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Failure Mode Classification for Tumor Endoprostheses: Retrospective Review of Five Institutions and a Literature Review

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Background: Massive endoprostheses provide orthopaedic oncologists with many reconstructive options after tumor resection, although failure rates are high. Because the number of these procedures is limited, failure of these devices has not been studied or classified adequately. This investigation is a multicenter review of the use of segmental endoprostheses with a focus on the modes, frequency, and timing of failure.

Methods: Retrospective reviews of the operative databases of five institutions identified 2174 skeletally mature patients who received a large endoprosthesis for tumor resection. Patients who had failure of the endoprosthesis were identified, and the etiology and timing of failure were noted. Similar failures were tabulated and classified on the basis of the risk of amputation and urgency of treatment. Statistical analysis was performed to identify dependent relationships among mode of failure, anatomic location, and failure timing. A literature review was performed, and similar analyses were done for these data.

Results: Five hundred and thirty-four failures were identified. Five modes of failure were identified and classified: soft-tissue failures (Type 1), aseptic loosening (Type 2), structural failures (Type 3), infection (Type 4), and tumor progression (Type 5). The most common mode of failure in this series was infection; in the literature, it was aseptic loosening. Statistical dependence was found between anatomic location and mode of failure and between mode of failure and time to failure. Significant differences were found in the incidence of failure mode Types 1, 2, 3, and 4 when polyaxial and uniaxial joints were compared. Significant dependence was also found between failure mode and anatomic location in the literature data.

Conclusions: There are five primary modes of endoprosthetic failure, and their relative incidences are significantly different and dependent on anatomic location. Mode of failure and time to failure also show a significant dependence. Because of these relationships, cumulative reporting of segmental failures should be avoided because anatomy-specific trends will be missed. Endoprosthetic design improvements should address failure modes specific to the anatomic location.

Level of Evidence: Therapeutic Level IV. See Instructions to Authors for a complete description of levels of evidence.

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A commentary by Dempsey Springfield, MD, is available at www.jbjs.org/commentary and is linked to the online version of this article.

Advances in nonsurgical treatments of malignant bone and soft-tissue tumors in the extremities have allowed successful reconstruction of upper and lower-extremity long bones after tumor resection[1,2]. Metallic endoprostheses for complex reconstructions involving joints have replaced allografts at many centers; component modularity, improved design and fixation, and quicker return to function favor endoprostheses as a reconstructive option[3-6].

Despite innovations in materials and component design, implant failure remains higher than that for primary joint arthroplasty in all anatomic sites and revision surgery is common[4,7-25]. While many investigators have reported the outcomes of patients receiving primary metallic endoprostheses for oncologic indications, few authors have specifically addressed the modes by which they fail[4,26]. Because of the limited patient numbers, these series lack meaningful analysis of site-specific modes of failure for endoprosthetic reconstruction. No large multicenter report or literature meta-analyses have been published on this subject.

This investigation is a retrospective review of the collective experience of five dedicated cancer centers with the use of large segmental endoprostheses following tumor resection over a period of thirty-four years as well as a review of the literature related to endoprosthetic failure. Data were analyzed to assess the incidence, mode, and temporal sequence of endoprosthetic component failure. We hypothesized that aseptic loosening would account for most failures when fixed hinged joints were used and that instability would be the primary mode of failure around polyaxial joints.

Materials and Methods

Patient Data

After institutional review board approval was obtained at the respective institutions of the authors, database searches were conducted for patients who underwent limb reconstruction with a metallic endoprosthesis. Between 1974 and 2008, 2367 patients underwent primary limb preservation with use of a metallic endoprosthesis at one of five institutions for the treatment of a benign or malignant tumor of an extremity. Patients receiving a segmental metallic endoprosthesis for diagnoses not related to a tumor were excluded. Skeletally immature patients who underwent reconstruction with an expandable endoprosthesis were also excluded. All patients were able to walk prior to surgery.

A total of 2174 patients were available for review. There were 1245 men and 929 women. The mean age was forty-one years (range, fourteen to ninety years). The diagnoses were osteosarcoma (956 patients), metastatic disease (367), chondrosarcoma (274), giant-cell tumor (136), Ewing sarcoma (104), malignant fibrous histiocytoma (eighty-four), leiomyosarcoma (thirty-one), multiple myeloma (twenty-four), and other (198) (Fig. 1). Of the endoprostheses, 348 (16%) were proximal humeral replacements; sixteen (0.7%), total humeral replacements; thirty-six (1.7%), distal humeral replacements; 403 (19%), proximal femoral replacements; seventy-eight (3.6%), total femoral replacements; 951 (44%), distal femoral replacements; forty-four (2.0%), combined distal femoral-proximal tibial replacements; and 298 (14%), proximal tibial replacements. The segmental endoprostheses that were used included the Global Modular Replacement System in 365 patients (17%), the Howmedica Modular Resection System in 1165 patients (54%), the Kotz Modular Replacement System in 199 patients (9.2%), and the Modular Replacement System in 402 patients (19%) (all endoprostheses were from Stryker Orthopaedics, Mahwah, New Jersey). The remaining forty-three endoprostheses (2.0%) were custom made.

