentages; survival and complications are reported as proportions to the included patients.

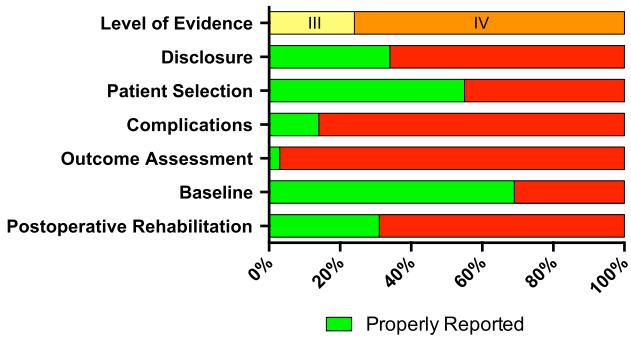

Fig. 2 Low reporting of patient and complication selection and outcome assessment increase the risk for selection and outcome bias.

Results

MSTS Scores

Twenty-four studies reported the MSTS scores for 28 reconstructive methods for a total of 398 patients. Functional score in prosthesis studies ranged from 61% to 77% (10 studies, 141 patients); osteoarticular grafts from 50% to 78% (eight studies, 84 patients); allograft-prosthesis composites from 57% to 91% (10 studies, 141 patients; Table 2).

Implant Survival

Implant survival and complications were calculated for 616 patients from 29 studies. Implant survival ranged from 0.38 to 1.0 in the prosthesis group (341 patients); 0.33 to 1.0 in the osteoarticular allograft group (143 patients), and 0.33 to 1.0 in allograft-prosthesis group (132 patients; Table 3).

