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RESEARCH ARTICLE

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Long term outcomes of total humeral replacement for oncological reconstructions: A single institution experience

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Abstract

Background: There is a paucity of data on long-term survivorship and outcomes for total humerus replacements (THR) with only two series reporting 10-year survival.

Patients and Methods: A review of 769 consecutive, prospectively collected endoprosthetic reconstructions for oncological diagnoses at a single-center between 1980 and 2019 was performed. Patients with THRs were isolated and analyzed for outcomes, complications, and modes of failure.

Results: Eighteen patients with 20 THR implants were identified. The median follow-up for surviving patients was 148 months (interquartile range [IQR] = 74-194) and 60 months (IQR = 17-155 months) for all patients. Two prostheses required revision for failure, both for symptomatic shoulder dislocation. There were three local recurrences. Revision-free survival at 5, 10, and 15 years was 100%, 86% and 86%, respectively. There were no cases of ulnar component failure, radial nerve palsy, or periprosthetic infection.

Conclusions: THR prosthesis survivorship is comparable to the previous series, with a longer follow-up than has previously been reported. Symptomatic shoulder instability was common (25%), and was the only cause of revision. Reverse total shoulder could be an important way to address this in the future. Local recurrence rates were high, as has been reported elsewhere for THR.

KEYWORDS
case series, endoprosthesis, total humerus replacement

1 | INTRODUCTION

While the humerus is among the most common locations of primary bone sarcoma, tumors requiring treatment with total humeral replacement (THR) are rare. In the oncological setting, THR is most often used when there is an extensive tumor of the humerus with insufficient proximal and distal bone stock, or for the failure of prior segmental reconstructions.[1,2] In these cases, techniques for sub-total humeral reconstruction including proximal or distal humerus endoprostheses, intercalary constructs, allograft prosthetic composites (APC) and claviculi-pro-humerus are not possible.[1-6] In most cases, THR is used with the intent to preserve a functional hand and elbow, preserving the limb as opposed to a shoulder disarticulation or forequarter amputation. Data describing the long-term survival and function of THR prostheses is sparse, however, making the decision to proceed with amputation vs salvage difficult.

We identified six studies reporting prosthesis survival and complications, including a total of 98 patients, with limited medium and long term follow-up information available.[7-12] In general, outcomes in these series showed dramatically reduced shoulder function with good function of the elbow and hand. The most commonly reported complications were shoulder instability and dislocation, radial nerve palsy, ulnar component loosening, and periprosthetic infection.

Here we report our institutional experience with a total humeral replacement for oncological diagnoses with the aim to address the paucity of long-term follow-up information for THR prostheses. We performed a retrospective review of THR prostheses implanted at our institution. A prior report on all upper extremity endoprosthetic reconstruction included a subset of these patients at shorter follow up.[13] Here, we have analyzed the survivorship of THR prostheses, Musculoskeletal Tumor Society (MSTS) scores for functional outcomes, and complications.

2 | PATIENTS AND METHODS

2.1 | Patients

The Univeristy of California, Los Angeles (UCLA) endoprosthesis database consisting of 769 consecutive endoprosthetic reconstructions performed for oncologic diagnoses between 1980 and 2019 at UCLA.[14,15] Research approval was granted by the Institutional Review Board. All endoprostheses were implanted by the senior or lead authors (JJE and NMB) at a single institution. Follow-up was performed at a single institution and data were prospectively entered into a single database. Demographic, oncological, procedural, and outcome information is collected and updated for each patient in the database. Primary tumors were staged according to the Enneking/MSTS staging system.[16] Functional outcomes are scored using the MSTS upper extremity scoring system.

Included in this study were patients who underwent THR for an original oncological diagnosis. Both primary and revision endoprostheses were included, and analysis was repeated for revisions in the same patient. Bushing changes and planned expansions of growing constructs were not considered failures. The primary outcome analyzed is THR failure requiring revision or amputation. Secondary outcomes analyzed are the presence of shoulder instability, radial nerve palsy, ulnar component loosening, and functional scores. MSTS scores available at most recent follow-up were included in analysis.[17] For revision operations, the reason for the failure of the primary prosthesis is coded according to the Henderson failure mode classification.[18] Duplicate coding was performed by three orthopedic surgeons for reliability.

