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CHAPTER 3

Outcome After Fixation Of Metastatic Proximal Femoral Fractures: A Systematic Review Of 40 Studies

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3

ABSTRACT

Objectives

To assess: (1) functional outcome, (2) local complication rate, and (3) systemic complication rate after surgery for proximal femoral metastases. These outcomes were compared between three commonly used surgical strategies: endoprosthetic reconstruction, intramedullary nailing, and open reduction and internal fixation (ORIF).

Design

Systematic review and meta-analysis.

Data Sources

On September 24th, 2015, we searched the Pubmed, Embase, and Cochrane libraries for studies (published after 1980) using the keywords: pathologic and fracture and surgery, including synonyms, in title and abstract, without any limits, yielding 7,670 publications.

Eligibility Criteria For Selecting Studies

Studies reporting on functional outcome or complications after surgery for impending or actual pathological proximal femoral fractures caused by metastatic disease. Exclusion criteria were: case-reports, studies with less than 10 patients within a treatment arm, reviews, letters to the editor, meeting abstracts, technique papers, revision procedures, and indiscernible treatment arms for proximal femoral metastasis.

Results

All three surgical strategies result in reasonable function on average; however, wide ranges indicate that both poor and good functional levels are obtained. We found that the overall reoperation rate was comparable for endoprosthesis and intramedullary nailing, but was higher after ORIF. Definitions and reporting of systemic complications varied widely among studies.

Conclusions

This study provides an overview of functional outcome and complications after common surgical strategies for impending and pathological fractures in proximal femoral metastasis. The results reported here can aid patients and their surgeons in the decision for surgical treatment.

INTRODUCTION

The proximal femur is commonly affected by bone metastases.[1,2] Bone metastases weaken the bone and reduce load bearing capabilities which can lead to pain and eventually a pathological fracture. Surgical treatment is often indicated in case of a pathological or impending fracture and aims to restore function in a single procedure while minimizing the risk of complications.[1-3]

Several surgical strategies are practiced for the treatment of proximal femoral fractures caused by bone metastasis.[4] The three mostly used concepts of treatment are: endoprosthetic reconstruction, intramedullary nailing, and open reduction and internal fixation with plate and screws.[1,2,4] The decision about whether to undergo surgery and the choice of surgical strategy is ideally made by the patient together with their doctor. This decision depends on many factors including estimated life expectancy, location and size of the lesion, and the expected functional outcome and complications. A survey among orthopaedic oncologists demonstrated large variation in preference for treatment and previous retrospective studies support the use of all three surgical techniques.[4] Outcomes such as reoperations and complications are relatively rare (<10%) and therefore require large cohorts to adequately compare surgical strategies.

This review aims to summarize current literature to help inform patients about expected outcome and compare the outcome between surgical strategies for proximal femoral fractures caused by bone metastasis. Specifically, we asked the following questions: (1) What is the functional outcome after surgery?, and (2) What is the local and systemic complication rate? We compared these outcomes between the three aforementioned surgical strategies.

METHODS

Article Selection

We report our results according to the PRISMA Statement and our review protocol was registered on PROSPERO prior to study selection (#2014:CRD42014007481).[5]

On 24 September 2015, we searched the Pubmed, Embase, and Cochrane libraries for studies, published after 1980 using the keywords: ("pathologic*" OR "impending") AND ("fracture*") AND ("surgery" OR "surgeries" OR "operation" OR "operations" OR "operativ*" OR "surgical*" OR "intramedull*" OR "fixation*" OR "resection*" OR "osteosynth*" OR "endoprosth*" OR "prosth*" OR "arthroplas*") in title and abstract, without any limits, yielding 7,670 publications (Figure 1).

Two reviewers (S.J., T.T.) independently screened titles and abstracts and subsequently full texts using predefined criteria. We included studies reporting on functional outcome

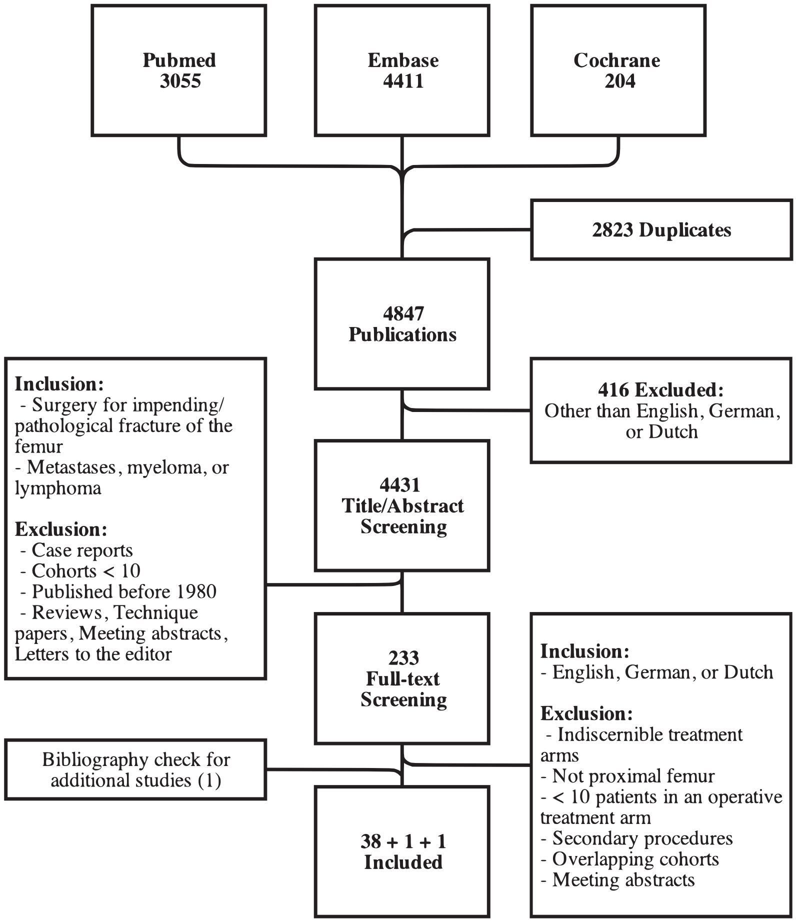

Figure 1: Flowchart demonstrating articles identified, excluded, and included in the systematic review. Thirty-eight studies were identified by our search, one was found through bibliography screening, and we included our recent retrospective study reviewing the cases at our institution.

or complications after surgery for impending or actual pathological proximal femoral fractures caused by metastatic disease. Myeloma and lymphoma were also included as these are commonly grouped with metastases and have similar mechanical implications.[6] We excluded: case-reports, studies with less than 10 patients within a treatment arm, reviews, letters to the editor, meeting abstracts, technique papers, revision procedures, and indiscernible treatment arms for proximal femoral metastasis (e.g. studies that also include primary tumors, other anatomical areas, or revision procedures without reporting results separately). We contacted authors if studies published after the year 2000 included indiscernible treatment arms but were otherwise eligible (20 studies).[6-25] Only one of these could eventually be included.[8] In case of overlapping cohorts (14 studies),[26-39] we included the most comprehensive or largest study.[33-39] Authors were contacted if studies published after the year 2000 insufficiently reported outcomes (14 studies).[33,35-38,40-47] Eight authors[36-38,41,42,44,45,47] responded and additional information on outcome was obtained for 4 studies which could then be included.[36,41,42,47] The bibliographies of included studies were checked for publications missed by our search; 1 additional study was found and included (Figure 1).[48]

Two reviewers (S.J., T.T.) independently appraised the quality of the studies using pre-determined criteria –study design, disclosure, direct comparison of surgical techniques, eligibility criteria for patient selection, baseline reporting, outcome reporting, attrition bias– and extracted data using a standardized sheet. Discordant judgments were resolved by consensus discussion.