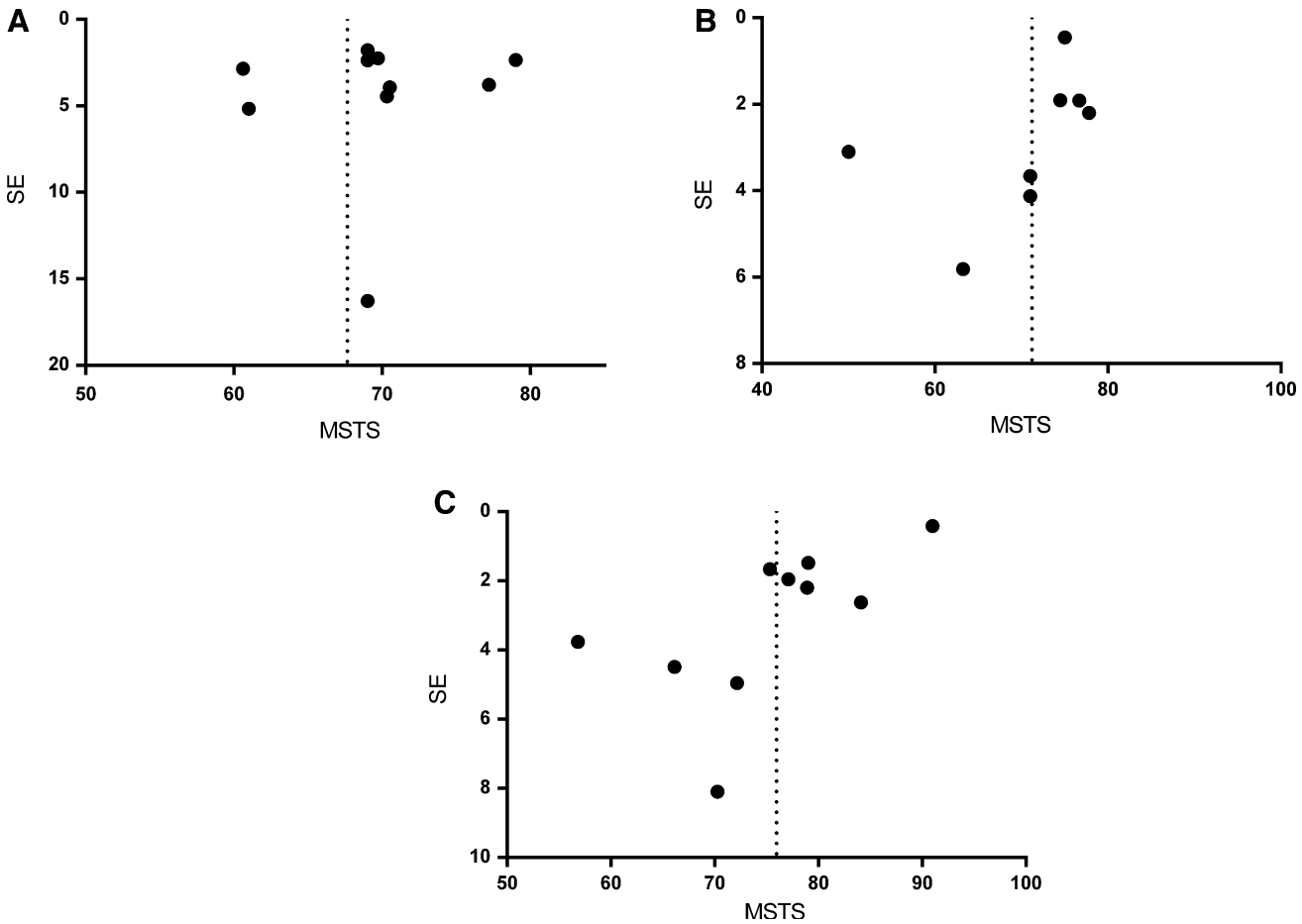

Fig. 3A–C The funnel plots show MSTS scores and standard errors for (**A**) prosthesis studies, (**B**) osteoarticular allograft studies, and (**C**) allograft-prosthesis composite studies. Asymmetry seems to reflect clinical and methodologic heterogeneity rather than publication bias.

Table 1. Characteristics of the included studies

Study	Type	Construct	Patients	Mean age (years)	Followup (years/range)	Malignant	Metastasis	Benign
Burrows et al. [11]	CS	P	7	47	13 (4–24)	57%	14%	29%
Bos et al. [10]	CS	P	15	29	6 (2–16)	67%	0%	33%
Malawer et al. [35]	CS	P	29	NR	4 (2–12)†	100%	0%	0%
O'Connor et al. [44]	RC	P	11	35*	5 (2–12)	NR	NR	NR
Meller et al. [41]	CS	P	8	34	3 (2–8)	88%	13%	0%
Voggenreiter et al. [57]	CS	P	19	49	5 (0–11)	89%	11%	0%
Fuhrmann et al. [22]	CS	P	22	57	4 (2–7)	23%	77%	0%
Wittig et al. [61]	CS	P	23	18†	10 (2–20)	100%	0%	0%
Kumar et al. [33]	CS	P	100	34	9 (2–20)	78%	18%	4%
Mayilvahanan et al. [39]	CS	P	57	28	6 (2–15)	65%	9%	26%
Kitagawa et al. [32]	CS	P	10	49	2 (0–9)	80%	0%	20%
Sharma et al. [50]	CS	P	21	41*	5 (0–13)*	100%	0%	0%
Potter et al. [45]	RC	P	16	54	8 (2–18)†	38%	56%	6%
Ioannou et al. [29]	CS	P	12	46	6 (4–9)	83%	17%	0%
Manfrini et al. [36]	RC	P	25	11	11 (SD 8)	100%	0%	0%