2.2 | Surgical approach

An extended deltopectoral approach was utilized in all cases, with resection of tumor following standard orthopedic oncological principles with the intent for complete local control. The shoulder was subsequently dislocated, with the goal of maximizing the length of retained rotator cuff while obtaining adequate margins. Subsequently, the elbow was dislocated. The preservation of all nerves and vessels not involved in the tumor was attempted. Involvement of the brachial artery or the median, ulnar, and radial nerves was considered a relative contraindication to THR.

In skeletally mature patients a stemmed ulnar component was utilized. Access to the ulnar canal was achieved by burring a trough for insertion of the component through the trochlear notch. The ulna was subsequently reamed and broached, and the ulnar component was cemented in the canal (Figures 1 and 2). In smaller, skeletally immature patients, a humeral implant was used with a condyle fitted to the patient's native olecranon as the ulnar canal was too narrow to accept a stem (Figure 3). Careful purse-string closure of the soft tissue around the condyles was used to increase subsequent stability.

All shoulders were nonconstrained. Shoulder reconstruction was achieved with native tissue of the preserved rotator cuff length if it allowed for complete coverage of the head of the prosthesis. If there was inadequate soft tissue coverage, a Gore-Tex (W. L. Gore & Associates, Inc, Newark, DE) mesh was sown to the base of the glenoid, wrapped and secured around the implant to achieve shoulder stability. Earlier in this series, dacron aorta graft was used in a similar fashion (Figure 4).

2.3 | Statistical analysis

The primary outcomes are prosthesis survival and mechanism of prosthetic failure according to the Henderson Failure Mode Classification. Prosthesis survival is analyzed at 5-year, 10-year, and 15-years using Kaplan-Meier analysis.[19] Analyses were repeated for THR revisions. Two-tailed Student *t*-tests and Mann-Whitney rank-sum tests were used to analyze differences within normally and non-normally distributed variables, respectively. A *P*-value of <.05 was considered to be significant. Analysis was carried out in R version 3.3.1.[20]

3 | RESULTS

3.1 | Patient characteristics

We identified 18 patients with 20 THR implants placed between December 1984 to September 2017 (Table 1). Eight patients were female, 10 patients were male. The mean age at the time of operation was 31 years-old. Thirteen endoprosthesis were implanted following primary resection of tumor (eight osteosarcoma (OS), three Ewing's sarcoma, one chondrosarcoma (CS), one malignant fibrous histiocytoma of bone). Ten were stage IIB and four were stage III at the time of operation. Representative pre- and post-operative radiographs for a patient who underwent THR following primary resection of OS can be found in Figures 1 and 2. Seven implants were used to revise a prior construct: one was the implantation of a larger expandable prosthesis, one for a failed distal humeral replacement (DHR), one for a failed intercalary prosthesis, one for a failed proximal humeral replacement (PHR) due to aseptic loosening, one for a failed PHR due to local recurrence, one for a failed open reduction and internal fixation (ORIF) of multiple myeloma (MM) pathological fracture, and one for a failed THR due to shoulder dislocation. In this latter patient (patient 18, Table 1), the expandable THR was shortened, the coracoid was removed and the surrounding soft tissues were revised to improve stability; however, the prosthesis was not