Outcome Measures

The following outcome measures were collected from the selected studies per treatment: physical function measured by an internationally accepted standardized instrument, local complications, and systemic complications.

Seven studies reported on functional outcome using a standardized measure; five used the Musculoskeletal Tumor Society (MSTS) score, one used the Toronto Extremity Salvage Score (TESS), and one used both. The MSTS score is a clinician completed assessment rating six domains, resulting in a score of 0 to 100% with a higher score indicating better function.[49] The TESS is a patient completed questionnaire containing 30 items resulting in a score of 0 to 100, with a higher score indicating better function.[50,51]

We only included those local complications that required reoperation and grouped these into: deep infection (e.g. incision and debridement with or without implant removal), fixation failure (including: implant or peri-implant fracture, nonunion, implant loosening, acetabular protrusion of hemiarthroplasty), dislocation (e.g. open reduction with or without component revision), tumor recurrence or progression, and total number of reoperations.

We included all reported systemic complications, regardless of treatment consequences.

The following data was extracted for all patients with femoral metastases: number of patients and affected femurs, number of reported actual and impending fractures, age, sex, minimum followup in months, percentage oneyear survival, and tumor distribution. We also extracted number of affected femurs, number of pathological and impending fractures, use of cement, and anatomic location of the lesion (head/neck, trochanteric, subtrochanteric, proximal shaft area) per treatment concept.

We considered the following surgical techniques (i.e. treatment arms): endoprosthetic reconstruction (including: total hip arthroplasty, hemiarthroplasty, and modular tumor prosthesis), intramedullary nailing, and ORIF (including: plate-screw fixation and dynamic hip screw).

Statistical Analysis

We reported the average functional outcome score with range and followup per surgical technique. No meta-analysis could be performed on these data because of the variation in outcome measures used, small number of studies, and varying followup.

Complication rates are reported as frequencies with percentages per surgical technique. We used a random-effects meta-analysis to generate pooled effect estimates for: (1) the total number of reoperations, (2) deep infections, and (3) fixation failures per surgical technique. The pooled effect estimate is a weighted average of included studies and presented as a percentage with 95% confidence interval (95% CI). Studies that did not report on these specific outcomes were not included in the calculations. We used the Freeman-Tukey double arcsine transformation to obtain 95% confidence intervals that are admissible when the complication rates are close to 0 or 100%.[52,53] The random-effects meta-analysis accounts for heterogeneity in effect estimates across studies (i.e. studies are permitted to have different effects and characteristics)[52]. We reported the I-squared statistic; an estimate of the percentage of the variation in the effect estimate due to the heterogeneity across studies.

No meta-analysis could be performed for systemic complications because of the low number of studies reporting on this outcome per treatment and substantial variation in definition of systemic complications among studies.

All statistical analyses were performed using Stata® 14.0 (StataCorp LP, College Station, TX, USA).

RESULTS

Study Characteristics

Forty studies were included (Figure 1); all had a retrospective design. Critical appraisal demonstrated that 32 (80%) studies had clear eligibility criteria and clear methods of selecting patients, leaving the remainder subject to selection bias. Only 11 (28%) studies described a clear definition of the outcomes to be reported, for the remaining studies outcome bias cannot be excluded. Overall, 17 (43%) of the studies were assessed as being at high or unclear risk of attrition bias due to possibly high loss to followup (Figure 2, Appendix 1).

Patient Characteristics

The 40 studies reported on 3,211 metastatic lesions in the complete femur; average age ranged from 54 to 78 years and 39% (range among studies: 15 to 55%) were men (Table 1). The oneyear survival percentage –reported in 23 studies– ranged from 0 to 62%. Breast (35%), Lung (15%), Prostate (10%), and Kidney (8.2%) were the most common

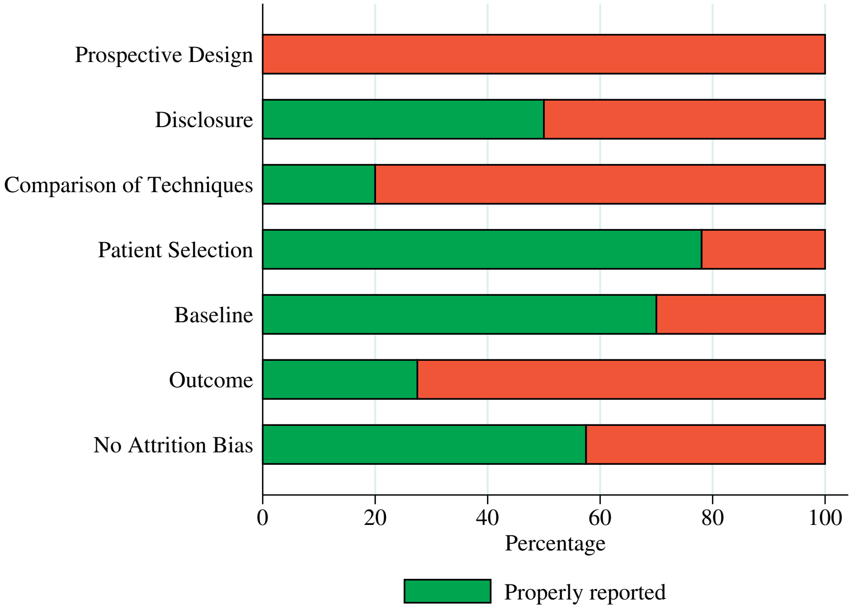

Figure 2: Overall quality of the included studies. All studies had a retrospective study design. (Appendix 1 includes the critical appraisal per study).

primary tumors (Figure 3, Appendix 2). Myeloma and lymphoma accounted for 9.8% of the tumors. The primary tumor type was unknown in 2.4% of the cases.

The 40 studies describe 58 treatments including 2,748 proximal femoral metastases: 23 studies reporting on 1,461 endoprostheses (664 [45%] pathological fractures, 347 [24%] impending fractures, and not specified in 450 [31%]); 24 studies reporting on 1,054 intramedullary nails (468 [44%] pathological fractures, 389 [37%] impending fractures, and not specified in 197 [19%] cases); and 11 studies reporting on 233 ORIFs (108 [46%] pathological fractures, 80 [34%] impending fractures, and not specified in 45 [19%] cases). Fracture location was head/neck in 17%, trochanteric/subtrochanteric in 34%, and not specified in 48% of the endoprosthetic reconstructions; head/neck in 3%, trochanteric/subtrochanteric in 75%, and not specified in 22% of the intramedullary nails; and head/neck in 3%, trochanteric/subtrochanteric in 55%, and not specified in 43% of the ORIFs. Cement was used in 87% of the endoprosthetic reconstructions (864/998, not specified in 463 cases), in 13% of the intramedullary nails (84/649, not specified in 405 cases), and in 71% of the ORIFs (113/160, not specified in 73 cases) (Appendix 3).