Literature Analysis

The literature review began with a search of MEDLINE for the terms "limb salvage," "endoprosthesis," "segmental endoprosthesis," "proximal humerus replacement," "total humerus replacement," "distal humerus replacement," "total elbow arthroplasty," "proximal femoral replacement," "total femoral replacement," "distal femoral replacement," and "proximal tibial replacement." Article inclusion required outcomes data for patients receiving segmental endoprostheses for preservation of any portion of the humerus, femur, or tibia including, but not limited to, number and anatomic location of procedures, complications, and number of failures. Intercalary resections were excluded from analysis. Further article partitioning was performed on the basis of the type of primary reconstruction, indication for primary reconstruction, and failure mode reporting. Data from manuscripts meeting the inclusion criteria were then tabulated with use of a spreadsheet (Microsoft Excel; Microsoft, Redmond, Washington). When manuscripts from the same institution with overlapping reporting dates of like procedures were noted, the most recent data were included and earlier reports were excluded. Our survey of

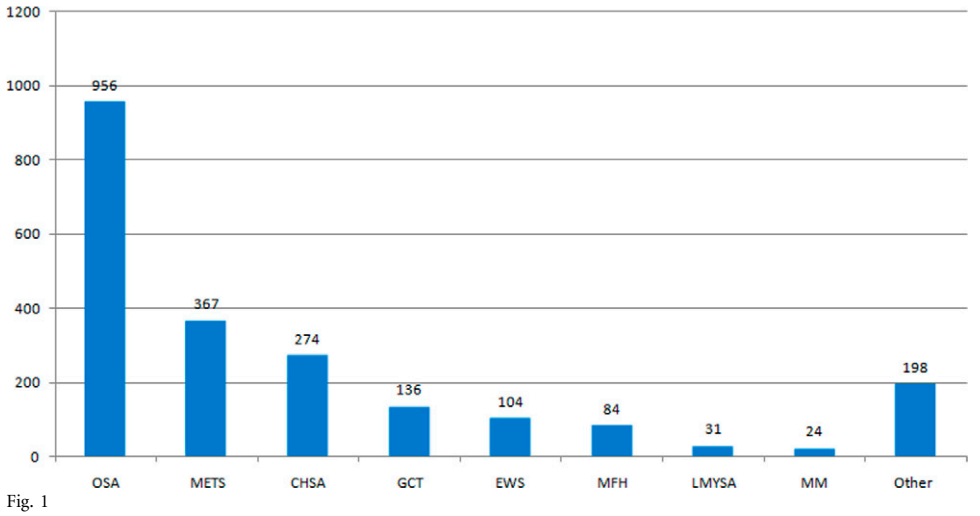

Fig. 1

Histologic diagnoses of the patients included in the current investigation. The bars indicate the number of patients. OSA = osteosarcoma, METS = metastatic disease, CHSA = chondrosarcoma, GCT = giant-cell tumor, EWS = Ewing sarcoma, MFH = malignant fibrous histiocytoma, LMYSA = leiomyosarcoma, and MM = multiple myeloma.

the orthopaedic literature yielded >200 manuscripts describing 8093 long-bone reconstructions with large endoprostheses. After exclusion of manuscripts that lacked appropriate follow-up information, described limb preservation for nononcologic conditions, involved expandable endoprostheses, and were redundant manuscripts from the same institution with overlapping time periods, data on 4359 patients were available for review[3,4,6-8,11-13,16,17,19,27-84].

Failure Classification

Patient records were reviewed for complications resulting in reconstruction failure. Failed reconstructions were defined as those requiring complete revision of the endoprosthesis, unplanned revision of a failed portion of the endoprosthesis, fixation of a periprosthetic fracture, soft-tissue reconstruction to restore joint stability, endoprosthetic removal without revision, and amputation.

Failures of segmental endoprosthetic reconstructions were categorized broadly as mechanical or nonmechanical[4]. Mechanical failures included those attributable to loss of normal function of the endoprosthesis and/or relationships between the endoprosthetic components and adjacent bone and soft-tissue attachments. Nonmechanical failures included conditions that necessitated endoprosthesis removal or revision that did not compromise the function of the endoprosthesis and its surrounding connective tissues. We divided failures in the current investigation and from the literature into these two general categories and further classified failures on the basis of the etiology of their mechanical or nonmechanical end points. When joint-type analysis was performed, total humeral replacements and total femoral replacements were excluded as these implants contain both uniaxial and polyaxial articulations.

Statistical Analysis

Endoprosthetic failures were compared by variables that included failure mode, joint type, and time to failure. Reported means are accompanied by standard deviations. The significance of the difference in means was calculated with the standard normal test, when appropriate. When adequate numbers were available, tests of independence were calculated with the chi-square test with use of a contingency table. Cross-tabulation significance testing was performed with the Fisher exact test, when appropriate. Statistical analysis was performed with Microsoft Excel software (Microsoft).

Source of Funding

No external funding was received for completion of any portion of this investigation.

Results

A total of 2174 skeletally mature patients received a segmental endoprosthesis for the treatment of an oncologic condition, with 534 primary procedures (24.5%) considered failures. The total number of failures by anatomic location included fifty-nine (17%) of the 348 proximal humeral replacements, three (19%) of the sixteen total humeral replacements, six (17%) of the thirty-six distal humeral replacements, sixty-four (16%) of the 403 proximal femoral replacements, twenty-one (27%) of the seventy-eight total femoral replacements, 261 (27%) of the 951 distal femoral replacements, nineteen (43%) of the forty-four combined distal femoral-proximal tibial replacements, and 101 (34%) of the 298 proximal tibial replacements. The relative occurrence of failure was lowest for proximal femoral replacement and highest for combined distal femoral-proximal tibial replacement (Fig. 2).