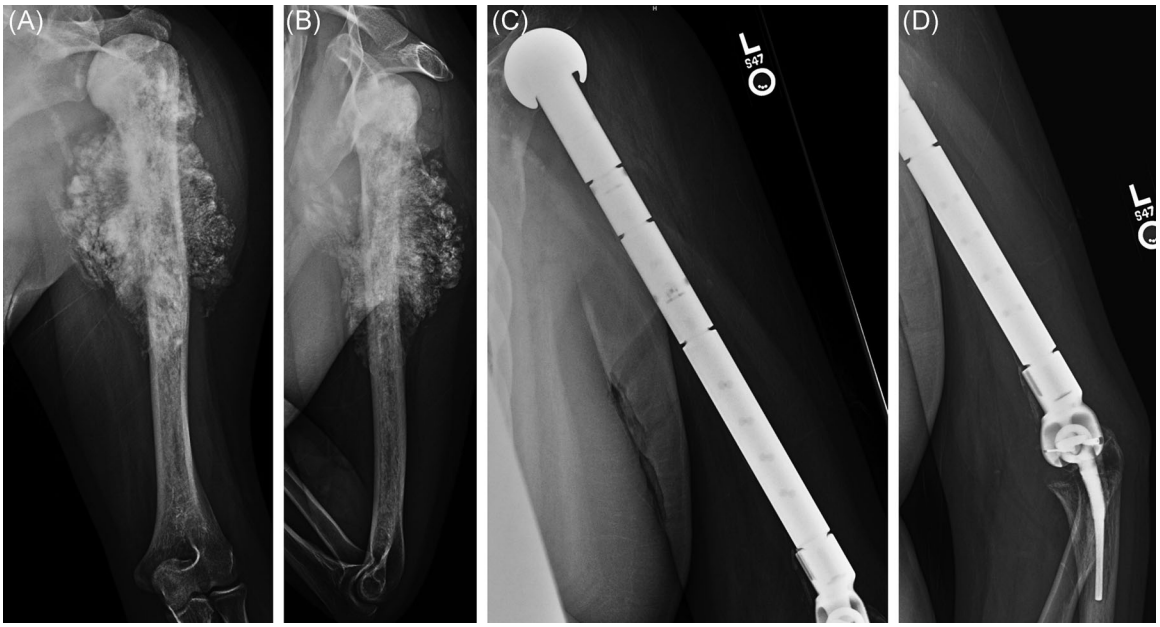

FIGURE 1 Pre- and post-operative plain films of 18-year-old male who underwent THR following primary resection of osteosarcoma. A-B, AP and lateral plain film of left humerus demonstrating large primary osteosarcoma. C-D, Lateral of left humerus 3 months after resection and reconstruction. AP, anterior-posterior; THR, total humerus replacement

removed (initial THR represented by patient 3, Table 1). Eight prostheses were expandable.

Ten patients were alive at the most recent follow-up. Seventeen patients had a minimum of 1-year follow-up. The median prothesis follow-up for surviving patients was 148 months (interquartile range [IQR] = 74-194), while the median prosthesis follow-up for all patients was 61 months (IQR = 17-155).

3.2 | Patient survival

A total of seven patients in our series died of their disease: five patients with osteosarcoma, one with Ewing's sarcoma, and one with multiple myeloma. Of patients with osteosarcoma, two were stage IIB and three were stage III at the time of surgery. Median survival was 15 months, and all patients died within 30 months of