Functional Outcome

Seven studies reported on functional outcome following endoprosthetic reconstruction: five studies reported the MSTS score in 95 patients; The average MSTS score ranged

Table 1: Characteristics of all patients with femoral metastases per study (%)

Author, Year	Implant	Patients	Femurs	Pathological fractures	Median Age	Men	Minimum followup#	Oneyear survival in %
Choy et al. 2015	IMN	19	19	19 (100)	66*	8 (42)	-	26
Hettwer et al. 2015	EPR	105	111	70 (63)	65*	45 (41)	0	42
Janssen et al. 2015	EPR, IMN, ORIF	417	417	173 (41)	62	163 (39)	0	58
Arvinius et al. 2014	IMN	65	65	44 (68)	68*	28 (43)	3	-
Piccioli et al. 2014	IMN	80	80	80 (100)	61*	42 (53)	36	40
Shemesh et al. 2014	IMN	19	21	11 (52)	63	8 (38)	4	28
Fakler et al. 2013	IMN	20	20	20 (100)	70	11 (55)	22	35
Sorensen et al. 2013	EPR	-	105	-	-	-	28	-
Weiss et al. 2013	IMN, EPR	194	196	151 (77)	68	101 (52)	0	33
Asavamongkolgul et al.	ORIF	27	27	9 (33)	58	10 (37)	2	42
Harvey et al. 2012	IMN, EPR	158	159	91 (57)	60*	72 (45)	C	51
Steensma et al. 2012	EPR, IMN, ORIF	298	298	112 (38)	-	-	0	-
Hattori et al. 2011	EPR	16	16	13 (81)	65	8 (50)	3	62
Parker et al. 2011	EPR, IMN, ORIF	137	145	145 (100)	72*	57 (39)	C	-
Zacherl et al. 2011	EPR, IMN, ORIF	59	64	64 (100)	64*	24 (38)	-	31
Potter et al. 2009	EPR	37	39	16 (41)	62*	-	24	-
Sarahrudi et al. 2009	EPR, ORIF	142	146	146 (100)	72	42 (29)	0	17
Chandrasekar et al. 2008	EPR	81	81	56 (69)	-	-	-	31
Selek et al. 2008	EPR	44	45	28 (62)	55*	21 (47)	2	27
Park et al. 2007	EPR	42	42	-	-	-	27	-
Rethnam et al. 2007	IMN	11	11	9 (82)	72	5 (45)	-	-
Wedin et al. 2005	EPR, IMN, ORIF	142	146	126 (86)	69	69 (47)	C	30

Table 1: Characteristics of all patients with femoral metastases per study (%) (*continued*)

Author, Year	Implant	Patients	Femurs	Pathological fractures	Median Age	Men	Minimum followup#	Oneyear survival in %
Datir et al. 2004	IMN	17	17	13 (76)	-	-	4	-
Moholkar et al. 2004	IMN	42	48	26 (54)	66*	12 (25)	-	-
Ramakrishnan et al. 2004	IMN	25	28	5 (18)	61	12 (43)	7	-
Piatek et al. 2003	IMN	-	28	26 (93)	-	-	0	-
Ward et al. 2003	EPR, ORIF	182	182	85 (47)	-	-	-	45
Assal et al. 2000	IMN	10	12	6 (50)	71	3 (25)	C	10
Giannoudis et al. 1999	IMN	27	30	23 (77)	68*	9 (30)	2	32
Chien et al. 1997	EPR	30	32	26 (81)	61*	14 (44)	1	20
Algan et al. 1996	IMN	27	27	-	57	-	-	-
Nargol et al. 1996	IMN	10	10	10 (100)	78	2 (20)	4	0
Rompe et al. 1994	EPR, ORIF	50	50	17 (34)	56*	11 (22)	-	50
Broos et al. 1993	EPR, ORIF	65	77	71 (92)	65*	12 (16)	-	-
Korkala et al. 1991	EPR	-	38	38 (100)	-	-	-	-
Borel Rinkes et al. 1990	EPR	34	34	27 (79)	61*	5 (15)	12	-
Yazawa et al. 1990	EPR, IMN	-	119	-	-	-	24	-
Fasano et al. 1988	IMN	10	11	9 (82)	70	5 (45)	7	22
Behr et al. 1985	IMN, ORIF	38	48	22 (46)	70*	14 (29)	7	-
Lane et al. 1980	EPR	163	167	125 (75)	54*	38 (23)	12	21

- = not available, * = Mean age, # = in months, C = complete followup, EPR = Endoprosthetic reconstruction, IMN = Intramedullary nailing, ORIF = Open reduction and internal fixation

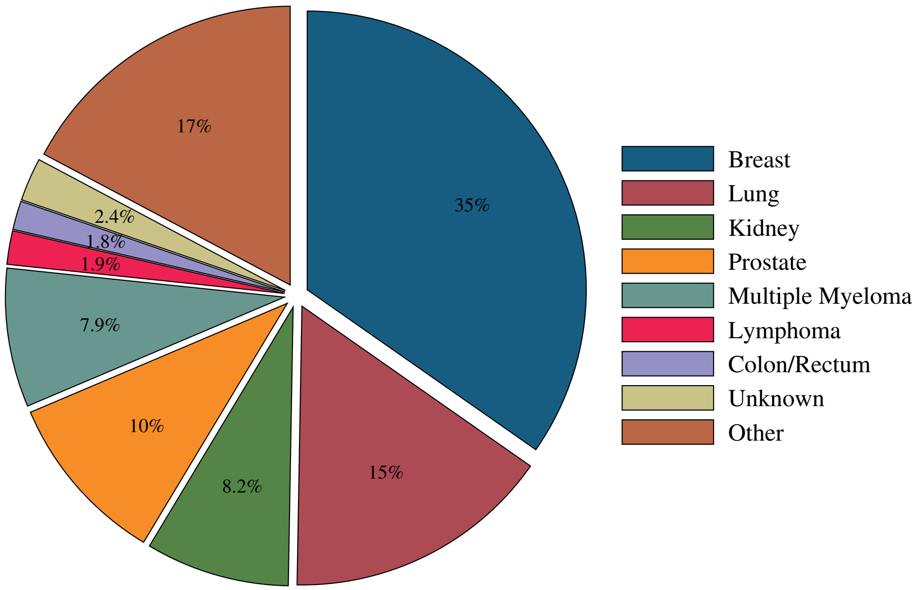

Figure 3: Primary tumor distribution (Appendix 2 includes the numbers).

from 51 to 74%, but followup varied from 6 to 27 months (Table 2). The score in individual patients ranged from 28 to 100%. Two studies reported TESS scores: one found a score of 67 (range 52 to 82) in 5 patients after 18 months, and another found a score of 71 (46 to 84) in 11 patients after 27 months.

Table 2: Functional outcome per implant type for proximal femur metastatic fractures (%)

Author, Year	Implant	Followup	Patients	Outcome measure	Median score (Range)
Harvey et al. 2012	EPR	9 months	21	MSTS	70* (40 - 90)
Hattori et al. 2011	EPR	6 months	12	MSTS	58 (28 - 100)
Potter et al. 2009	EPR	24 months	39	MSTS	67* (43 - 90)
Chandrasekar et al. 2008	EPR	18 months	5	TESS	67* (52 - 82)
Selek et al. 2008	EPR	2 months	29	MSTS	51*
		12 months	12	MSTS	66*
Park et al. 2007	EPR	27 months	11	MSTS	74 (57 - 83)
		27 months	11	TESS	71 (46 - 84)
Harvey et al. 2012	IMN	9 months	24	MSTS	80* (27 - 100)
Asavamongkolgul et al. 2012	ORIF	3 months	17	MSTS	80 (25 - 96)

* = Mean score, MSTS = Musculoskeletal Tumor Society Score, TESS = Toronto Extremity Salvage Score, EPR = Endoprosthetic reconstruction, IMN = Intramedullary nailing, ORIF = Open reduction and internal fixation. Range was not available for the patients in the study by Selek et al.

One study reported the MSTS score after intramedullary nailing; the average score was 80% in 24 patients with a followup of 9 months (range 27 to 100%).

One study reported the MSTS score after ORIF; the average score was 80% in 17 patients with a followup of 3 months (range 28 to 96%).

Local Complications

The overall reoperation rate varied from 0 to 31% after endoprosthetic reconstruction, 0 to 26% after intramedullary nailing, and 0 to 42% after ORIF (Table 3). Meta-analysis demonstrates pooled reoperation rates of 5.2% (95% CI 2.9 to 8.1%) for endoprostheses, 4.2% (95% CI 2.0 to 6.8%) for intramedullary nails, and 14% (95% CI 7.3 to 22%) for ORIF (Figure 4, left column).