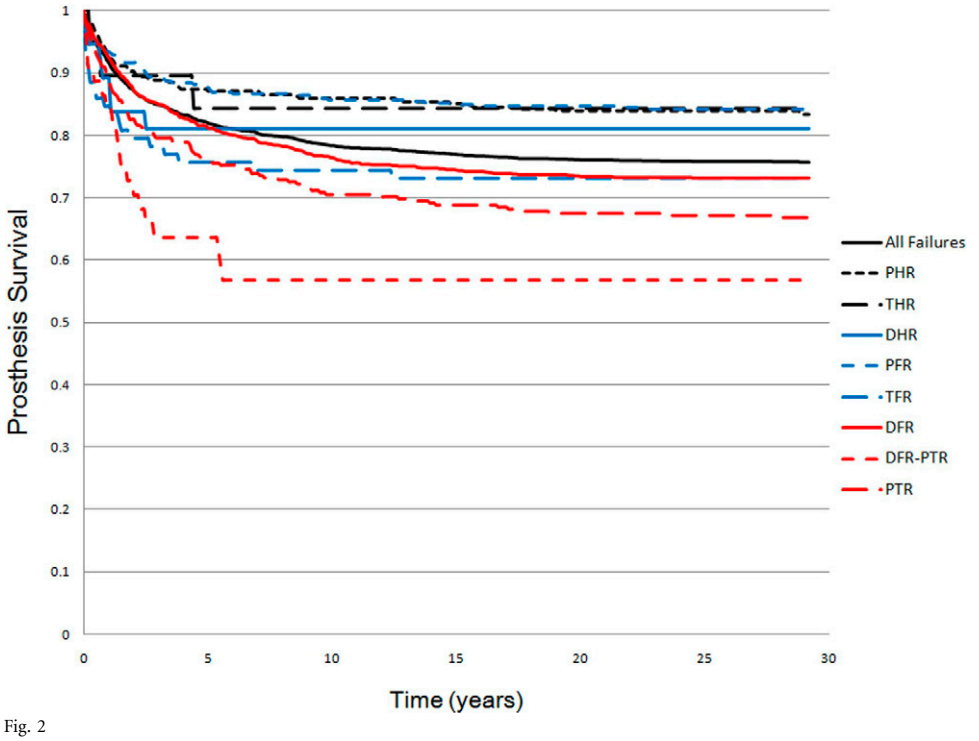

Fig. 2

Kaplan-Meier survival graph for survival of all endoprostheses, stratified by anatomic site. PHR = proximal humeral replacement, THR = total humeral replacement, DHR = distal humeral replacement, PFR = proximal femoral replacement, TFR = total femoral replacement, DFR = distal femoral replacement, and PTR = proximal tibial replacement.

TABLE I Classification of Segmental Endoprosthetic Failure

Type of Failure	Mode of Failure	Description
Mechanical		
1	Soft-tissue failure	Instability, tendon rupture, or aseptic wound dehiscence
2	Aseptic loosening	Clinical and radiographic evidence of loosening
3	Structural failure	Periprosthetic or prosthetic fracture or deficient osseous supporting structure
Nonmechanical		
4	Infection	Infection about endoprosthesis necessitating removal of device
5	Tumor progression	Recurrence or progression of tumor with contamination of endoprosthesis

Mode of Failure

Two hundred and fifty-nine (49%) of all 534 failures were mechanical. Sixty-four (12%) of all failures were due to problems related to the soft tissues about the implant. These failures included functional issues, such as chronic instability and dislocation, as well as implant coverage problems, such as aseptic wound dehiscence. One hundred and two failures (19%) were from aseptic loosening at the bone-implant interface, and ninety-three failures (17%) were due to periprosthetic or prosthetic fractures. These modes of failure were classified as Type 1 (soft-tissue failure), Type 2 (aseptic loosening), and Type 3 (structural failure), respectively (Table I).

Nonmechanical causes accounted for 275 (51%) of all failures (Fig. 3). These included ninety-three failures (17%) that were due to tumor progression and 182 failures (34%) that were from infection, the most common mode of failure for all anatomic sites. Nonmechanical failures were classified as Type 4 (infection) and Type 5 (tumor progression). The absolute risks of failure modes Type 1 through 5 for all anatomic locations were 2.9%, 4.7%, 4.2%, 8.4%, and 4.3%, respectively.

Soft-tissue (Type-1) failures accounted for 12% of all failures (Table II). The highest rates of Type-I failures were observed in reconstruction of the shoulder and hip, with most due to instability (Figs. 4 and 5). When combined, soft-tissue failures for endoprostheses with only polyaxial joints (proximal humeral and proximal femoral replacements) were 29% of all failures for these locations. The combined soft-tissue failures about uniaxial joints at the elbow and knee were 5.7% of all failures for these locations; the difference was significant ($p < 0.0001$, Table III). Soft-tissue failures were more likely to occur

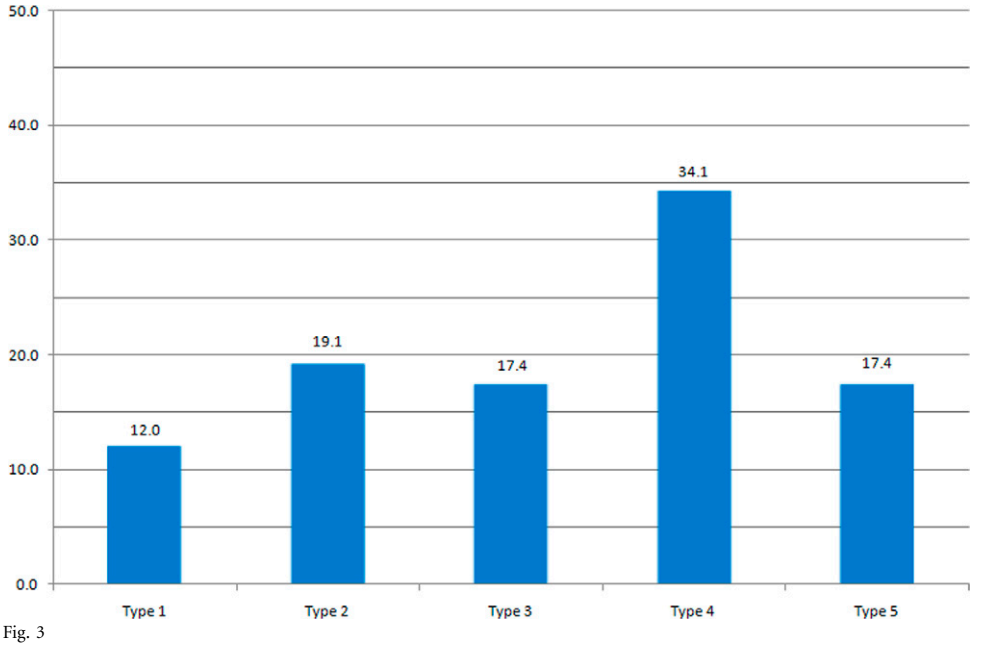

Fig. 3

Chart demonstrating the overall incidence (%) of endoprosthetic failure according to the five failure modes for all anatomic sites. Type I = soft-tissue failure, Type 2 = aseptic loosening, Type 3 = structural failure, Type 4 = infection, and Type 5 = tumor progression.