van de Sande et al. [56]	RC	P	14	44	17 (3–25)	57%	21%	21%
Wang et al. [60]	RC	P	25	19*	7 (3–16)	100%	0%	0%
Gebhardt et al. [23]	CS	OA	20	42*	16 (2–28)*	65%	5%	30%
Aho et al. [3]	CS	OA	4	NR	6 (3–20)*	25%	0%	75%
Alman et al. [4]	CS	OA	3	13	5 (3–7)	100%	0%	0%
O'Connor et al. [44]	RC	OA	8	35*	5 (2–12)	NR	NR	NR
Probyn et al. [46]	CS	OA	11	34	4 (2–7)	100%	0%	0%
Getty & Peabody [24]	CS	OA	16	35	4 (1–11)	88%	0%	13%
DeGroot et al. [15]	CS	OA	31	30	6 (2–12)	55%	10%	35%
Potter et al. [45]	RC	OA	17	37	8 (2–18)†	59%	24%	18%
Manfrini et al. [36]	RC	OA	3	12	3 (NR)	100%	0%	0%
van de Sande et al. [56]	RC	OA	13	33	17 (3–25)	69%	0%	31%
Aponte-Tinao et al. [6]	RC	OA	21	32*	5 (1–20)	81%	0%	19%
Jensen & Johnston [30]	CS	APC	14	43	5 (2–12)	93%	0%	7%
Suk et al. [52]	CS	APC	6	26	4 (3–5)	100%	0%	0%
Black et al. [9]	CS	APC	6	41	5 (2–6)	83%	17%	0%
Potter et al. [45]	RC	APC	16	56	8 (2–18)†	50%	38%	13%
Abdeen et al. [1]	CS	APC	36	23*	5 (0–11)	89%	8%	3%
Moran & Stalley [42]	CS	APC	11	22	6 (2–9)	100%	0%	0%
Manfrini et al. [36]	RC	APC	3	9	4 (NR)	100%	0%	0%
van de Sande et al. [56]	RC	APC	10	34	17 (3–25)	70%	10%	20%
Wang et al. [60]	RC	APC	14	19*	7 (3–16)	100%	0%	0%
Aponte-Tinao et al. [6]	RC	APC	16	42	5 (1–20)	100%	0%	0%