Table 3: Local and systemic complication rates per implant type for proximal femur metastatic fractures (%)

Author, Year	Implant	Femurs	Pathological fractures	Deep infection	Fixation Failure	Disloc.	Recurr.	Reop.	Sys. Comp.
Hettwer et al. 2015	EPR	111	70 (63)	4 (4)	1 (1)	6 (5)	1 (1)	13 (12)	-
Janssen et al. 2015	EPR	70	55 (79)	6 (9)	0 (0)	1 (1)	0 (0)	8 (11)	-
Sorensen et al. 2013	EPR	105	-	1 (1)	0 (0)	3 (3)	0 (0)	4 (4)	-
Weiss et al. 2013	EPR	82	-	0 (0)	4 (5)	1 (1)	0 (0)	5 (6)	1 (1)
Harvey et al. 2012	EPR	113	70 (62)	10 (9)	0 (0)	8 (7)	0 (0)	16 (14)	-
Steensma et al. 2012	EPR	197	80 (41)	0 (0)	0 (0)	5 (3)	1 (1)	6 (3)	-
Hattori et al. 2011	EPR	16	13 (81)	0 (0)	0 (0)	-	0 (0)	-	-
Parker et al. 2011	EPR	54	54 (100)	-	3 (6)	2 (4)	0 (0)	5 (9)	-
Zacherl et al. 2011	EPR	13	13 (100)	2 (15)	0 (0)	1 (8)	0 (0)	4 (31)	-
Potter et al. 2009	EPR	39	16 (41)	-	-	-	-	-	-
Sarahrudi et al. 2009	EPR	23	23 (100)	0 (0)	2 (9)	1 (4)	1 (4)	5 (22)	1 (4)
Chandrasekar et al. 2008	EPR	81	56 (69)	-	0 (0)	0 (0)	1 (1)	1 (1)	-
Selek et al. 2008	EPR	45	28 (62)	1 (2)	2 (4)	0 (0)	0 (0)	3 (7)	1 (2)
Park et al. 2007	EPR	31	-	0 (0)	0 (0)	1 (3)	0 (0)	1 (3)	-
Wedin et al. 2005	EPR	109	-	0 (0)	5 (5)	3 (3)	0 (0)	9 (8)	6 (6)
Ward et al. 2003	EPR	46	-	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	-
Chien et al. 1997	EPR	12	10 (83)	-	0 (0)	0 (0)	-	-	-
Rompe et al. 1994	EPR	25	9 (36)	0 (0)	1 (4)	1 (4)	0 (0)	3 (12)	2 (8)
Broos et al. 1993	EPR	36	-	0 (0)	0 (0)	1 (3)	0 (0)	1 (3)	-
Korkala et al. 1991	EPR	15	15 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	-
Borel Rinkes et al. 1990	EPR	34	27 (79)	0 (0)	1 (3)	0 (0)	1 (3)	1 (3)	-
Yazawa et al. 1990	EPR	41	-	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)
Lane et al. 1980	EPR	163	125 (77)	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)	2 (1)
Choy et al. 2015	IMN	10	10 (100)	0 (0)	1 (10)	0 (0)	0 (0)	1 (10)	-

Table 3: Local and systemic complication rates per implant type for proximal femur metastatic fractures (%) (*continued*)

Author, Year	Implant	Femurs	Pathological fractures	Deep infection	Fixation Failure	Disloc.	Recurr.	Reop.	Sys. Comp.
Janssen et al. 2015	IMN	302	100 (33)	6 (2)	9 (3)	0 (0)	2 (1)	16 (5)	-
Arvinius et al. 2014	IMN	56	37 (66)	-	2 (4)	0 (0)	2 (4)	2 (4)	6 (11)
Piccioli et al. 2014	IMN	80	80 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	13 (16)
Shemesh et al. 2014	IMN	21	11 (52)	1 (5)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)
Fakler et al. 2013	IMN	12	12 (100)	0 (0)	2 (17)	0 (0)	0 (0)	2 (17)	-
Weiss et al. 2013	IMN	108	-	0 (0)	10 (9)	0 (0)	1 (1)	11 (10)	2 (2)
Harvey et al. 2012	IMN	46	21 (46)	1 (2)	10 (22)	0 (0)	0 (0)	12 (26)	-
Steensma et al. 2012	IMN	82	27 (33)	0 (0)	2 (2)	0 (0)	3 (4)	5 (6)	-
Parker et al. 2011	IMN	40	40 (100)	-	1 (3)	0 (0)	0 (0)	1 (3)	-
Zacherl et al. 2011	IMN	37	37 (100)	0 (0)	2 (5)	0 (0)	0 (0)	3 (8)	-
Rethnam et al. 2007	IMN	11	9 (82)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (27)
Wedin et al. 2005	IMN	24	-	0 (0)	3 (13)	0 (0)	0 (0)	3 (13)	0 (0)
Datir et al. 2004	IMN	17	13 (76)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Moholkar et al. 2004	IMN	48	26 (54)	1 (2)	1 (2)	0 (0)	0 (0)	2 (4)	6 (13)
Ramakrishnan et al. 2004	IMN	28	5 (18)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (7)
Piatek et al. 2003	IMN	18	-	1 (6)	2 (11)	0 (0)	0 (0)	3 (17)	-
Assal et al. 2000	IMN	12	6 (50)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)
Giannoudis et al. 1999	IMN	17	-	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Algan et al. 1996	IMN	12	-	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	-
Nargol et al. 1996	IMN	10	10 (100)	-	0 (0)	0 (0)	0 (0)	-	-
Yazawa et al. 1990	IMN	18	-	0 (0)	1 (6)	0 (0)	0 (0)	1 (6)	0 (0)
Fasano et al. 1988	IMN	11	9 (82)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (36)
Behr et al. 1985	IMN	34	15 (44)	0 (0)	1 (3)	0 (0)	0 (0)	1 (3)	-
Janssen et al. 2015	ORIF	45	18 (40)	0 (0)	6 (13)	0 (0)	1 (2)	6 (13)	-
Asavamongkolgul et al.	ORIF	27	9 (33)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	-
Steensma et al. 2012	ORIF	19	6 (32)	0 (0)	5 (26)	0 (0)	3 (16)	8 (42)	-
Parker et al. 2011	ORIF	35	35 (100)	-	6 (17)	0 (0)	0 (0)	6 (17)	-
Zacherl et al. 2011	ORIF	12	12 (100)	0 (0)	2 (17)	0 (0)	0 (0)	3 (25)	-
Sarahrudi et al. 2009	ORIF	15	15 (100)	0 (0)	3 (20)	0 (0)	-	3 (20)	0 (0)
Wedin et al. 2005	ORIF	13	-	0 (0)	3 (23)	0 (0)	0 (0)	3 (23)	0 (0)
Ward et al. 2003	ORIF	13	-	0 (0)	1 (8)	0 (0)	0 (0)	1 (8)	-
Rompe et al. 1994	ORIF	25	8 (32)	0 (0)	0 (0)	0 (0)	3 (12)	4 (16)	2 (8)
Broos et al. 1993	ORIF	19	-	0 (0)	1 (5)	0 (0)	0 (0)	1 (5)	-
Behr et al. 1985	ORIF	10	5 (50)	0 (0)	1 (10)	0 (0)	0 (0)	1 (10)	-

- = not available, Disloc. = dislocation, Recurr. = Recurrence, Reop. = total reoperations, Sys. Compl. = Systemic Complications. EPR = Endoprosthetic reconstruction, IMN = Intramedullary nailing, ORIF = Open reduction and internal fixation.