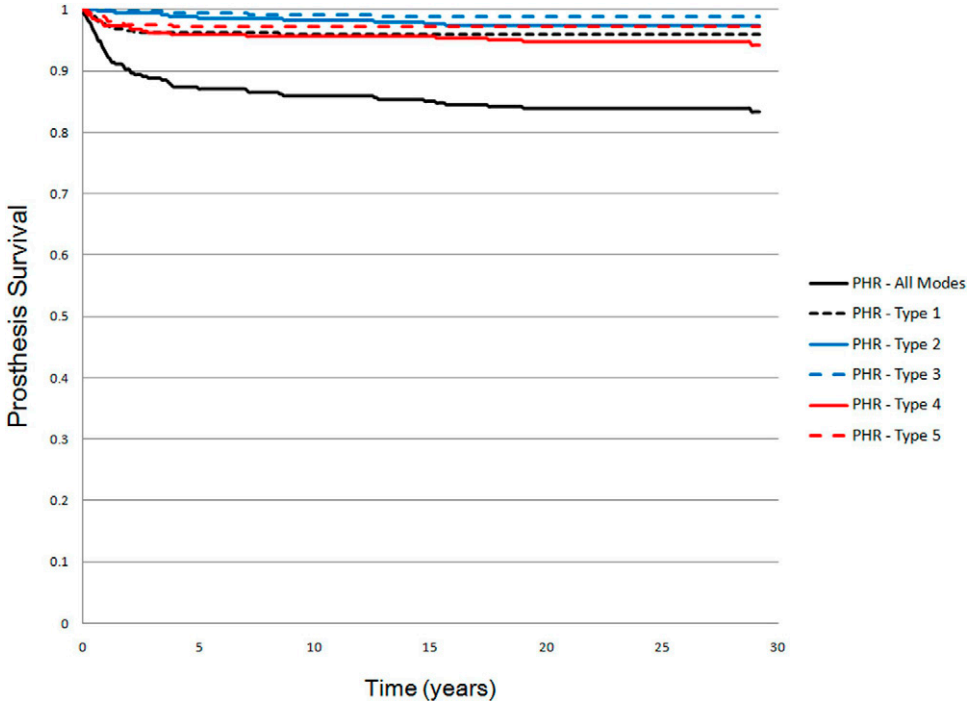

Fig. 4

Kaplan-Meier survival graph for proximal humeral replacements (PHR), stratified by mode of failure.

in the upper extremity than the lower extremity ($p = 0.03$), reflecting the preponderance of soft-tissue failures following proximal humeral replacement.

Aseptic loosening (Type 2) accounted for 19% of all failures. Aseptic loosening in the distal part of the femur accounted for 6.8% of the failures and was the highest of all locations

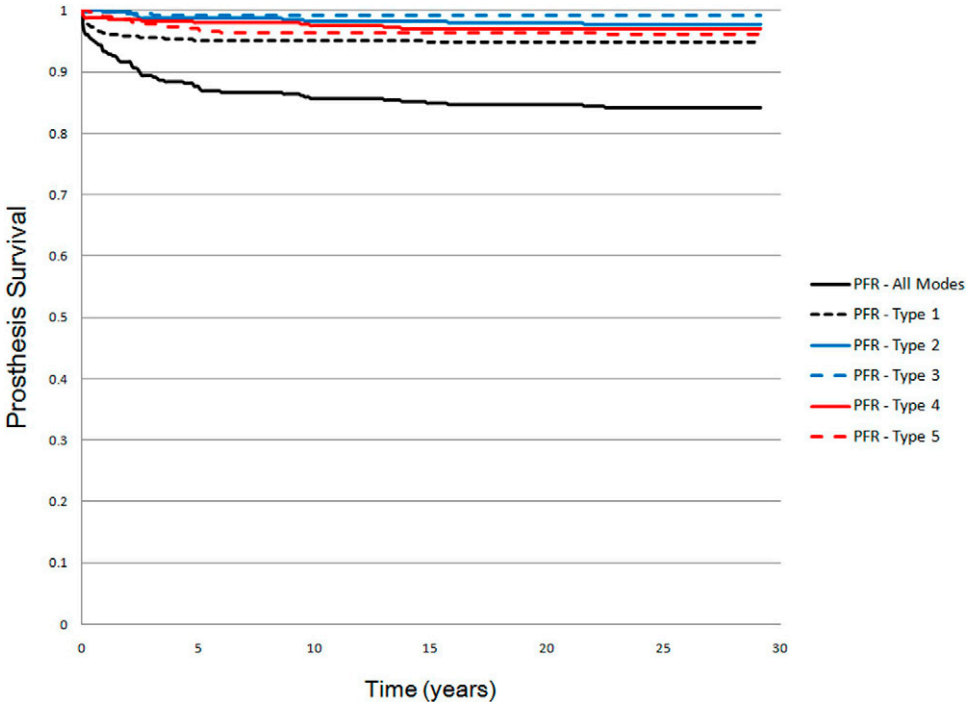

Fig. 5

Kaplan-Meier survival graph for proximal femoral replacements (PFR), stratified by mode of failure.