CS = case series; RC = retrospective cohort; P = prosthesis; OA = osteoarticular allograft; APC = allograft-prosthesis composite; NR = not reported; * cohort, †median.

Complications

Overall complications per patient varied between 0.045 and 0.85 in the prosthesis group, 0 and 1.5 in the osteoarticular graft group, and 0.19 and 0.79 in the prosthesis-composite graft group. In particular, the fracture rate varied among groups; proportions ranged from 0.05 to 0.17 with prostheses and 0 to 0.67 with osteoarticular grafts and composite-prosthesis allografts. However, when only including studies with more than 10 patients the fracture rates ranged from 0 to 0.05 in the prosthesis group, 0.08 to 0.62 in the osteoarticular allograft group, and 0 and 0.06 in the allograft-prosthesis composite group (Table 3). Other complications were similar between constructs (Appendix

Table 2. Functional outcome

Study	Construction	Sample size	MSTS score (%)	Standard deviation
O'Connor et al. [44]	Prosthesis	6	61	13
Meller et al. [41]	Prosthesis	6	71	10
Voggenreiter et al. [57]	Prosthesis	10	70	14
Fuhrmann et al. [22]	Prosthesis	22	61	13
Kumar et al. [33]	Prosthesis	30	79	13
Kitagawa et al. [32]	Prosthesis	3	69	28
Potter et al. [45]	Prosthesis	16	69	9
Manfrini et al. [36]	Prosthesis	21	70	10
van De Sande et al. [56]	Prosthesis	10	77	12
Wang et al. [60]	Prosthesis	17	69	7
O'Connor et al. [44]	Allograft	6	71	10
Probyn et al. [46]	Allograft	10	50	10
Getty & Peabody [24]	Allograft	8	63	16
DeGroot et al. [15]	Allograft	23	74	9.1
Potter et al. [45]	Allograft	12	71	13
Manfrini et al. [36]	Allograft	3	78	3.8
van De Sande et al. [56]	Allograft	6	77	4.7
Aponte-Tinao et al. [6]	Allograft	16	75	1.8
Jensen & Johnston [30]	APC	14	77	7.3
Suk et al. [52]	APC	6	57	9.2
Black et al. [9]	APC	4	70	16
Potter et al. [45]	APC	15	79	5.7
Abdeen et al. [1]	APC	34	91	2.4
Moran & Stalley [42]	APC	8	66	13
Manfrini et al. [36]	APC	3	79	3.8
van de Sande et al. [56]	APC	7	72	13
Wang et al. [60]	APC	10	75	5.3
Aponte-Tinao et al. [6]	APC	13	84	9.4

MSTS = Musculoskeletal Tumor Society; APC = allograft-prosthesis composite.

2, Supplemental material is available with the online version of CORR).

Discussion

Tumors of the appendicular skeleton commonly affect the proximal humerus, and complete resection impedes shoulder function. As there is no consensus regarding the best reconstructive technique after proximal humerus resection, reviewing the literature in the absence of quality randomized prospective trials might offer some insight into the best reconstructive option. We aimed to identify which surgical reconstruction offers (1) the best functional outcome measured by the MSTS score, and (2) has the longest survival rate and (3) lowest complication rate after proximal humerus resection. Because of the limited literature available we were able to compare only arthroplasty prostheses, osteoarticular allografts, and allograft-prosthesis composites.