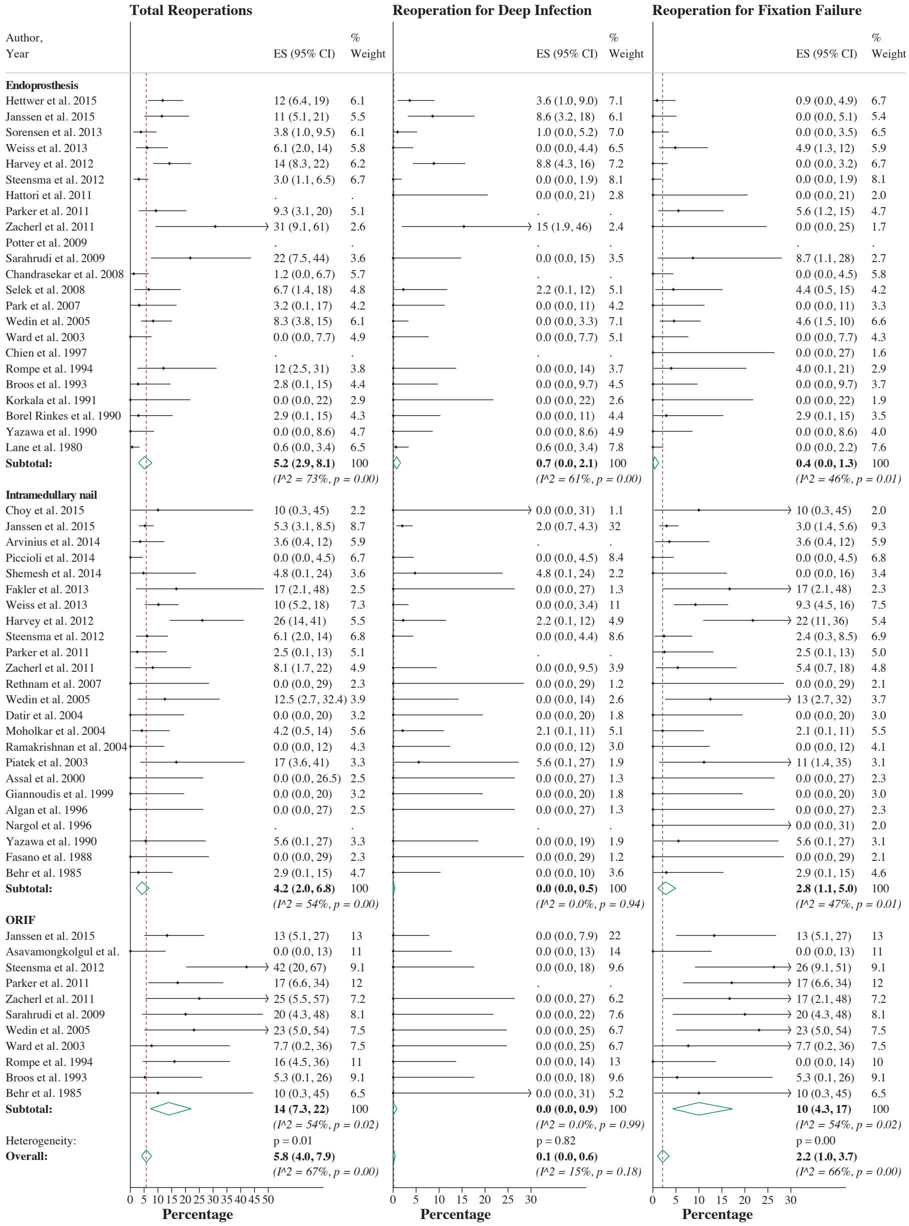

Figure 4: Random-effects meta-analysis with reoperation rates (solid black diamonds) per study per treatment arm including the 95% confidence interval [95% CI] (black horizontal lines crossing the solid diamonds). The green open diamonds are the pooled reoperation rates based on all studies per treatment arm (subtotal). The vertical red dashed lines indicate the reoperation rate for all treatment arms (overall). The left column includes all reoperations, the middle column includes reoperations for deep infections, and the right column includes reoperations for fixation failure. ES = effect estimate, ORIF = Open reduction and internal fixation. The I-squared statistic demonstrates the estimate of the percentage of the variation in the effect estimate due to the heterogeneity across studies. Note the varying percentage-scale on the x-axis.

The reoperation rate for deep infection varied from 0 to 15% after endoprosthetic reconstruction, 0 to 6% after intramedullary nailing, and was 0% in all studies after ORIF (Table 3). Meta-analysis demonstrates pooled deep infection rates of 0.68% (95% CI 0.0 to 2.05%) for endoprostheses, 0.04% (95%CI 0.00 to 0.54%) for intramedullary nails, and 0.00% (95%CI 0.00 to 0.92%) for ORIF (Figure 4, middle column).

The reoperation rate for fixation failure varied from 0 to 9% after endoprosthetic reconstruction, 0 to 22% after intramedullary nailing, and 0 to 26% after ORIF (Table 3). Meta-analysis demonstrates pooled fixation failure rates of 0.4% (95% CI 0.0 to 1.3%) for endoprostheses, 2.8% (95% CI 1.1 to 5.0%) for intramedullary nails, and 10% (95% CI 4.3 to 17%) for ORIF (Figure 4, right column).

Dislocations requiring reoperation in the endoprosthesis group ranged from 0 to 8% (Table 3). Tumor recurrence or progression requiring reoperation was reported in 20 patients; distribution of the recurring tumors was: 2 kidney, 2 breast, 1 bladder, 1 lung, 1 esophageal, 1 multiple myeloma, and not specified in the remaining 12 cases. Other reasons for reoperation (included in the overall reoperation rates) were: an exostosis (1), massive hematoma (1), wound healing problems (2), and a loose piece of cement in the hip joint after endoprosthetic reconstruction;[37,38,74,76] bursitis (1), wound healing problems (1), and painful hardware, after intramedullary nailing;[48,76] and wound healing (2) after ORIF.[37,76]

Systemic Complications

Only fourteen studies reported on systemic complications after 16 treatments. The systemic complication rate varied from 1 to 8% after endoprosthetic reconstruction, 0 to 27% after intramedullary nailing, and 0 to 8% after ORIF. There were 54 systemic complications reported in 53 patients: deep venous thrombosis (17), pneumonia (9), pulmonary embolism (6), respiratory failure (5), intraoperative mortality (3), fat-embolism (2), cardiac failure (2), urinary tract infection (2), perforated colon (1), cerebrovascular accident (1), multi-organ failure (1), ileus (1), respiratory arrest (1), cardiovascular embolism (1), and not specified (2). Fat-embolism and intraoperative mortality occurred in the same case.[55]

DISCUSSION

Endoprosthetic reconstruction, intramedullary nailing, and ORIF are common treatments for pathological proximal femoral fracture caused by bone metastasis; all aim to preserve the patient's independence and quality of the remaining life. Most studies are relatively small hampering comparison of outcomes among these surgical techniques. We aimed to establish functional outcome and complications –both local and systemic– and compared these among common surgical strategies. We found that only seven studies reported functional outcome and that on average all three techniques result in good function.

In terms of local complications, we found that the pooled overall reoperation rate was comparable for endoprosthesis and intramedullary nailing, but was substantially higher for ORIF. Deep infection seems to occur more commonly after endoprosthetic reconstruction, while fixation failure more commonly occurred after intramedullary nailing and ORIF. Deep venous thrombosis, pneumonia, and pulmonary embolism were the most commonly reported systemic complications. These findings could aid in surgical decision making and help inform the patient.