TABLE II Segmental Endoprosthetic Failures by Location in the Current Investigation

Location	Primary Procedures*	Soft-Tissue Failure†	Aseptic Loosening†	Structural Failure†	Infection†	Tumor Progression†	Total‡
Proximal end of humerus	348 (16.0)	14 (4.0, 23.7)	9 (2.6, 15.3)	4 (1.1, 6.8)	22 (6.3, 37.3)	10 (2.9, 16.9)	59 (17.0)
Total humerus	16 (0.7)	0 (0, 0)	0 (0, 0)	0 (0, 0)	3 (18.8, 100)	0 (0, 0)	3 (18.8)
Distal end of humerus	36 (1.7)	0 (0, 0)	0 (0, 0)	2 (5.6, 33.3)	2 (5.6, 33.3)	2 (5.6, 33.3)	6 (16.7)
Proximal end of femur	403 (18.5)	21 (5.2, 32.8)	11 (2.7, 17.2)	4 (1.0, 6.3)	12 (3.0, 18.8)	16 (4.0, 25.0)	64 (15.9)
Total femur	78 (3.6)	7 (9.0, 33.3)	2 (2.6, 9.5)	1 (1.3, 4.8)	9 (11.5, 42.9)	2 (2.6, 9.5)	21 (26.9)
Distal end of femur	951 (43.7)	12 (1.3, 4.6)	65 (6.8, 24.9)	60 (6.3, 23.0)	79 (8.3, 30.3)	45 (4.7, 17.2)	261 (27.4)
Distal end of femur and proximal end of tibia	44 (2.0)	3 (6.8, 15.8)	1 (2.3, 5.3)	3 (6.8, 15.8)	10 (22.7, 52.6)	2 (4.5, 10.5)	19 (43.2)
Proximal end of tibia	298 (13.7)	7 (2.3, 6.9)	14 (4.7, 13.9)	19 (6.4, 18.8)	45 (15.1, 44.6)	16 (5.4, 15.8)	101 (33.9)
All locations	2174 (100)	64 (2.9, 12.0)	102 (4.7, 19.1)	93 (4.3, 17.4)	182 (8.4, 34.1)	93 (4.3, 17.4)	534 (24.6)

*The values are given as the number of patients who had a procedure, with the percentage of all procedures in parentheses. †The values are given as the number of procedures, with the percentage of all primary procedures that failed by location and the percentage of total failures by location in parentheses. ‡The values are given as the number of procedures that failed, with the percentage in parentheses.

(Fig. 6). The rate of aseptic loosening failures for segmental endoprostheses was significantly higher in hinged joints than polyaxial articulations ($p = 0.0004$, Table III). Aseptic loosening was also higher with all lower extremity prostheses compared with all upper extremity prostheses, but the difference was not significant ($p = 0.12$).

Structural failures (Type 3) accounted for 17% of all failures and were highest with distal humeral and distal femoral replacements. Structural failure was lowest for proximal humeral and total femoral replacements. The rate of structural failure was significantly increased in the uniaxial endoprostheses compared with the polyaxial endoprostheses ($p < 0.0001$, Table III). Structural failures also occurred more often in the lower extremity compared with the upper extremity ($p = 0.002$).

Infection (Type 4) was the most common mode of failure overall and was the most common cause of failure at all locations except the proximal part of the femur. Infection accounted for all total humeral replacement failures. Type-4

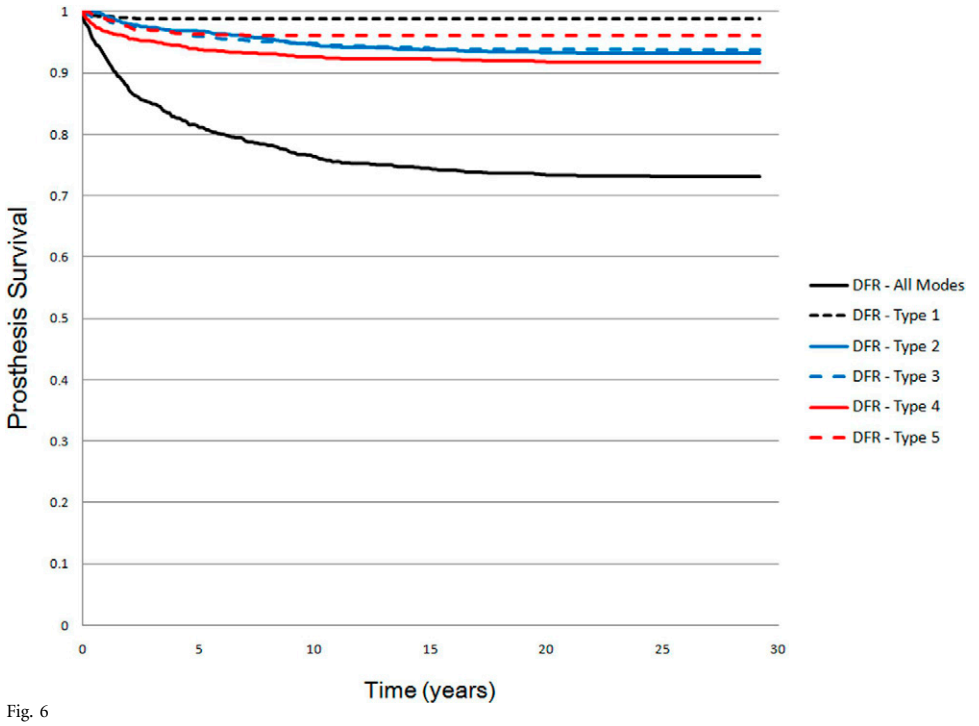

Fig. 6

Kaplan-Meier survival graph for distal femoral replacements (DFR), stratified by mode of failure.