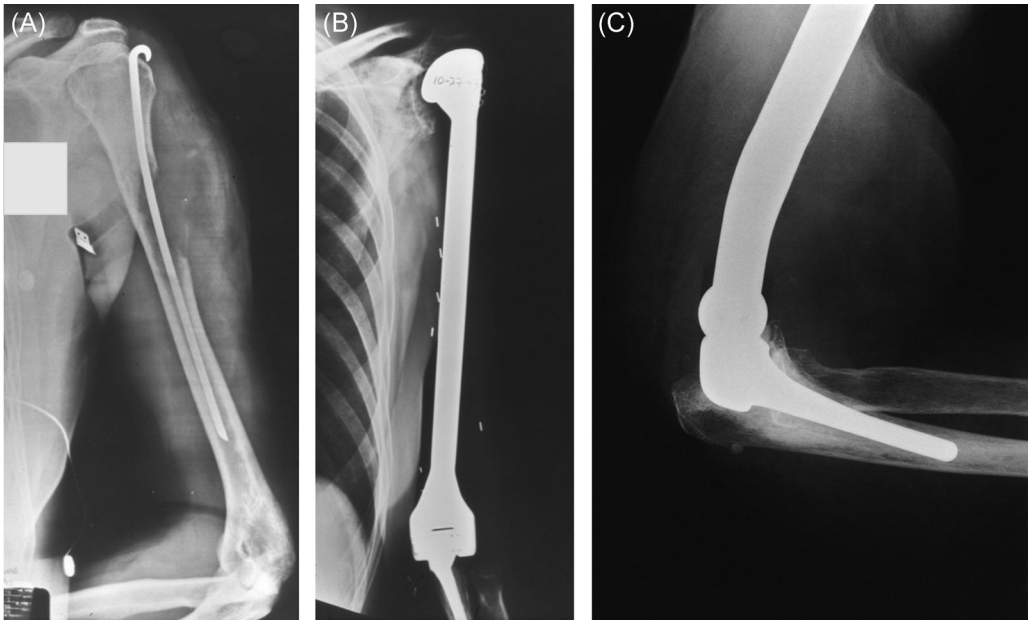

FIGURE 2 Pre- and post-operative plain films of 75-year-old male who underwent THR following primary resection of osteosarcoma which had previously received intermeduallary nail for assumed pathologic fracture. A, Lateral plain film of left humerus demonstrating large lytic lesion. B, AP plain fulm of humerus after reconstruction. C, Lateral of the elbow after reconstruction. AP, anterior-posterior; THR, total humerus replacement

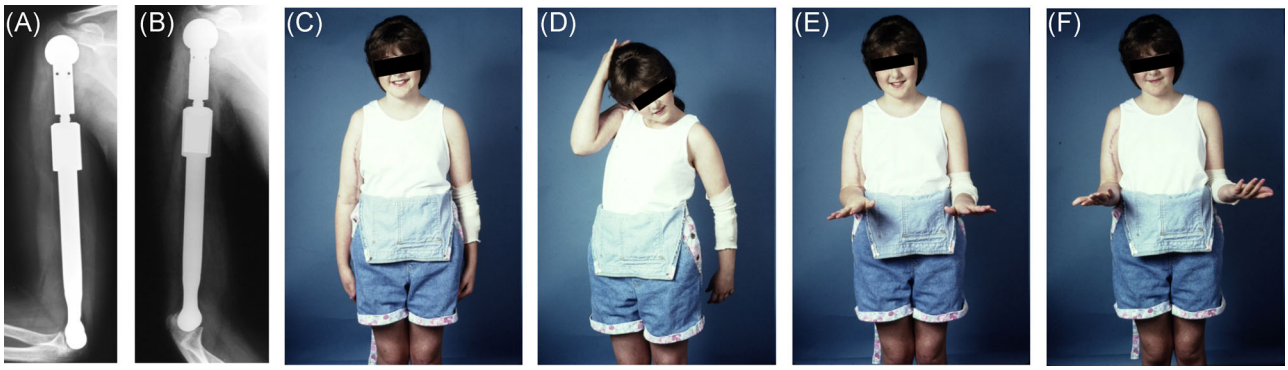

FIGURE 3 Demonstration of functional ability in 10-year-old female 12 months after THR. A-B, Lateral and AP plain film of left humerus demonstrating expandable THR component without the ulnar stem. C-F, Picture of the patient demonstrating a range of motion at elbow and shoulder. THR, total humerus replacement [Color figure can be viewed at wileyonlinelibrary.com]

their operation. Overall survival at 5, 10, and 15 years was therefore 60% (Figure 5).

3.3 | Analysis of implant survivorship

Analysis of the primary outcome showed an overall prosthesis survival at 5, 10, and 15 years of 100%, 86%, and 86% (Figure 6). Two (2/20, 10%) failures requiring implant revision of THR prostheses were documented at the final follow-up. Both failures were soft-tissue failures leading to symptomatic shoulder dislocation (Henderson type 1). Survival for these implants was 112 and 259 months (patients 6 and 3 respectively, Table 1). There were no cases of infection, local recurrence, structural failure, or aseptic loosening of the ulnar component requiring revision. Notably, three of the 13 patients (23%) receiving THR for resection of primary sarcoma had local recurrence. These were treated with wide local excision of the recurrent lesion and post-operative radiation. Patient 6 was disease-free at most recent follow-up; patient 5 at initial resection had positive margins with vascular invasion and was found to be metastatic shortly after resection, for this reason, amputation was not pursued and the patient died of disease 15 months after surgery; patient 12 presented with lung metastasis and died of disease 12 months after surgery.