Our study has limitations. First, although three large literature databases have been used, we might have missed possible relevant publications that are not listed in these libraries. Additionally, our search missed one relevant paper –identified by bibliography screening of included studies–; this means that other relevant studies might have been missed as well.[48] However, we see these as a minor limitations because this was the only study identified after extensive screening of the bibliographies of the included studies. Second, the type of implants used within the three treatment concepts vary; the surgical technique, experience of the surgeons, and postoperative rehabilitation probably varied as well. We see this as an important limitation as we were not able to stratify for this; however, we feel that this affects all three treatment arms and reflects clinical practice. Third, indications –fracture type, location of the fracture, extend of bone destruction– for the specific strategies vary and selection bias can therefore not be ignored. We tried to minimize this by focusing on proximal femoral metastases. Furthermore, we described fracture types and location per surgical technique to help understand the variation in indications. Fourth, adjuvant treatment –radiation therapy and chemotherapy– can influence complication rates; These are poorly reported in the included studies and we were therefore not able to stratify for this, we consider this as an important limitation. Fifth, definitions of outcome, such as complications, might have varied between studies and we therefore only included local complications that required reoperation. Sixth, followup varied between studies and was not always clearly reported. We see this as an important limitation as short followup or loss to followup –attrition bias– might preclude identification of a complication. This might result in underestimating the complication rates; however, all three treatment arms are affected by this. Despite these limitations, we feel that meta-analysis is justified for estimation of pooled reoperation rates per surgical strategy as this outcome is often the primary outcome of interest and therefore generally well reported.

The limited number of studies assessing functional outcome and variation in use of outcome measures and duration of followup did not allow us to directly compare surgical strategies. All three techniques seem to result in reasonable function on average; however, the range is wide indicating that both poor and good functional levels are obtained. The MSTS score is most commonly used;[49] however, it is a clinician completed assessment of the patients' functional level and results might therefore be biased as clinicians tend to overestimate function and underestimate pain.[51,77-79] Future studies assessing function should therefore focus on patient reported outcome measures, such as the TESS score or a more general instrument like the PROMIS Physical Function Cancer questionnaire.[51,80,81] Furthermore, studies should aim to measure both preoperative and postoperative functional levels in order to establish the efficacy of surgical fixation. Lastly, including measures of quality of life (e.g. the EQ-5D or SF-36 instruments) would help us to understand how treatment impacts the overall wellbeing of the patient.[77]

Acknowledging the limitations of directly comparing local complications among surgical strategies, we found that ORIF results in the highest overall reoperation rate. These reoperations after ORIF were predominantly performed for failure of fixation. We found comparable overall reoperation rates when comparing endoprosthetic reconstruction with intramedullary nailing. However, reoperation for deep infection seems to be more common after endoprosthetic reconstruction, while reoperation for failure of fixation is more common after intramedullary nailing. Dislocations can technically only occur after endoprosthetic reconstruction and required reoperation in 0 to 8% of the cases. The finding of comparable overall reoperation rates but different reasons for reoperation are confirmed when focusing on the seven studies that describe both endoprosthetic reconstructions and intramedullary nailing.[44,46-48,62,74-76] Four out of these seven studies describe timing of the reoperations; deep infections seem to occur early (within the first months), while fixation failures seem to occur late.[47,48,62,74] Based on these findings, we feel that intramedullary nailing is an acceptable option for treatment of proximal femoral metastasis in the trochanteric and subtrochanteric area with limited bone loss in patients with poor life expectancy. Endoprosthetic reconstruction should be considered in patients with femoral head/neck lesions, lesions with substantial bone loss in the trochanteric or subtrochanteric area, radioresistant lesions (e.g. renal cell carcinoma), and in patients with reasonable life expectancy. Several algorithms exist to help the surgeon estimate life expectancy.[82-85]

Deep venous thrombosis, pneumonia, and pulmonary embolism were the most commonly reported systemic complications. Intraoperative mortality was rare (3 cases described). Measures should be taken to prevent systemic complications from occurring and to limit their consequences in these patients. Unfortunately, poor quality of reporting systemic complications did not allow direct comparison of this outcome between surgical strategies using a meta-analysis approach. Future studies should be more clear about: which systemic complications are to be reported, what the treatment consequences are, and the timing and followup of the systemic complications.[86] Lastly, studies should only include 1 limb per 1 patient as to avoid violation of the statistical rule of independence; or authors should use adequate statistical method to account for this.[87]

In conclusion, this study provides an overview of functional outcome and complications after common surgical strategies for impending and pathological fractures in proximal femoral metastasis. All three surgical strategies result in reasonable function on average; however, functional levels vary substantially. ORIF results in a high reoperation rate, while reoperation rates for endoprosthesis and intramedullary nailing are comparable. The results reported here can aid patients and their surgeons in the decision for surgical treatment.

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Appendix 1: Critical appraisal of included studies (Figure 2)

Author, Year	Prospective Design	Disclosure	Comparison of Techniques	Patient Selection	Baseline	Outcome	No Attrition Bias
Choy et al. 2015	0	1	0	1	1	0	0
Hettwer et al. 2015	0	1	0	1	1	0	0
Janssen et al. 2015	0	1	1	1	1	1	1
Arvinius et al. 2014	0	0	0	0	0	0	0
Piccioli et al. 2014	0	1	0	1	1	1	1
Shemesh et al. 2014	0	1	0	1	1	0	0
Fakler et al. 2013	0	1	0	1	1	0	1
Sorensen et al. 2013	0	1	0	1	0	1	1
Weiss et al. 2013	0	1	0	1	1	1	0
Asavamongkolgul et al. 2012	0	1	0	0	1	0	1
Harvey et al. 2012	0	1	1	1	1	1	1
Steensma et al. 2012	0	1	1	1	1	1	0
Hattori et al. 2011	0	1	0	1	1	0	1
Parker et al. 2011	0	1	1	1	1	0	1
Zacherl et al. 2011	0	1	1	1	1	1	1
Potter et al. 2009	0	1	0	1	0	0	1
Sarahrudi et al. 2009	0	0	0	1	0	0	1
Chandrasekar et al. 2008	0	1	0	1	0	1	1
Selek et al. 2008	0	1	0	1	1	0	1
Park et al. 2007	0	0	0	1	0	0	1
Rethnam et al. 2007	0	1	0	1	1	0	0
Wedin et al. 2005	0	0	1	1	1	1	1
Datir et al. 2004	0	0	0	1	0	1	0
Moholkar et al. 2004	0	0	0	1	1	0	1
Ramakrishnan et al. 2004	0	0	0	1	1	0	0
Piatek et al. 2003	0	0	0	1	0	0	0
Ward et al. 2003	0	1	0	0	0	0	0
Assal et al. 2000	0	1	0	1	1	0	1
Giannoudis et al. 1999	0	0	0	1	1	0	1
Chien et al. 1997	0	0	0	0	0	0	1
Algan et al. 1996	0	0	0	0	1	0	0
Nargol et al. 1996	0	0	0	1	1	0	0
Rompe et al. 1994	0	0	1	1	1	0	0
Broos et al. 1993	0	0	0	1	1	0	0
Korkala et al. 1991	0	0	0	0	0	0	0
Borel Rinkes et al. 1990	0	0	0	0	1	0	1

Appendix 1: Critical appraisal of included studies (Figure 2) (*continued*)

Author, Year	Prospective Design	Disclosure	Comparison of Techniques	Patient Selection	Baseline	Outcome	No Attrition Bias
Yazawa et al. 1990	0	0	0	1	0	1	1
Fasano et al. 1988	0	0	0	0	1	0	1
Behr et al. 1985	0	0	1	1	1	0	0
Lane et al. 1980	0	0	0	1	1	0	1

