Surgical decision-making for long bone metastases

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CHAPTER 8

Management Of Metastatic Humeral Fractures: Variations According To Orthopedic Subspecialty, Tumor Characteristics

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Orthopaedics & Traumatology: Surgery & Research 2018 Feb; 104(1):59-65

Presented at:
European Musculoskeletal Oncology Society Annual Meeting 2016, La Baule, France.
Musculoskeletal Tumor Society Annual Meeting 2016, Detroit, Michigan, USA.

ACKNOWLEDGMENTS:

The authors thank the Skeletal Oncology Research Group* and Science Of Variation Group†

* members of the Skeletal Oncology Research Group: Albert J. Aboulafia; John A. Abraham; Dimosthenis Andreou; Luis A. Aponte-Tinao; Robert U. Ashford; Tessa Balach; Nicholas M. Bernthal; David J. Biau; Susan V. Bukata; George T. Calvert; Felix H. Cheung; Paul W. Clarkson; Matthew W. Colman; Judd E. Cummings; Francis Cyran; Timothy A. Damron; Will Eward; German L. Farfalli; Peter C. Ferguson; Marco Ferrone; Joerg Friesenbichler; Philipp T. Funovics; Mark C. Gebhardt; Michelle Ghert; Parker Gibbs; Francois Gouin; Robert J. Grimer; James B. Hayden; John H. Healey; Eric Henderson; Robert M. Henshaw; Marc H. Isler; Shintaro Iwata; Lee M. Jeys; Muchael J. Joyce; Johnny Keller; Piya Kiatisevi; David M. King; Nitin Kukkar; Minna K. Laitinen; Andreas Leithner; Adam S. Levin; Edward A. Levine; Dieter Lindskog; Santiago A. Lozano Calderon; Joel Mayerson; Corey O. Montgomery; Carol D. Morris; John C. Neilson; Lukas Nystrom; Vania Oliveira; Eduardo J. Ortiz-Cruz; Joshua C. Patt; Robert H. Quinn; Rajiv Rajani; Lor R. Randall; John E. Ready; Peter S. Rose; Matt Steensma; Gwen M.L. Sys; Richard M. Terek; Frank Traub; Takafumi Ueda; Rikard Wedin; Kurt R. Weiss; Jay Wunder; Daniel Wurtz; and Rosanna L. Wustrack

† members of the Science of Variation Group: Jeffrey Abrams; Lars E. Adolfsson; Michael H. Amini; Paul Appleton; George C. Babis; Efstathios G. Ballas; Flamarion Dos Santos Batista; Grant J. Bayne; Thierry Begue; Arne Berner; Jan Biert; Lars C. Borris; Maarten W.G.A. Bronkhorst; Richard Buckley; Tim Chesser; Joseph M. Conflitti; Brett D. Crist; Brian J. Cross; Thomas DeCoster; Derek F.P. van Deurzen; Thomas Dienstknecht; Percy V. van Eerten; Nelson Elias; Denise Eygendaal; Christos Garnavos; Peter Giannoudis; Vincenzo Giordano; Hans Goost; Roger G. Hackney; Jeremy Hall; Eric Mark Hammerberg; Ian Harris; Steven J. Hattrup; Robert Haverlag; Huub van der Heide; Svenhjalmar van Helden; Edward F. Ibrahim; Prashanth Inna; Vishwanath M. Iyer; Richard Jenkinson; Kyle Jeray; Clifford Jones; Axel Jubel; Koroush Kabir; Nikolaos K. Kanakaris; Matej Kastelec; Jack Elias Kazanjian; Cyrus Klostermann; Georges Kohut; Peter Krause; Anze Kristan; Paul Levin; Iain McGraw; Matthew Menon; Milind Merchant; Ladislav Mica; Thomas Mittlmeier; Jesus Moreta; Matt Mormino; Betsy M. Nolan; Timothy Omara; Richard S. Page; Emilija Stojkovska Pemovska; Rodrigo Pesantez; Marinis Pirpiris; Lodewijk M.S.J. Poelhekke; Michael Prayson; Michael Quell; Radzeli Mohd Ramli; Martin Richardson; Edward K. Rodriguez; Juan Miguel Rodríguez Roiz; Nigel Rossiter; Parag Sancheti; Michiel A.J. van de Sande; Wojciech Satora; Peter Schandelmaier; John A. Scolaro; Adam B. Shafritz; Raymond Malcolm Smith; Andy B. Spoor; Marc Swiontkowski; Lisa Taitsman; Theodoros Tosounidis; Michael Verhofstad; Anne J.H. Vochteloo; Richard Wallensten; Mohammad Waseem; Yoram Weil; and David Weiss

ABSTRACT

Objectives

To assess: (1) if there is a difference between orthopaedic oncology surgeons and other orthopaedic surgeons in their recommendation for treatment of metastatic humeral lesions, and (2) what patient and tumor characteristics were associated with the decision for treatment.