This study has some limitations. Because this is a review of nonrandomized studies, there is an increased risk of selection bias, variation in the way in which confounding is considered in the analysis, and greater risk of other biases. All of these biases would tend to increase apparent benefits of treatments and deemphasize the problems and complications associated with these treatments. Additionally, the most commonly used score in the papers reviewed in this investigation used the MSTS score, resulting in a possibly overstated physician-perceived function, instead of a true patient-reported outcome. The MSTS score is not a validated tool and may not adequately reflect upper extremity function, as it mainly measures impairment instead of activity limitation. Moreover, the MSTS score is a physician-rated instrument and a couple studies stress its subsequent limitations [2, 53].

Owing to the limited information reported, the current results do not allow for subgroup analysis on different clinical scenarios (eg, tumor type and stage, age, soft tissue resection, or radiographic findings). This impedes the predictive value of our results for specific patients. We include previously missing, and therefore unpublished, MSTS score standard deviations and baseline characteristics from seven studies that were not verified by peer review [6, 9, 17, 27, 36, 45, 56].

Although allograft-prosthesis composites resulted in the largest range in MSTS scores, the majority of the scores for all three constructs were between 60% and 79%, making them seem largely comparable in functional outcome.

Implant survival looks similar between the three constructs.

The number of overall complications per patient seems greater in the osteoarticular allograft group (range, 0–1.5 versus 0.045–0.85 in the prosthesis group and 0.19–0.79 in the allograft-prosthesis composite group). The increased complication rate seems to be based on higher osteoarticular allograft fracture rates, as all other specific complications were comparable. Fracture rates between the osteoarticular allograft group and allograft-prosthesis composite group might appear similar (both 0–0.67); however, the upper limits with allograft-prosthesis composite fractures are based on relatively small studies. When comparing only studies with more than 10 patients, the allograft-prosthesis composite fracture rates (0–0.06) are comparable to those of the prosthesis (0–0.05).

Performance of a (superior) randomized controlled trial is hindered by several practical difficulties; one is the necessity of a surgeon or group of surgeons being able to confidently perform highly specialized operations such fibular transplantation, including vascular microsurgery

Table 3. Implant survival and complications

Study	Construct	Sample size	Implant survival	Proportion	Complications	Proportion	Fractures	Proportion
Burrowes et al. [11]	Prosthesis	6	5	0.83	5	0.83	1	0.17
Bos et al. [10]	Prosthesis	13	5	0.38	11	0.85	2	0.15
Malawer et al. [35]	Prosthesis	29	26	0.9	NR	NR	NR	NR
O'Conner et al. [44]	Prosthesis	11	7	0.63	9	0.82	1	0.091
Meller et al. [41]	Prosthesis	8	8	1.0	NR	NR	NR	NR
Voggenreiter et al. [57]	Prosthesis	19	17	0.89	4	0.21	2	0.11
Fuhrmann et al. [22]	Prosthesis	22	22	1.0	1	0.045	0	0
Wittig et al. [61]	Prosthesis	15	15	1.0	2	0.13	1	0.067
Kumar et al. [33]	Prosthesis	45	39	0.87	10	0.22	0	0
Mayilvahanan et al. [39]	Prosthesis	55	50	0.91	16	0.29	3	0.055
Kitagawa et al. [32]	Prosthesis	5	4	0.8	3	0.60	0	0
Sharma et al. [50]	Prosthesis	21	14	0.67	3	0.14	0	0
Potter et al. [45]	Prosthesis	16	16	1.0	5	0.31	0	0
Ioannou et al. [29]	Prosthesis	12	NR	NR	2	0.17	0	0
Manfrini et al. [36]	Prosthesis	25	20	0.80	15	0.60	0	0
van de Sande et al. [56]	Prosthesis	14	14	1.0	7	0.50	0	0
Wang et al. [60]	Prosthesis	25	23	0.92	22	0.88	0	0
Gebhardt et al. [23]	Allograft	20	16	0.80	10	0.50	5	0.25
Aho et al. [3]	Allograft	4	2	0.50	5	1.3	2	0.50
Alman et al. [4]	Allograft	3	1	0.33	3	1.0	2	0.67
O'Conner et al. [44]	Allograft	8	6	0.75	4	0.50	4	0.50
Probyn et al. [46]	Allograft	10	4	0.40	10	1.0	4	0.40
Getty & Peabody [24]	Allograft	13	8	0.61	20	1.5	8	0.62
DeGroot et al. [15]	Allograft	31	23	0.74	16	0.52	11	0.35
Potter et al. [45]	Allograft	17	12	0.71	14	0.82	9	0.53
Manfrini et al. [36]	Allograft	3	3	1.0	0	0	0	0
van de Sande et al. [56]	Allograft	13	8	0.62	11	0.85	1	0.077
Aponte-Tinao et al. [6]	Allograft	21	16	0.76	5	0.24	5	0.24
Jensen & Johnston [30]	APC	14	14	1.0	3	0.21	0	0
Suk et al. [52]	APC	6	5	0.83	2	0.33	1	0.17
Black et al. [9]	APC	6	5	0.83	2	0.33	0	0
Potter et al. [45]	APC	16	15	0.94	7	0.44	1	0.063
Abdeen et al. [1]	APC	36	33	0.92	10	0.28	1	0.028
Moran & Stalley [42]	APC	11	11	1.0	6	0.55	0	0
Manfrini et al. [36]	APC	3	1	0.33	2	0.67	2	0.67
van de Sande et al. [56]	APC	10	9	0.90	15	1.5	2	0.20
Wang et al. [60]	APC	14	12	0.86	11	0.79	0	0
Aponte-Tinao et al. [6]	APC	16	13	0.81	3	0.19	1	0.063