Prospective design
1, Prospective design
0, Retrospective design
Disclosure
1, Disclosure is reported
0, Disclosure is not reported
Comparison of Techniques
1, Direct comparison of surgical techniques
0, Single treatment arm or not a comparison
Patient selection
1, Clear eligibility criteria
0, Potential selection bias or eligibility criteria unclear

Baseline
1, Detailed baseline characteristics per treatment arm
0, Mixed or unspecified baseline characteristics
Outcome
1, Clear definition of outcomes to be reported
0, Outcomes not specified or unclear
Completeness of outcome data (no attrition bias)
1, <20% Lost to followup within a year
0, >20% Lost to followup within a year, or unclear

Appendix 2: Primary tumor characteristics of all patients with femoral metastases per study (Figure 3) (%)

Author, Year	Patients	Femurs	Breast	Lung	Kidney	Prostate	MM	Lymph.	Colon/ Rectum	Unknown	Other
Choy et al. 2015	19	19	6 (32)	3 (16)	3 (16)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	6 (32)
Hettwer et al. 2015	105	111	35 (33)	19 (18)	13 (12)	10 (10)	8 (8)	4 (4)	4 (4)	3 (3)	9 (9)
Janssen et al. 2015	417	417	125 (30)	95 (23)	26 (6)	29 (7)	57 (14)	0 (0)	7 (2)	13 (3)	65 (16)
Piccioli et al. 2014	80	80	23 (29)	8 (10)	2 (3)	12 (15)	16 (20)	4 (5)	6 (8)	0 (0)	9 (11)
Shemesh et al. 2014	19	21	9 (47)	5 (26)	0 (0)	1 (5)	3 (16)	0 (0)	1 (5)	0 (0)	0 (0)
Fakler et al. 2013	20	20	8 (40)	1 (5)	0 (0)	2 (10)	2 (10)	0 (0)	1 (5)	2 (10)	4 (20)
Weiss et al. 2013	194	196	70 (36)	19 (10)	27 (14)	34 (18)	0 (0)	0 (0)	0 (0)	16 (8)	28 (14)
Asavamongkolgul et al. 2012	27	27	10 (37)	3 (11)	0 (0)	2 (7)	1 (4)	0 (0)	2 (7)	1 (4)	8 (30)
Harvey et al. 2012	158	159	41 (26)	19 (12)	19 (12)	10 (6)	14 (9)	2 (1)	7 (4)	3 (2)	43 (27)
Steensma et al. 2012	298	298	75 (25)	50 (17)	39 (13)	12 (4)	26 (9)	12 (4)	12 (4)	0 (0)	72 (24)
Hattori et al. 2011	16	16	8 (50)	1 (6)	2 (13)	3 (19)	0 (0)	0 (0)	0 (0)	1 (6)	1 (6)
Parker et al. 2011	137	145	52 (36)*	17 (12)*	4 (3)*	33 (23)*	9 (6)*	13 (9)*	2 (1)*	11 (8)*	4 (3)*
Zacherl et al. 2011	59	64	24 (41)	10 (17)	5 (8)	8 (14)	0 (0)	0 (0)	2 (3)	0 (0)	10 (17)
Sarahrudi et al. 2009	142	146	66 (46)	14 (10)	7 (5)	11 (8)	6 (4)	0 (0)	0 (0)	0 (0)	38 (27)
Selek et al. 2008	44	45	17 (39)	13 (30)	2 (5)	3 (7)	0 (0)	0 (0)	0 (0)	0 (0)	9 (20)
Rethnam et al. 2007	11	11	5 (45)	2 (18)	0 (0)	3 (27)	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)
Wedin et al. 2005	142	146	45 (32)	16 (11)	8 (6)	36 (25)	0 (0)	0 (0)	0 (0)	0 (0)	37 (26)
Moholkar et al. 2004	42	48	24 (50)*	7 (15)*	2 (4)*	5 (10)*	6 (13)*	1 (2)*	1 (2)*	0 (0)*	2 (4)*
Ramakrishnan et al. 2004	25	28	8 (29)*	4 (14)*	0 (0)*	9 (32)*	5 (18)*	0 (0)*	1 (4)*	0 (0)*	1 (4)*
Ward et al. 2003	182	182	39 (21)	41 (23)	16 (9)	17 (9)	28 (15)	9 (5)	0 (0)	3 (2)	29 (16)
Assal et al. 2000	10	12	5 (50)	3 (30)	1 (10)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Giannoudis et al. 1999	27	30	15 (56)	8 (30)	2 (7)	2 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Appendix 2: Primary tumor characteristics of all patients with femoral metastases per study (Figure 3) (%) (*continued*)

Author, Year	Patients	Femurs	Breast	Lung	Kidney	Prostate	MM	Lymph.	Colon/ Rectum	Unknown	Other
Chien et al. 1997	30	32	14 (44)	4 (13)	2 (6)	1 (3)	0 (0)	0 (0)	0 (0)	6 (19)	5 (16)
Algan et al. 1996	27	27	16 (59)	1 (4)	5 (19)	0 (0)	3 (11)	0 (0)	0 (0)	1 (4)	1 (4)
Nargol et al. 1996	10	10	5 (50)	1 (10)	0 (0)	1 (10)	2 (20)	0 (0)	0 (0)	1 (10)	0 (0)
Rompe et al. 1994	50	50	36 (72)	0 (0)	14 (28)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Broos et al. 1993	65	77	49 (75)	3 (5)	4 (6)	4 (6)	0 (0)	0 (0)	0 (0)	1 (2)	4 (6)
Borel Rinkes et al. 1990	34	34	27 (79)	2 (6)	0 (0)	3 (9)	2 (6)	0 (0)	0 (0)	0 (0)	0 (0)
Fasano et al. 1988	10	11	4 (40)	2 (20)	1 (10)	2 (20)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)
Behr et al. 1985	38	48	17 (45)	4 (11)	2 (5)	1 (3)	9 (24)	0 (0)	1 (3)	1 (3)	3 (8)
Lane et al. 1980	163	167	100 (61)	12 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	51 (31)

MM = Multiple Myeloma, Lymph. = Lymphoma. Primary tumor type for femur metastases not available for the following studies: Arvinius et al. 2014, Sorensen et al. 2013, Potter et al. 2009, Chandrasekar et al. 2008, Park et al. 2007, Datir et al. 2004, Piatek et al. 2003, Korkala et al. 1991, Yazawa et al. 1990

3

Appendix 3: Affected anatomical area and use of cement per implant type for proximal femur metastatic fractures (%)