Design

Cross sectional survey study.

Setting

Online survey sent to two international groups of orthopaedic surgeons.

Participants

78 (48%) orthopaedic oncologists and 83 (52%) orthopaedic surgeons that were not regularly involved in the treatment of bone tumors.

Outcome Measures

Recommendation for treatment. Twenty-four case scenarios were created by combining: tumor type, life expectancy, fracture type, and anatomical location. Participants were asked for every case: what treatment would you recommend?

Results

There was a difference between orthopaedic oncologists and other subspecialty surgeons in recommendation for specific treatments: intramedullary nailing was less often recommended by orthopaedic oncologists (53%, 95% CI: 47-59) compared to other surgeons (62%, 95% CI: 57-67) (p = 0.023); while endoprosthetic reconstruction (orthopaedic oncologists: 8.8% [95% CI: 6.6-11], other surgeons: 3.6%[95% CI: 2.3-4.8], $p < 0.001$) and plate-screw fixation (orthopaedic oncologists: 19%[95% CI: 14-25], other surgeons: 9.5%[95% CI: 5.9-13], $p = 0.003$) were more often recommended by orthopaedic oncologists. There was no difference in recommendation for nonoperative management. There were differences in recommendation for specific treatments based on tumor type, life expectancy, and anatomical location, but not fracture type.

Conclusions

Subspecialty training and patient and tumor characteristics influence the decision for surgical management and the decision for a specific implant in metastatic humeral fractures.

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INTRODUCTION

Treatment of metastatic humeral lesions is a challenge as indications vary, several implant options exist, different types of adjuvant treatment are available, and many patient and tumor factors need to be considered. Commonly used implants are intramedullary nails, endoprostheses, and plate and screws.[1,2] Case-series and retrospective studies support the use of each of these implants and high quality comparative studies are lacking.[1] Commonly cited patient and tumor factors that are considered in surgical decision making are: tumor type, life expectancy, location of the tumor, and fracture type.[2-5] Several orthopaedic subspecialties take care of patients with metastatic humeral lesions, including orthopaedic oncology surgeons, trauma surgeons, and general orthopaedic surgeons. As training among these subspecialties differs, their surgical approach might differ as well. We therefore investigated if orthopaedic oncology surgeons approach metastatic humeral lesions differently than surgeons who are not regularly involved in the treatment of bone tumors.

It is unclear to what extend these patient, tumor, and surgeon factors influence surgical decision making. Better understanding of what treatment is recommended and the factors that have the greatest influence on recommending specific treatment for metastatic humeral lesions would help: development of guidelines, highlight areas that require further (comparative) study, create techniques to improve measurement of these criteria (e.g. techniques to estimate life expectancy or fracture risk), and educate trainees.

Specifically, we assessed: (1) if there was a difference between orthopaedic oncology surgeons and other orthopaedic surgeons in their recommendation for treatment, and (2) what patient and tumor characteristics were associated with the decision for treatment.[6]

METHODS

Study Design

Our institutional review board exempted this study from review and informed consent was not needed. We created 24 case scenarios by combining four categorical variables: tumor type (breast, renal cell, lung; 8 cases each), estimated life expectancy (<3, >3 months; 12 cases each), fracture type (displaced pathological, impending; 12 cases each), and anatomical location (proximal, diaphyseal; 12 cases each). Humeral metastases from breast, renal cell, and lung tumors were chosen because these are most common.[1] We explained for every case that the patient had activity related pain, that the tumor was widely metastatic, that the patient walked with a walker, and that he or she has not had radiotherapy. We searched our institutions' humeral metastases database for the first random radiograph that matched the constructed case scenario (i.e. matched tumor type, fracture type, and anatomical location).

We used SurveyMonkey (Palo Alto, CA, USA), a web-based assessment tool, to develop a survey including the 24 case scenarios. For all cases, we asked: *what treatment would you recommend: Intramedullary nailing, Endoprosthetic reconstruction, Plate-screw fixation, or Nonoperative management?* In addition, we asked for the 12 impending fracture cases: *What is the fracture risk on a scale from 0 to 100%?* We collected the following demographics from participants: year finished residency, sex, country, subspecialties, and the proportion of practice dedicated to oncology.

This was the first study of a new collaborative in musculoskeletal oncology, named the Skeletal Oncology Research Group (SORG). The idea to develop this collaborative was based on the existing Science of Variation Group (SOVG, an international group of upper extremity and trauma surgeons).[7] The objective of this new group is to study variation in interpretation and management of musculoskeletal tumors. We invited people to this new group by emailing the members of two professional organizations (the European MusculoSkeletal Oncology Society [n = 156] and the Connective Tissue Oncology Society [n = 783]) and we also reached out to our colleagues, friends, and acquaintances (n = 83); we welcome all interested physicians involved in treatment of musculoskeletal tumors who wish to join. Eighty-five people subscribed (8.3% [85/1,022]) and 71 orthopaedic oncology surgeons completed this study.