3.4 | Functional outcomes and complications

Thirteen patients had MSTS scores recorded at the final follow up. The average MSTS score in these patients was 77% (range 34%-100%). The majority of points lost were due to a poor range of

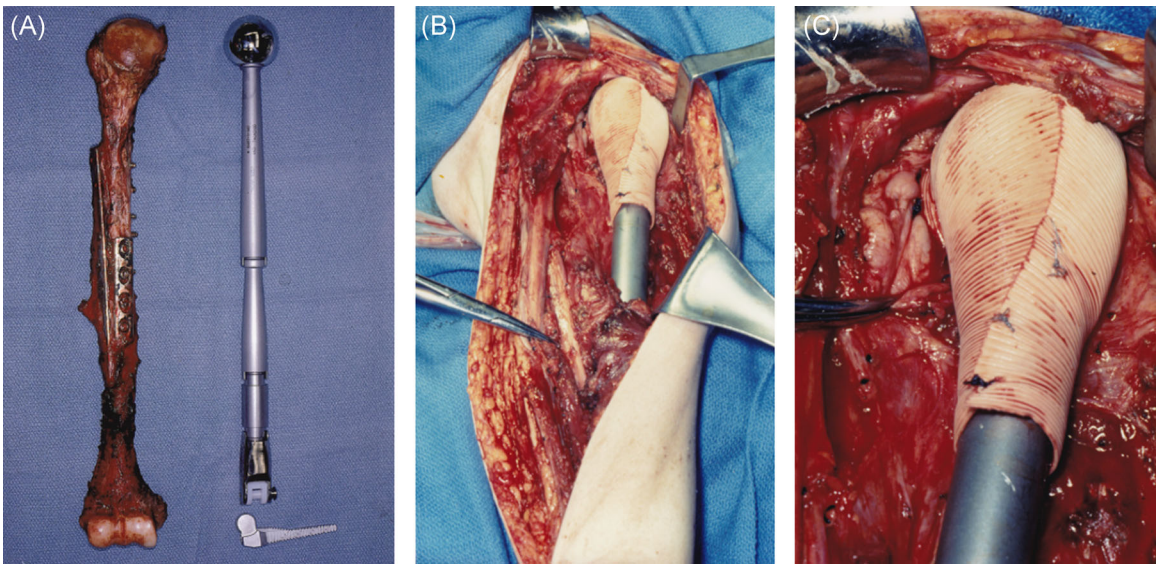

FIGURE 4 Intra-operative photos from 67-year-old female with MM who underwent THR following the failure of previous ORIF. A, Photo of specimen and implant used. B-C, Photos demonstrating dacron aortic graft sown to inferior glenoid originally used to improve shoulder stability. MM, multiple myeloma; ORIF, open reduction and internal fixation. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Patient demographics and surgical details

Case	Sex	Age (y)	Diagnosis	Stage	Previous Tx	Manufacturer	Expandable	Failure	LR	Complications	Follow-up (mo)	Status
Primary												
1	M	17	OS	IIB	Cx	TM					7	DOD
2	M	76	OS	IIB	Cx, Xrt, IMN	INT-M					88	Died
3	F	6	Ewing's	IIB	Cx, Xrt	TM	Yes	Yes		Shoulder instability, radial head overgrowth	382	CDF
4	F	84	CS	IIB	Cx	TM					79	Died
5	M	8	OS	IIB	Cx	DCW	Yes		Yes		15	DOD
6	F	57	Fibrous histiocytoma of bone	IIB	Cx	TM		Yes	Yes	Shoulder instability	148	Died
7	M	3	Ewing's	IIB	Cx	DCW	Yes				184	CDF
8	F	10	OS	III	Cx	DCW	Yes				17	DOD
9	M	13	OS	IIB	Cx, Xrt	HM					204	CDF
10	M	10	Ewing's	IIB	Cx	DCW	Yes				29	DOD
11	F	8	OS	III	Cx	DCW	Yes				236	CDF
12	M	13	OS	III	Cx	HM			Yes	Shoulder instability	12	DOD
13	M	18	OS	III	Cx	ZB					16	DOD
Revision				*Reason*								
14	F	29	Ewing's	Soft tissue failure THR		TM	Yes			Shoulder instability	106	CDF
15	F	74	MM	Failed intercalary		TM					12	DOD
16	F	41	OS	Aseptic loosening DHR		HM/TM					134	CDF
17	F	13	OS	Larger expandable prosthesis		DCW	Yes				174	CDF
18	M	69	CS, recurrent	Local recurrence PHR allograft		HM				Shoulder instability	43	AWD
19	F	67	MM	Failed ORIF, pathological fx		ZB					25	AWD
20	M	11	Ewing's	Aseptic loosening PHR		ZB					22	CDF