Author, Year	Implant	Femurs	Pathological fractures	Cement	Head /Neck	Troch. Area	Subtroch. Area	Prox. Shaft	Unspec.
Hettwer et al. 2015	EPR	111	70 (63)	-	0 (0)	0 (0)	0 (0)	0 (0)	111 (100)
Janssen et al. 2015	EPR	70	55 (79)	68 (97)	28 (40)	30 (43)	12 (17)	0 (0)	0 (0)
Sorensen et al. 2013	EPR	105	-	-	0 (0)	0 (0)	0 (0)	0 (0)	105 (100)
Weiss et al. 2013	EPR	82	-	-	0 (0)	0 (0)	82 (100)	0 (0)	0 (0)
Harvey et al. 2012	EPR	113	70 (62)	113 (100)	0 (0)	0 (0)	0 (0)	0 (0)	113 (100)
Steensma et al. 2012	EPR	197	80 (41)	197 (100)	0 (0)	115 (58)	82 (42)	0 (0)	0 (0)
Hattori et al. 2011	EPR	16	13 (81)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	16 (100)
Parker et al. 2011	EPR	54	54 (100)	29 (54)	0 (0)	0 (0)	0 (0)	0 (0)	54 (100)
Zacherl et al. 2011	EPR	13	13 (100)	13 (100)	0 (0)	0 (0)	0 (0)	0 (0)	13 (100)
Potter et al. 2009	EPR	39	16 (41)	39 (100)	0 (0)	0 (0)	0 (0)	0 (0)	39 (100)
Sarahrudi et al. 2009	EPR	23	23 (100)	23 (100)	0 (0)	0 (0)	0 (0)	0 (0)	23 (100)
Chandrasekar et al. 2008	EPR	81	56 (69)	81 (100)	0 (0)	0 (0)	0 (0)	0 (0)	81 (100)
Selek et al. 2008	EPR	45	28 (62)	45 (100)	0 (0)	0 (0)	0 (0)	0 (0)	45 (100)
Park et al. 2007	EPR	31	-	-	0 (0)	0 (0)	0 (0)	0 (0)	31 (100)
Wedin et al. 2005	EPR	109	-	106 (97)	54 (50)	28 (26)	27 (25)	0 (0)	0 (0)
Ward et al. 2003	EPR	46	-	-	0 (0)	0 (0)	0 (0)	0 (0)	46 (100)
Chien et al. 1997	EPR	12	10 (83)	-	11 (92)	1 (8)	0 (0)	0 (0)	0 (0)
Rompe et al. 1994	EPR	25	9 (36)	-	0 (0)	0 (0)	0 (0)	0 (0)	25 (100)
Broos et al. 1993	EPR	36	-	-	15 (42)	10 (28)	11 (31)	0 (0)	0 (0)
Korkala et al. 1991	EPR	15	15 (100)	-	8 (53)	7 (47)	0 (0)	0 (0)	0 (0)
Borel Rinkes et al. 1990	EPR	34	27 (79)	34 (100)	27 (79)	0 (0)	0 (0)	0 (0)	0 (0)
Yazawa et al. 1990	EPR	41	-	41 (100)	27 (66)	14 (34)	0 (0)	0 (0)	0 (0)

Appendix 3: Affected anatomical area and use of cement per implant type for proximal femur metastatic fractures (%) (*continued*)

Author, Year	Implant	Femurs	Pathological fractures	Cement	Head /Neck	Troch. Area	Subtroch. Area	Prox. Shaft	Unspec.
Lane et al. 1980	EPR	163	125 (77)	75 (46)	78 (48)	55 (34)	30 (18)	0 (0)	0 (0)
Choy et al. 2015	IMN	10	10 (100)	10 (100)	0 (0)	2 (20)	8 (80)	0 (0)	0 (0)
Janssen et al. 2015	IMN	302	100 (33)	7 (2)	28 (9)	146 (48)	128 (42)	0 (0)	0 (0)
Arvinius et al. 2014	IMN	56	37 (66)	-	0 (0)	0 (0)	0 (0)	0 (0)	56 (100)
Piccioli et al. 2014	IMN	80	80 (100)	8 (10)	0 (0)	30 (38)	22 (28)	28 (35)	0 (0)
Shemesh et al. 2014	IMN	21	11 (52)	0 (0)	0 (0)	11 (52)	5 (24)	5 (24)	0 (0)
Fakler et al. 2013	IMN	12	12 (100)	3 (25)	0 (0)	0 (0)	0 (0)	0 (0)	12 (100)
Weiss et al. 2013	IMN	108	-	-	0 (0)	0 (0)	108 (100)	0 (0)	0 (0)
Harvey et al. 2012	IMN	46	21 (46)	-	0 (0)	0 (0)	0 (0)	0 (0)	46 (100)
Steensma et al. 2012	IMN	82	27 (33)	31 (38)	0 (0)	7 (9)	75 (91)	0 (0)	0 (0)
Parker et al. 2011	IMN	40	40 (100)	-	0 (0)	0 (0)	0 (0)	0 (0)	40 (100)
Zacherl et al. 2011	IMN	37	37 (100)	4 (11)	0 (0)	8 (22)	14 (38)	10 (27)	5 (14)
Rethnam et al. 2007	IMN	11	9 (82)	-	0 (0)	0 (0)	0 (0)	0 (0)	11 (100)
Wedin et al. 2005	IMN	24	-	6 (25)	0 (0)	4 (17)	20 (83)	0 (0)	0 (0)
Datir et al. 2004	IMN	17	13 (76)	-	0 (0)	0 (0)	17 (100)	0 (0)	0 (0)
Moholkar et al. 2004	IMN	48	26 (54)	-	0 (0)	0 (0)	0 (0)	0 (0)	48 (100)
Ramakrishnan et al. 2004	IMN	28	5 (18)	-	0 (0)	0 (0)	28 (100)	0 (0)	0 (0)
Piatek et al. 2003	IMN	18	-	0 (0)	0 (0)	0 (0)	0 (0)	6 (33)	12 (67)
Assal et al. 2000	IMN	12	6 (50)	0 (0)	1 (8)	1 (8)	7 (58)	3 (25)	0 (0)
Giannoudis et al. 1999	IMN	17	-	-	0 (0)	0 (0)	0 (0)	17 (100)	0 (0)
Algan et al. 1996	IMN	12	-	0 (0)	1 (8)	4 (33)	5 (42)	0 (0)	2 (17)
Nargol et al. 1996	IMN	10	10 (100)	0 (0)	0 (0)	5 (50)	5 (50)	0 (0)	0 (0)

Appendix 3: Affected anatomical area and use of cement per implant type for proximal femur metastatic fractures (%) (*continued*)

Author, Year	Implant	Femurs	Pathological fractures	Cement	Head /Neck	Troch. Area	Subtroch. Area	Prox. Shaft	Unspec.
Yazawa et al. 1990	IMN	18	-	12 (67)	0 (0)	18 (100)	0 (0)	0 (0)	0 (0)
Fasano et al. 1988	IMN	11	9 (82)	3 (27)	0 (0)	0 (0)	11 (100)	0 (0)	0 (0)
Behr et al. 1985	IMN	34	15 (44)	-	0 (0)	8 (24)	7 (21)	19 (56)	0 (0)
Janssen et al. 2015	ORIF	45	18 (40)	27 (60)	3 (7)	27 (60)	15 (33)	0 (0)	0 (0)
Asavamongkolgul et al. 2012	ORIF	27	9 (33)	19 (70)	0 (0)	27 (100)	0 (0)	0 (0)	0 (0)
Steensma et al. 2012	ORIF	19	6 (32)	8 (42)	0 (0)	16 (84)	3 (16)	0 (0)	0 (0)
Parker et al. 2011	ORIF	35	35 (100)	-	0 (0)	0 (0)	0 (0)	0 (0)	35 (100)
Zacherl et al. 2011	ORIF	12	12 (100)	12 (100)	0 (0)	0 (0)	0 (0)	0 (0)	12 (100)
Sarahrudi et al. 2009	ORIF	15	15 (100)	-	0 (0)	0 (0)	0 (0)	0 (0)	15 (100)
Wedin et al. 2005	ORIF	13	-	3 (23)	1 (8)	8 (62)	4 (31)	0 (0)	0 (0)
Ward et al. 2003	ORIF	13	-	-	0 (0)	0 (0)	0 (0)	0 (0)	13 (100)
Rompe et al. 1994	ORIF	25	8 (32)	25 (100)	0 (0)	0 (0)	0 (0)	0 (0)	25 (100)
Broos et al. 1993	ORIF	19	-	19 (100)	0 (0)	5 (26)	14 (74)	0 (0)	0 (0)
Behr et al. 1985	ORIF	10	5 (50)	-	2 (20)	5 (50)	3 (30)	0 (0)	0 (0)

- = not available, Troch. = Trochanteric, Subtroch = Subtrochanteric, Prox. Shaft = Proximal shaft, Unspec. = Unspecified, EPR = Endoprosthesis, IMN = Intramedullary nail, ORIF = Open reduction internal fixation