TABLE III Segmental Endoprosthetic Failures by Joint Type in the Current Investigation

Joint Type	Primary Procedures* *(no. of patients)*	Soft-Tissue Failure†	Aseptic Loosening†	Structural Failure†	Infection†	Tumor Progression†	Total No. (%) of Procedures
Uniaxial joint prosthesis	1329	22 (1.7, 5.7)	81 (6.1, 20.9)	84 (6.3, 21.7)	136 (10.2, 35.1)	64 (4.8, 16.5)	387 (29.1)
Polyaxial joint prosthesis	751	35 (4.7, 28.7)	20 (2.7, 16.4)	7 (0.9, 5.7)	34 (4.5, 27.9)	26 (3.5, 21.3)	122 (16.2)
Significance‡ *(p value)*		0.0001	0.0004	0.007	0.0001	0.18	<0.0001

*Total humeral replacements and total femoral replacements were excluded as these implants contain both uniaxial and polyaxial articulations. †The values are given as the number of procedures, with the percentage of all primary procedures that failed and the percentage of failures by location in parentheses. ‡Significance is defined as $p < 0.05$.

failures occurred significantly more often in hinged prostheses than in polyaxial prostheses ($p = 0.0001$, Table III).

The relative incidence of endoprosthetic failures due to tumor progression (Type 5) was greatest with the distal humeral and proximal femoral replacements and least with total femoral and combined distal femoral-proximal tibial replacements; however, overall tumor progression rates were similar for all locations. Tumor progression failures occurred more often after primary tumor resection (4.7%) than after treatment of metastatic disease (2.2%); the difference was significant ($p = 0.03$). There were no significant differences in tumor progression when joint type or extremity was considered.

A chi-square test of independence was performed with a contingency table considering mode of failure and anatomic location. Mode of failure demonstrates significant dependence on anatomic location for all locations except total humeral replacement ($p < 0.0001$). The number of total humeral replacements was insufficient to be included in this analysis.

When failure incidence was analyzed chronologically in five-year increments, the rates of endoprosthetic failure decreased over time (Fig. 7). Failure rates for replacements of the proximal part of the humerus, proximal part of the femur, distal end of the femur, and proximal part of the tibia implanted from 1974 to 1988 were compared with those implanted from 1994 to 2008. The overall failure rate of endoprostheses implanted from 1974 to 1988 was 36%, whereas the failure rate from 1994 to 2008 was 20.9% ($p < 0.0001$). Significant reductions in failure incidence were seen for each anatomic location except the proximal part of the humerus, for which failure was reduced from 22% to 14% ($p = 0.09$).

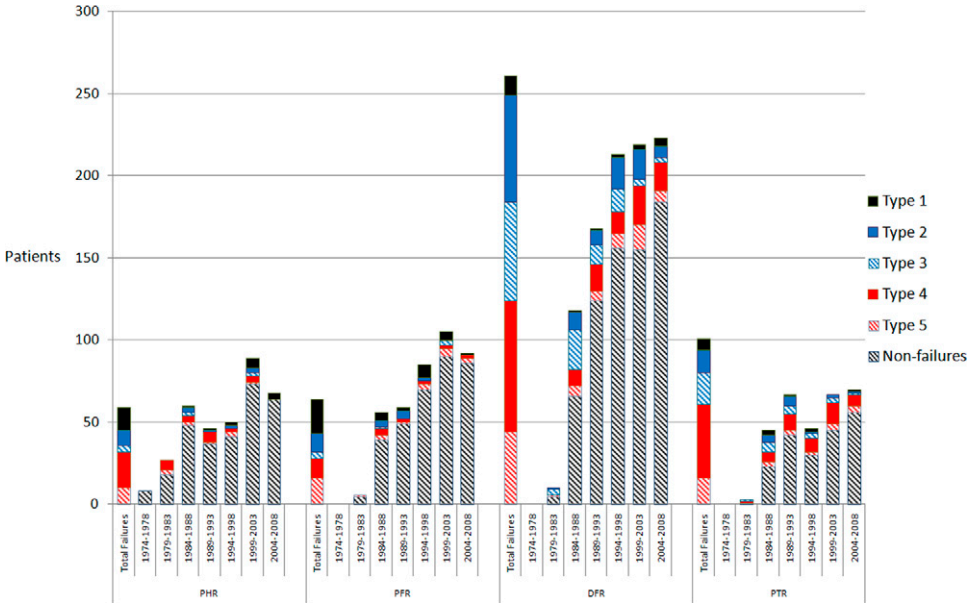

Fig. 7

Chart representing the chronological evolution of failure modes for proximal humeral replacement (PHR), proximal femoral replacement (PFR), distal femoral replacement (DFR), and proximal tibial replacement (PTR).

TABLE IV Time to Failure of Segmental Endoprostheses

Location	Time to Failure* *(mo)*					
	Soft-Tissue Failure	Aseptic Loosening	Structural Failure	Infection	Tumor Progression	Total for All Failure Types
Proximal end of humerus	16 ± 26	88 ± 69	74 ± 60	80 ± 115	15 ± 13	53 ± 81
Total humerus	NA	NA	NA	21 ± 28	NA	21 ± 28
Distal end of humerus	NA	NA	11 ± 3.5	16 ± 20	11 ± 2.8	11 ± 9.9
Proximal end of femur	19 ± 40	88 ± 87	19 ± 18	55 ± 65	47 ± 63	43 ± 61
Total femur	7 ± 8.0	83 ± NA	39 ± NA	29 ± 48	10 ± 10	22 ± 36
Distal end of femur	8.8 ± 9.9	75 ± 62	59 ± 59	45 ± 56	23 ± 19	51 ± 57
Distal end of femur and proximal end of tibia	32 ± 29	11 ± NA	17 ± 7.5	19 ± 21	44 ± 33	23 ± 22
Proximal end of tibia	28 ± 38	76 ± 56	76 ± 67	46 ± 74	23 ± 25	51 ± 65
All locations	16 ± 29	76 ± 63	59 ± 59	47 ± 69	26 ± 33	47 ± 61

*The values are given as the mean and the standard deviation. NA = not applicable.