Abbreviations: AWD, alive with disease; CDF, continue disease free; DCW, Dow Corning Wright (now Wright Medical, Memphis, TN); DOD, died of disease; HM, Howmedica (now Stryker, Kalamazoo, MI); INT-M, Intermedics Orthopedics (Arlington, TN); LR, local recurrence; TM, Techmedica (now DePuy Synthes, Warsaw, IN); Zimmer Biomet (Warsaw, IN).

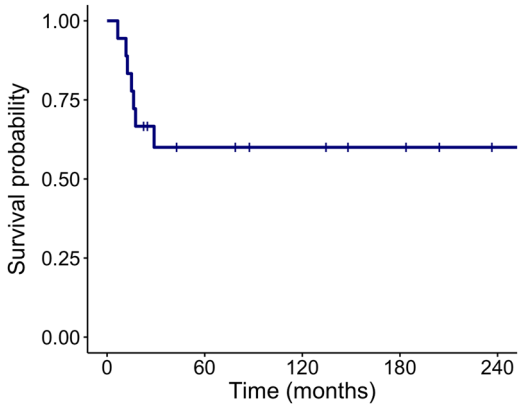

FIGURE 5 Patient oncological survival. Hash marks represent censoring [Color figure can be viewed at wileyonlinelibrary.com]

motion at the shoulder. An example of one patient's postoperative function is summarized in Figure 4. One patient with an expandable prosthesis developed radial head overgrowth causing local pain and neuralgia, requiring a radial head excision, as well as an elbow contracture after multiple operations to the arm. A total of three patients (3/20, 15%) experienced chronic shoulder instability that did not require a revision operation. There were no cases of permanent radial, ulnar or median nerve palsies or intra-operative ulnar fracture in our cohort.

4 | DISCUSSION

Total humeral replacement is a rare procedure in the field of Orthopedic Oncology, with limited survival and outcomes data reported in the literature. Of the nearly 800 endoprosthetic reconstructions for oncological diagnoses in our database, only 20 THR prostheses have been implanted at our institution over the course of more than 30 years. This paucity of data makes the decision to proceed with THR vs amputation difficult. In this series, THR proved to be a durable construct with good functional outcomes. Function at the hand was reliably preserved, while shoulder function was limited and was the only cause of revision. Prosthesis survival was 86% at 15 years, with all revisions occurring because of recurrent shoulder dislocation. There were an additional three patients with chronic shoulder instability that did not require revision. There were three cases of local recurrence, although none of these were treated with implant revision or amputation. There were no cases of ulnar component loosening or clinically significant radial nerve palsy. As expected, functional outcomes were best at the elbow and hand, with an average overall MSTS score of 77%. To our knowledge, this series represents the longest follow-up reported in the literature. Given these results, we believe that THR represents a viable option for upper extremity limb salvage for oncological diagnoses, particularly in cases when the only alternative option is amputation.

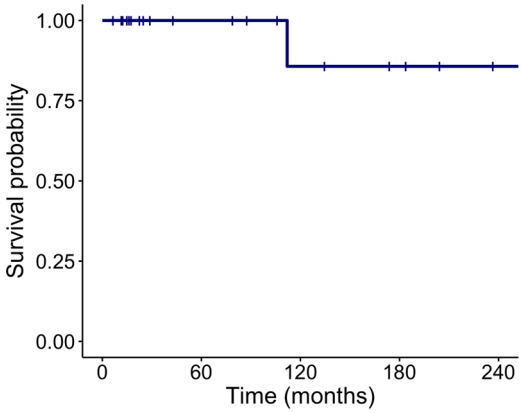

FIGURE 6 Survival of THR prostheses. Hash marks represent censoring. THR, total humerus replacement [Color figure can be viewed at wileyonlinelibrary.com]