MSTS = Musculoskeletal Tumor Society; APC = allograft-prosthesis composite; NR = not reported

and adequate tumor resection. Another major problem is the number of patients presenting with oncologic conditions requiring resection of the proximal humerus. A power analysis of three reconstructive methods, assuming a difference in MSTS score of 10%, shows a required sample size of 969 patients (alpha 0.05; power 0.8; G*Power 3.1.7). Because the cohort studies in our review reported an average of 1.6 to 5.3 patients per year [6, 32, 36, 44, 45, 56, 57, 60, 61], a randomized controlled trial would be an elongated, if not impossible, endeavor at any institution. Nonetheless, according to the IDEAL recommendations [40] to evaluate surgical innovations, all surgical procedures for proximal humerus replacement are far from validated. The next step would be assessment by inclusion of large groups of patients using standardized surgeries, postoperative care, and outcome reporting. Because a

randomized controlled trial might be difficult to conduct, several other options are available, for example, matching procedures or an expertise-based randomized trial. The latter involves a study in which patients are randomly assigned by a third party to surgeons, who then treat their patients with their preferred intervention [40]. This design prevents the exigency of different highly specialized surgeons at one institution and does not require any surgeon to abandon his or her preferred method.

The limitations of the literature we surveyed suggest strongly to us that multicenter studies are warranted if we are to establish the optimal treatment for oncologic replacement of the complex shoulder. A prospective database including patients from specialized treatment centers would be an important first step. Strengths of our systematic review of the available retrospective literature were its restriction to followup of at least 2 years and restriction to studies that accounted for 80% or greater of the patients they included. Conscious of the limitations of our systematic review in coming to firm conclusions, allograft-prosthesis composites and prostheses probably are indistinguishable based on the literature, and both seem to avoid the problem of fracture that is observed with osteoarticular allografts.