Time to Failure

Time to failure differed significantly on the basis of the location of the endoprosthesis. The mean overall time to failure was forty-seven months (Table IV). The shortest mean time to failure by anatomic location (10.9 months) was observed in the distal humeral replacements. The longest mean time to failure was fifty-three months, observed in proximal humeral replacements. Intervals to failure were similar for proximal tibial and distal femoral replacements. A chi-square test of independence was performed with the use of a contingency table considering time to failure and anatomic location. Time to failure demonstrates significant dependence on anatomic location for all locations except total humeral replacement ($p < 0.0001$), but there was an insufficient number of total humeral replacements to be included in this analysis.

The interval from prosthetic reconstruction to failure varied widely with respect to the mode of failure. Soft-tissue failures were associated with the shortest mean time to failure (sixteen months), while aseptic loosening had the longest mean time to failure (seventy-six months). A chi-square test of independence with the use of a contingency table considering mode of failure and time to failure was performed. Time to failure demonstrates significant dependence on mode of failure for all locations except total humeral replacement ($p < 0.0001$).

Literature Review

Our literature review was based on 4359 patients who underwent limb preservation surgery following tumor resection[3,4,6-8,11-13,16,17,19,27-84]. Of these subjects, 237 (5.4%) had proximal humeral replacements; nine (0.2%), total humeral replacements; thirty-five (0.8%), distal humeral replacements with total elbow arthroplasty; 452 (10%), proximal femoral replacements; sixty-three (1.4%), total femoral replacements; 2861 (66%), distal femoral replacements; and 702 (16%), proximal tibial replacements (Table V).

TABLE V Segmental Endoprosthetic Failures by Location Reported in the Orthopaedic Literature

Location	Total Procedures*	Soft-Tissue Failure†	Aseptic Loosening†	Structural Failure†	Infection†	Tumor Progression†	Total‡
Proximal end of humerus	237 (5.4)	16 (6.8, 20.5)	16 (6.8, 20.5)	2 (0.8, 2.6)	5 (2.1, 6.4)	39 (16.5, 50.0)	78 (32.9)
Total humerus	9 (0.2)	1 (11.1, 20.0)	0 (0, 0)	2 (22.2, 40.0)	0 (0, 0)	2 (22.2, 40.0)	5 (55.6)
Distal end of humerus	35 (0.8)	0 (0, 0)	2 (5.7, 11.8)	3 (8.6, 17.6)	0 (0, 0)	12 (34.3, 70.6)	17 (48.6)
Proximal end of femur	452 (10.4)	15 (3.3, 16.5)	24 (5.3, 26.4)	5 (1.1, 5.5)	32 (7.1, 35.2)	15 (3.3, 16.5)	91 (20.1)
Total femur	63 (1.4)	0 (0, 0)	4 (6.3, 13.3)	1 (1.6, 3.3)	11 (17.5, 36.7)	14 (22.2, 46.7)	30 (47.6)
Distal end of femur	2861 (65.6)	4 (0.1, 0.5)	328 (11.5, 43.1)	163 (5.7, 21.4)	155 (5.4, 20.4)	111 (3.9, 14.6)	761 (26.6)
Proximal end of tibia	702 (16.1)	0 (0, 0)	62 (8.8, 21.5)	52 (7.4, 18.0)	138 (19.7, 47.8)	37 (5.3, 12.8)	289 (41.2)
All locations	4359 (100)	36 (0.8, 2.8)	436 (10.0, 34.3)	228 (5.2, 17.9)	341 (7.8, 26.8)	230 (5.3, 18.1)	1271 (29.2)

*The values are given as the number of patients, with the percentage in parentheses. †The values are given as the number of patients, with the percentage of failure for all primary procedures by location and the percentage of total failures by location in parentheses. ‡The values are given as the total number of failures, with the percentage of all procedures that failed at the location in parentheses.

Overall, 1271 primary procedures (29%) were considered failures. Total failure occurrences by anatomic location included seventy-eight (33%) of the 237 proximal humeral replacements, five of nine total humeral replacements, seventeen (49%) of thirty-five distal humeral replacements, ninety-one (20%) of 452 proximal femoral replacements, thirty (48%) of sixty-three total femoral replacements, 761 (27%) of 2861 distal femoral replacements, and 289 (41%) of 702 proximal tibial replacements (Table V).

Mode of failure demonstrated significant dependence on anatomic location for all locations ($p < 0.0001$). Soft-tissue failures were most common for endoprostheses located about the shoulder and hip, whereas aseptic loosening was the most common mode of failure in the lower extremities, especially with hinged knee arthroplasty. Time to failure for individual failure modes and anatomic sites was not commonly reported and could not be analyzed reliably.

Discussion

Segmental metallic endoprostheses play an increasingly important role in limb reconstruction following tumor surgery. Reconstructive failures are common, and no large investigations have analyzed these failures and enabled their classification[4,7,27,28,85]. Several factors may contribute to failure. Soft-tissue stripping, wide excision of normal adjacent muscle and bone, and patient deconditioning predispose to joint instability[86]. The substantial lengths of these endoprostheses create high bending stresses at the prosthesis-bone interface and may contribute to loosening and periprosthetic or component fracture[87]. Constrained joint designs also impart substantial stress between the endoprosthesis and cement or endoprosthesis and bone, increasing the incidence of loosening[87]. Tumor progression remains a persistent threat to endoprosthesis and limb survival[57,68]. Extensive dissections, longer operative times, large endoprosthetic volume, and exposure to chemotherapy and radiation place patients at a higher risk of infection[88-90].