The prosthesis survival described here is comparable to what has been described previously, though survival at 15 years has not been reported to our knowledge (Table 2). Prosthesis survival at 5 years has previously been reported at 78% to 95%, compared to 100% reported here. Ten-year survival rates reported in the literature range from 65% to 90%, compared to 86% reported here. As all existing case series are relatively small - the largest of which contains 34 prostheses[8] - a certain amount of variability is expected. The only mode of failure in our series was shoulder instability, and this differs from other series where infection and ulnar stem loosening also lead to revision. Our functional outcomes for available patients were comparable to previously reported as well: the average MSTS score was 77%, which is comparable to other series (71%-83%) (Table 2). In our series, elbow and hand function were universally normal, while shoulder function was routinely fair and occasionally good as is often the case in nonconstrained shoulder reconstuctions.

Significant shoulder instability was the most common complication in this series with five patients (5/20, 25%) experiencing instability, two of which required revision surgery. Shoulder instability is a well-known complication of THR, as well as proximal humerus replacement particularly when resection of the rotator cuff is necessary, or in older patients with incompetent stabilizing structures. Notably, reverse shoulder arthroplasty was not utilized at our institutions during the period that this cohort underwent THR. Surgeons have incorporated reverse total shoulder designs into PHR prostheses and achieved encouraging functional outcomes.[21-24] Small series have achieved outcomes scores comparable to reverse total shoulder replacements performed for non-oncological purposes, supplemented by latissimus dorsi and teres major muscle transfer. No studies were identified regarding reverse shoulder reconstruction with THR. THR functional scores and survivorship may improve with the utilization of reverse total shoulder replacement, however, the function of a reverse THR given the complete resection of the deltoid insertion as well possible deltoid muscle resection is unknown. Further study in this area is required.

High rates of local recurrence in patients undergoing THR - ranging from 15%-26%[10-12] - have been reported in the literature. Local recurrence in this series was similar, occurring in 23% (3/13) of patients

TABLE 2 Review of the literature of THR endoprostheses

Citation	Prostheses	Follow-up	Survival	Outcomes	Complications
Kotwal et al[7]	20 Unknown expandable 11 primary sarc	43 mo	87% 5 y, 65% 10 y mechanical survival	MSTS 72%	1 infection 1 loosening ulnar component 7 subluxation 2 shoulder dislocation 2 radial n palsy
Wafa et al[8]	34 10 expandable 29 primary sarc	98 mo	90% cumulative 10 y survival	MSTS 83% (min 1 y)	1 radial n palsy 4 infection 3 subluxation
Natarajan et al[9]	11 2 expandable 10 primary sarc	66 mo	91% 1 y, 78% 5 y survival	MSTS 80%	1 ulnar stem loosening (10 y) 1 subluxation All with some instability
Puri and Gluia[10]	20 2 expandable All primary sarc	41 mo	95% 5 y survival	MSTS 73%	2 intra-op ulna fx
Weber et al[11]	7 Unknown expandable Unknown primary	43 mo	Unknown	MSTS 71%	1 ulnar peri-prosthetic lysis Possible n palsy (4 of 23) Possible infection (2 of 23)
Ayoub et al[12]	6 All expandable All primary sarc	80 mo	83% cumulative 5 y survival	MSTS 80% (2 pts)	1 radial n palsy
This study	20 8 expandable 14 primary	148 mo	100% 5 y, 86% 10 and 15 y survival	MSTS 77%	5 shoulder instability 1 radial head overgrowth

Abbreviations: MSTS, Musculoskeletal Tumour Society; THR, total humeral replacement.

who underwent primary THR after resection of sarcoma. These occurred in two patients with osteosarcoma and one with malignant fibrous histiocytoma of bone. Each of these patients was treated with re-excision, implant retention, and postoperative radiation. One of the osteosarcoma patients was metastatic at presentation, and the other had positive margins with vascular invasion and was found to be metastatic shortly after resection. Because patients were metastatic, amputation was not purused; these two patients died of disease at 12 and 15 months. This high rate of local recurrence may reflect the high tumor burden inherent in patients requiring THR. However, this contrasts with lower rates of local recurrence reported in the lower extremity. In total femur replacements for primary bone sarcoma where tumor burden is also high, rates of local recurrence have been reported as 0% to 2%, indicating that there may be another factor contributing to high rates of LR in THR[25,26] Local recurrence has been associated with poor survival,[27,28] however it is not clear that amputation increases survival.[29] A larger sample is required to determine if high rates of local recurrence in total humerus replacement impact survival and if amputation may yield improved results.