References

1. Abdeen A, Hoang BH, Athanasian EA, Morris CD, Boland PJ, Healey JH. Allograft-prosthesis composite reconstruction of the proximal part of the humerus: functional outcome and survivorship. *J Bone Joint Surg Am.* 2009;91:2406–2415.
2. Acquadro C, Berzon R, Dubois D, Leidy NK, Marquis P, Revicki D, Rothman M; PRO Harmonization Group. Incorporating the patient's perspective into drug development and communication: an ad hoc task force report of the Patient-Reported Outcomes (PRO) Harmonization Group meeting at the Food and Drug Administration, February 16, 2001. *Value Health.* 2003;6:522–531.
3. Aho AJ, Ekfors T, Dean PB, Aro HT, Ahonen A, Nikkanen V. Incorporation and clinical results of large allografts of the extremities and pelvis. *Clin Orthop Relat Res.* 1994;307:200–213.
4. Alman BA, De Bari A, Krajbich JI. Massive allografts in the treatment of osteosarcoma and Ewing sarcoma in children and adolescents. *J Bone Joint Surg Am.* 1995;77:54–64.
5. Amin SN, Ebeid WA. Shoulder reconstruction after tumor resection by pedicled scapular crest graft. *Clin Orthop Relat Res.* 2002;397:133–142.
6. Aponte-Tinao LA, Ayerza MA, Muscolo DL, Farfalli GL. Allograft reconstruction for the treatment of musculoskeletal tumors of the upper extremity. *Sarcoma.* 2013;2013:925413.
7. Bernd L, Sabo D, Zahlten-Hinguranage A, Niemeyer P, Daecke W, Simank HG. [Experiences with vascular pedicled fibula in reconstruction of osseous defects in primary malignant bone tumors][in German]. *Orthopade.* 2003;32:983–993.
8. Bilgin SS. Reconstruction of proximal humeral defects with shoulder arthrodesis using free vascularized fibular graft. *J Bone Joint Surg Am.* 2012;94:e94.
9. Black AW, Szabo RM, Titelman RM. Treatment of malignant tumors of the proximal humerus with allograft-prosthesis composite reconstruction. *J Shoulder Elbow Surg.* 2007;16:525–533.
10. Bos G, Sim F, Pritchard D, Shives T, Rock M, Askew L, Chao E. Prosthetic replacement of the proximal humerus. *Clin Orthop Relat Res.* 1987;224:178–191.
11. Burrows HJ, Wilson JN, Scales JT. Excision of tumours of humerus and femur, with restoration by internal prostheses. *J Bone Joint Surg Br.* 1975;57:148–159.
12. Camnasio F, Scotti C, Peretti GM, Fontana F, Fraschini G. Prosthetic joint replacement for long bone metastases: analysis of 154 cases. *Arch Orthop Trauma Surg.* 2008;128:787–793.
13. Campanacci M, Baldini N, Boriani S, Sudanese A. Giant-cell tumor of bone. *J Bone Joint Surg Am.* 1987;69:106–114.
14. Coleman BD, Khan KM, Maffulli N, Cook JL, Wark JD. Studies of surgical outcome after patellar tendinopathy: clinical significance of methodological deficiencies and guidelines for future studies. Victorian Institute of Sport Tendon Study Group. *Scand J Med Sci Sports.* 2000;10:2–11.
15. DeGroot H, Donati D, Di Liddo M, Gozzi E, Mercuri M. The use of cement in osteoarticular allografts for proximal humeral bone tumors. *Clin Orthop Relat Res.* 2004;427:190–197.
16. De Wilde L, Boileau P, Van der Bracht H. Does reverse shoulder arthroplasty for tumors of the proximal humerus reduce impairment? *Clin Orthop Relat Res.* 2011;469:2489–2495.
17. De Wilde LF, Plasschaert FS, Audenaert EA, Verdonk RC. Functional recovery after a reverse prosthesis for reconstruction of the proximal humerus in tumor surgery. *Clin Orthop Relat Res.* 2005;430:156–162.
18. Dorfman HD, Czerniak B. Bone cancers. *Cancer.* 1995; 75(1 suppl):203–210.
19. El-Sherbiny M. Reconstruction of the proximal humerus after wide resection of tumors: comparison of three reconstructive options. *J Egypt Natl Canc Inst.* 2008;20:369–378.
20. Enneking WF, Dunham W, Gebhardt MC, Malawar M, Pritchard DJ. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. *Clin Orthop Relat Res.* 1993;286:241–246.
21. Fuchs B, O'Connor MI, Padgett DJ, Kaufman KR, Sim FH. Arthrodesis of the shoulder after tumor resection. *Clin Orthop Relat Res.* 2005;436:202–207.
22. Fuhrmann RA, Roth A, Venbrocks RA. Salvage of the upper extremity in cases of tumorous destruction of the proximal humerus. *J Cancer Res Clin Oncol.* 2000;126:337–344.
23. Gebhardt MC, Roth YF, Mankin HJ. Osteoarticular allografts for reconstruction in the proximal part of the humerus after excision of a musculoskeletal tumor. *J Bone Joint Surg Am.* 1990;72: 334–345.
24. Getty PJ, Peabody TD. Complications and functional outcomes of reconstruction with an osteoarticular allograft after intra-articular resection of the proximal aspect of the humerus. *J Bone Joint Surg Am.* 1999;81:1138–1146.
25. Gosheger G, Gebert C, Ahrens H, Streitbuerger A, Winkelmann W, Hardes J. Endoprosthetic reconstruction in 250 patients with sarcoma. *Clin Orthop Relat Res.* 2006;450:164–171.
26. Greenspan A. Benign bone-forming lesions: osteoma, osteoid osteoma, and osteoblastoma. Clinical, imaging, pathologic, and differential considerations. *Skeletal Radiol.* 1993;22:485–500.
27. Hartigan DE, Veillette CJ, Sanchez-Sotelo J, Sperling JW, Shives TC, Cofield RH. Reconstruction of the proximal humerus for bone neoplasm using an anatomic prosthesis-bone graft composite. *Acta Orthop Belg.* 2012;78:450–457.
28. Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions.* The Cochrane Collaboration; 2011. Available at: http://handbook.cochrane.org/. Accessed January 9, 2014.
29. Ioannou M, Papanastassiou J, Athanassiou AE, Ziras N, Kottakis S, Demertzis N. Surgical options in cases of tumorous destruction