Despite the high failure rates of these devices, the epidemiology of their failure has not been addressed sufficiently because of the paucity of procedures performed annually. The current study combines the collective experience of five institutions that perform a high volume of these procedures, and the investigation was done with two goals. The first was to analyze a large cohort of patients who had undergone limb preservation surgery with metallic segmental endoprostheses to delineate the incidence and mode of failure. The second goal was to derive a classification system based on these failure modes to facilitate understanding and uniform reporting of segmental failures as well as provide information for treatment decisions.

The results from the present study and a review of the literature indicate that there are five major modes of segmental endoprosthetic failure. These five modes are based on the categories of mechanical and nonmechanical failures[4]. We classified mechanical failures as soft-tissue failure (Type 1), aseptic loosening (Type 2), and structural breakage (Type 3). Nonmechanical failures were classified as infection (Type 4) and tumor progression (Type 5). In the present study, infection was the most common cause of failure, followed by aseptic loosening, tumor progression, structural failure, and soft-tissue failure, respectively.

Data from this study and a comprehensive literature review demonstrated significant dependence of failure mode on anatomic location. Risk of Type-1 failures for polyaxial joints was over five times that for uniaxial joints, and risk of Type-2 failures for distal femoral replacement was over twice that for proximal femoral replacement. Previous investigations of outcomes after reconstruction with segmental endoprostheses have generally taken a cumulative approach to reporting failures[7,12,37,57,83]; however, on the basis of the results in the current investigation, this should be avoided as it dilutes significant location-specific trends that could guide endoprosthetic design improvements.

Overall, the reports in the literature had results similar to our findings. The least common failure mode in the literature and in the current investigation was soft-tissue failure, predominantly about the hip and shoulder, reflecting the intrinsic instability of these joints. The proportion of patients who had structural failure of a prosthesis or failure due to disease progression was nearly identical in the literature and the current study.

The most striking difference between the current investigation and literature involved aseptic loosening. The overall incidence of aseptic loosening failures in the literature was 10%; the incidence in the current study was 4.7%. The incidence of aseptic loosening for distal femoral replacement was 12% in the literature and 6.8% in the current study. This finding may reflect the trend toward use of press-fit stems, which have a lower incidence of aseptic loosening than cement in the short term[72], although some series have found that the differences are not significant and the comparatively short duration of press-fit use compared with cement does not allow for adequate comparison[91]. This difference may also be explained by different levels of expertise in complex reconstruction between the dedicated centers in this study and the wide variation in experience among individuals and groups reported in the literature. Lastly, this difference may also be explained by technological advances in the detection of latent infections, curtailing the onset of loosening that would have been judged previously to be aseptic; this would also help to explain the relative increase in failures due to infection in the present study compared with previous reports.

Infection was the most common mode of failure in the current study. Larger endoprostheses (total humeral, total femoral, and combined distal femoral-proximal tibial replacements) had a higher failure rate due to infection than the smaller endoprostheses, demonstrating the effect of the extensive dissections and longer operative times accompanying these procedures[88,92]. Proximal femoral replacement demonstrated the lowest infection rate in the current study, which may be due to the more robust vascular supply and soft-tissue envelope surrounding this joint. A similar trend was demonstrated by Jeys et al., who reported an infection rate of 23.1% about the tibia and 6.7% about the proximal part of the femur[92].

Time to failure was also significantly dependent on anatomic location and mode of failure. Soft-tissue failures generally occurred early in the postoperative period but then

leveled off by the end of the second postoperative year (Figs. 4, 5, and 6). Kabukcuoglu et al. reported similar findings in that proximal femoral replacement dislocation usually occurred within the first three months after surgery[59].

Infection failures presented at an average of forty-seven months; however, half of all infections occurred within the first two years. Therefore, failures due to infection generally occur early in the postoperative period, but late infections are not uncommon. Jeys et al. reported a high incidence of infection in the first two years, with most infections occurring within the first ten years after surgery; however, they did not comment on a rationale for this trend[92]. We hypothesize that the effects of ongoing treatment for oncologic disease are likely responsible for these findings, but the data reported by Jeys et al. are inconsistent in this matter; radiation has been shown to be a significant risk factor, but chemotherapy has not. Regardless of etiology, these findings reinforce the importance of patient education, surveillance, and continuing preventive measures such as antibiotic prophylaxis for dental and invasive procedures over the lifetime of the patient.

While the relative incidence of tumor failures showed some variance, the absolute incidence of tumor progression failures ranged from 2.6% for total femoral replacement to 5.6% for distal humeral replacement, which was not significant. Therefore, no obvious recommendations to prevent progression in various anatomic sites can be made. The significant difference in tumor progression failures for patients with primary tumors and those with metastatic disease is likely due to the relatively shorter survival of the patients with metastatic disease.

The authors acknowledge limitations to this study. While the volume of patients reported is a strength of this investigation, the procedures were performed at multiple centers by surgeons using nonstandardized techniques and instrumentation. This investigation spans three and a half decades; therefore, adjuvant treatment of these tumors, and consequently patient and prosthesis survival, has evolved over the course of the period reviewed. Endoprosthetic designs and fixation methods have also evolved. Failure rates of cemented and noncemented segmental endoprostheses, however, have not been shown to be significantly different in medium-term follow-up[91].

The classification system presented in this study is intended to place greatest emphasis on the most devastating causes of segmental endoprosthetic failure and, therefore, those that require the most urgent intervention. Among the five failure modes, infection (Type 4) and tumor progression (Type 5) are the most likely to result in amputation[4,93]. Soft-tissue failures (Type 1), aseptic loosening (Type 2), and structural failures (Type 3) may compromise function, but their occurrence is rarely threatening to life or limb, and the classification system was derived accordingly[4]. Future application of this classification system for reporting segmental outcomes will facilitate clearer communication of failure modes and a better understanding of their causes. ■

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