As osteosarcoma and other primary bone tumors often occur in skeletally immature patients, epiphyseal resection in these patients can lead to limb length discrepancies. While the upper extremity is less sensitive to these alterations than the lower extremity, expandable prostheses may be considered in very young patients with significant expected discrepancies. Indeed, all series on THR we have identified include patients with expandable prostheses (Table 2). We encountered one unique complication in such a patient-radial overgrowth requiring radial head excision. This patient was 8-years old at the time of surgery, and early age likely contributed to this complication. Functional ability was not significantly affected by the radial head excision.

Of note, no cases of ulnar component loosening were identified in this series, and few such cases are reported in the THR literature (Table 2). In contrast, loosening and instability of the ulnar component occur frequently in total elbow replacement for nononcological diagnoses and are amongst the most common complications.[29,30] This discrepancy may be due to the inherent functional limitations of patients undergoing THR for oncological reconstructions, resulting in reduced stress at the ulnar component when compared to total elbow replacements.

The use of THR may decrease as new technologies allow for better fixation into short residual bone segments following tumor resection. One such method, compressive oseointegration, has been successfully applied to the upper extremity in a small number of cases allowing for preservation of the patient's native elbow or shoulder.[31,32] In general, reconstruction of the upper extremity is

more forgiving than the lower extremity as length matching is less essential, rotational forces on the bone-stem interface are decreased, and a limited range of motion is more accepted.

There are several limitations to this study. First, it is a single institution experience with the operations carried out by two surgeons. Also, it is a retrospective case review with no control or comparison group. Institutional and patient factors have not been controlled and these could contribute to differences in outcomes between studies. Second, as is the case with many studies involving mega prosthetic reconstruction - and certainly THR - the number of patients included in this study is small. Larger multi-institution prospective endoprosthetic databases would help resolve this limitation common to many studies in our field. Third, while patients obtained good functional outcomes at the hand and wrist, an average MSTS score of 77% given very little shoulder function demonstrates the opportunity for a more discerning physical function outcome score. The development of a different system to assess extremity function following oncologic reconstructions is an area of needed ongoing research. Finally, this series does not reflect the use of newer implant designs. Specifically, reverse total shoulder arthroplasty may be expected to improve outcomes in this cohort of patients, while compressive osseointegration may reduce the indication for THR.

5 | CONCLUSIONS

Total humerus endoprosthetic replacement is a durable reconstruction option for preserving a functional upper extremity in patients who require complete excision of the humerus for malignant bone tumors. THR offers acceptable functional outcomes with highest scores at the hand and elbow, and lowest scores at the shoulder. In our study, survivorship is comparable to the previous series. Soft tissue failure at the shoulder necessitating revision was the only mode of failure (Henderson type I) in this series. The previous series have cited periprosthetic infection as the most common cause of failure, but there were no infections requiring revision in this series. The local recurrence rate was relatively high in our series, as has been reported elsewhere. This may reflect the significant tumor burden inherent in any patient requiring a THR. More study is required to determine how local recurrence in the humerus impacts survival as the current study is not sufficiently powered to address this question. There were no nerve palsies or failures of the ulnar component as have been documented previously. Despite the expected range of motion and strength limitations, total humeral reconstruction offers preservation of upper extremity function with a low rate of complications and failure and can be considered as a viable alternative to amputation. Newer implant designs, such as reverse total shoulder arthroplasty may further improve the outcomes in this patient cohort.

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AUTHOR CONTRIBUTIONS

Study design: NMB, AUB, ZDCB, and JJE. Study conduct and data collection: NMB and JJE. Data summarization: AUB, ZDCB, DG, and RH. Data interpretation: NMB, AUB, ZDCB, BC, and JJE. Drafting manuscript: NMB, AUB, and ZDCB. Approving final version of manuscript: NMB, AUB, ZDCB, DG, RH, BC, and JJE.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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