of the proximal humerus: twenty-one patients followed from 4–9 years. *J BUON.* 2009;14:57–61.
30. Jensen KL, Johnston JO. Proximal humeral reconstruction after excision of a primary sarcoma. *Clin Orthop Relat Res.* 1995;311:164–175.
31. Kiss J, Sztrinkai G, Antal I, Kiss J, Szendroi M. Functional results and quality of life after shoulder girdle resections in musculoskeletal tumors. *J Shoulder Elbow Surg.* 2007;16:273–279.
32. Kitagawa Y, Thai DM, Choong PF. Reconstructions of the shoulder following tumour resection. *J Orthop Surg (Hong Kong).* 2007;15:201–206.
33. Kumar D, Grimer RJ, Abudu A, Carter SR, Tillman RM. Endoprosthetic replacement of the proximal humerus: long-term results. *J Bone Joint Surg Br.* 2003;85:717–722.
34. Kumar VP, Satku SK, Mitra AK, Pho RW. Function following limb salvage for primary tumors of the shoulder girdle: 10 patients followed 4 (1–11) years. *Acta Orthop Scand.* 1994;65:55–61.
35. Malawer MM, Chou LB. Prosthetic survival and clinical results with use of large-segment replacements in the treatment of high-grade bone sarcomas. *J Bone Joint Surg Am.* 1995;77:1154–1165.
36. Manfrini M, Tiwari A, Ham J, Colangeli M, Mercuri M. Evolution of surgical treatment for sarcomas of proximal humerus in children: retrospective review at a single institute over 30 years. *J Pediatr Orthop.* 2011;31:56–64.
37. Mankin HJ, Doppelt SH, Sullivan TR, Tomford WW. Osteoarticular and intercalary allograft transplantation in the management of malignant tumors of bone. *Cancer.* 1982;50:613–630.
38. Mayer D, ed. *Essential Evidence-Based Medicine*. Ed 2. Cambridge, UK: Cambridge University Press; 2010.
39. Mayilvahanan N, Paraskumar M, Sivaseelam A, Natarajan S. Custom mega-prosthetic replacement for proximal humeral tumours. *Int Orthop.* 2006;30:158–162.
40. McCulloch P, Altman DG, Campbell WB, Flum DR, Glasziou P, Marshall JC, Nicholl J; Balliol Collaboration, Aronson JK, Barkun JS, Blazeby JM, Boutron IC, Clavien PA, Cook JA, Ergina PL, Feldman LS, Maddern GJ, Nicholl J, Reeves BC, Seiler CM, Strasberg SM, Meakins JL, Ashby D, Black N, Bunker J, Burton M, Campbell M, Chalkidou K, Chalmers I, de Leval M, Deeks J, Grant A, Gray M, Greenhalgh R, Jenicek M, Kehoe S, Lilford R, Littlejohns P, Loke Y, Madhock R, McPherson K, Meakins J, Rothwell P, Summerskill B, Taggart D, Tekkis P, Thompson M, Treasure T, Trohler U, Vandenbroucke J. No surgical innovation without evaluation: the IDEAL recommendations. *Lancet.* 2009;374:1105–1112.
41. Meller I, Bickels J, Kollender Y, Ovadia D, Oren R, Mozes M. Malignant bone and soft tissue tumors of the shoulder girdle: a retrospective analysis of 30 operated cases. *Acta Orthop Scand.* 1997;68:374–380.
42. Moran M, Stalley PD. Reconstruction of the proximal humerus with a composite of extracorporeally irradiated bone and endoprosthesis following excision of high grade primary bone sarcomas. *Arch Orthop Trauma Surg.* 2009;129:1339–1345.
43. Mourikis A, Mankin HJ, Hornicek FJ, Raskin KA. Treatment of proximal humeral chondrosarcoma with resection and allograft. *J Shoulder Elbow Surg.* 2007;16:519–524.
44. O'Connor MI, Sim FH, Chao EY. Limb salvage for neoplasms of the shoulder girdle: intermediate reconstructive and functional results. *J Bone Joint Surg Am.* 1996;78:1872–1888.
45. Potter BK, Adams SC, Pitcher JD Jr, Malinin TI, Temple HT. Proximal humerus reconstructions for tumors. *Clin Orthop Relat Res.* 2009;467:1035–1041.
46. Probyn LJ, Wunder JS, Bell RS, Griffin AM, Davis AM. A comparison of outcome of osteoarticular allograft reconstruction and shoulder arthrodesis following resection of primary tumours of the proximal humerus. *Sarcoma.* 1998;2:163–170.
47. Rodl RW, Gosheger G, Gebert C, Lindner N, Ozaki T, Winkelmann W. Reconstruction of the proximal humerus after wide resection of tumours. *J Bone Joint Surg Br.* 2002;84:1004–1008.
48. Ruggieri P, Mavrogenis AF, Guerra G, Mercuri M. Preliminary results after reconstruction of bony defects of the proximal humerus with an allograft-resurfacing composite. *J Bone Joint Surg Br.* 2011;93:1098–1103.
49. Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ.* 2010;340:c332.
50. Sharma S, Turcotte RE, Isler MH, Wong C. Experience with cemented large segment endoprostheses for tumors. *Clin Orthop Relat Res.* 2007;459:54–59.
51. Shin KH, Park HJ, Yoo JH, Hahn SB. Reconstructive surgery in primary malignant and aggressive benign bone tumor of the proximal humerus. *Yonsei Med J.* 2000;41:304–311.
52. Suk KS, Shin KH, Hahn SB. Limb salvage using original low heat-treated tumor-bearing bone. *Clin Orthop Relat Res.* 2002;397:385–393.
53. Tarlov AR, Ware JE Jr, Greenfield S, Nelson EC, Perrin E, Zubkoff M. The Medical Outcomes Study: an application of methods for monitoring the results of medical care. *JAMA.* 1989;262:925–930.
54. Teunis T, Nota S, Lozano-Calderón S, Schwab J, Hornicek F. Functional outcome after surgical reconstruction of the proximal humerus for tumor resection: a systematic review and meta-analysis. PROSPERO: CRD42013005626. Available at: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42013005626. Accessed September 17, 2013.
55. University of York Centre for Reviews and Dissemination. Welcome to PROSPERO: International prospective register of systematic reviews. Available at: http://www.crd.york.ac.uk/NIHR_PROSPERO/. Accessed September 4, 2013.
56. van de Sande MA, Dijkstra PD, Taminiau AH. Proximal humerus reconstruction after tumour resection: biological versus endoprosthetic reconstruction. *Int Orthop.* 2011;35:1375–1380.
57. Voggenreiter G, Assenmacher S, Schmit-Neuerburg KP. Tikhoff-Linberg procedure for bone and soft tissue tumors of the shoulder girdle. *Arch Surg.* 1999;134:252–257.
58. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol.* 2008;61:344–349.
59. Wada T, Usui M, Isu K, Yamawakii S, Ishii S. Reconstruction and limb salvage after resection for malignant bone tumour of the proximal humerus: a sling procedure using a free vascularised fibular graft. *J Bone Joint Surg Br.* 1999;81:808–813.
60. Wang J, Shen J, Dickinson IC. Functional outcome of arthrodesis with a vascularized fibular graft and a rotational latissimus dorsi flap after proximal humerus sarcoma resection. *Ann Surg Oncol.* 2011;18:1852–1859.
61. Wittig JC, Bickels J, Kellar-Graney KL, Kim FH, Malawer MM. Osteosarcoma of the proximal humerus: long-term results with limb-sparing surgery. *Clin Orthop Relat Res.* 2002;397:156–176.
62. Yang Q, Li J, Yang Z, Li X, Li Z. Limb sparing surgery for bone tumours of the shoulder girdle: the oncological and functional results. *Int Orthop.* 2010;34:869–875.