We also invited all trauma surgeons and shoulder and elbow surgeons of the SOVG (n = 441) and specifically asked them to only complete the survey if they treat metastatic humeral lesions. One hundred thirty (29%) members responded: 22 indicated that they do not treat this condition, and 18 did not complete all questions, leaving 90 (20%) complete surveys. However, 7 SOVG members indicated that orthopaedic oncology was one of their subspecialties and we therefore grouped them with the orthopaedic oncologists from the SORG; of the 161 participants in total, 78 (48%) were orthopaedic oncologists (surgeons), the remaining 83 (52%) participants were not.

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Statistical Analysis

An ante-hoc power calculation determined that 122 participants (61 per group) would provide 80% statistical power (beta 0.20; alpha 0.05) to detect a difference in proportion of recommendation for a specific treatment of 20% assuming a proportion of 10% in one group, and 30% in the other.

We assessed if there was a difference in baseline characteristics between groups using a Fisher exact test for categorical variables and an unpaired T-test for continuous variables.

We calculated treatment scores per specific treatment per surgeon by dividing the amount of cases they recommend a specific treatment for by the number 24 (i.e. the total number of cases) and presented this as a percentage. The score ranges from 0 to 100% with a higher score indicating a higher likelihood of choosing a specific treatment. We used an unpaired T-test to compare the scores for the four specific treatments between the two study groups. We also calculated the observed proportion of agreement and did a Fleiss' kappa analysis for choosing: (1) operative treatment versus nonoperative treatment, and (2) specific implants. Kappa is a quantitative measure of agreement among observers and is adjusted for the amount of agreement that can be expected to occur by chance alone.[8,9] Bootstrapping (resamples = 1,000) was used to calculate a standard error, z statistic, *p* value, and 95% confidence interval.[10]

Subsequently, we calculated treatment scores per specific treatment per case by dividing the amount of surgeons choosing a treatment by the total number of surgeons within the study group. We used an unpaired T-test to assess the difference in treatment score based on dichotomous patient characteristics and one-way analysis of variance (ANOVA) for categorical patient characteristics.

Intraclass correlation coefficient (ICC) was used to demonstrate interobserver agreement for the estimated fracture risk. The ICC was calculated though a two-way mixed-effects model with absolute agreement. Absolute agreement assesses how much each fracture risk estimate per observer differs from the other observers. As with kappa, a score of 1 reflects perfect agreement in ICC, whereas 0 reflects no agreement. Fisher's z transformation was used to calculate *p* values.[11]

All statistical analyses were performed using Stata® 14.0 (StataCorp LP, College Station, TX, USA). A two-tailed *p* value less than 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

Of the 161 participants, 149 (93%) were men and the mean years in practice was 15 (Table 1). There was no difference in sex and years in practice between groups. Most participants were from North America (49%) and Europe (39%). There was a difference in location of practice between the two study groups; most participating orthopaedic oncology surgeons were from North America, while the majority of the other orthopaedic surgeons was from Europe ($p = 0.001$). We also found –as expected– differences in subspecialty training between both groups (Table 1). Among those not involved in treating bone tumors (other subspecialty orthopaedic surgeons); the majority was subspecialized in trauma surgery (88%).

Recommendation For Specific Treatment Based On Subspecialty

We found a difference between orthopaedic oncology surgeons and other subspecialty surgeons in recommendation for specific treatments: endoprosthetic reconstruction and plate-screw fixation were more often recommended by orthopaedic oncology surgeons, while intramedullary nailing was more often recommended by other subspecialty surgeons.

Table 1: Baseline characteristics of participating surgeons per group

	Group 1: Orthopaedic oncology surgeons (n = 78)	Group 2: Other subspecialty orthopaedic surgeons (n = 83)	
	Mean (±SD)	**Mean (±SD)**	**p value**
Years in practice	15 (10)	16 (8.9)	*0.495*
	n (%)	**n (%)**	
Sex			
Men	70 (90)	79 (95)	*0.235*
Women	8 (10)	4 (4.8)	
Location of practice			
North America	50 (64)	29 (35)	
Europe	22 (28)	40 (48)	
Asia	3 (3.8)	6 (7.2)	***0.001***
Autralia	0 (0)	5 (6)	
South America	3 (3.8)	3 (3.6)	
Percentage of practice dedicated to orthopaedic oncology surgery			
0 - 25%	8 (10)	-	
25 - 50%	6 (7.7)	-	-
50 - 75%	15 (19)	-	
75 - 100%	49 (63)	-	
Surgical Subspecialties*			
Orthopaedic oncology	78 (100)	0 (0)	***<0.001***
Trauma	8 (10)	73 (88)	***<0.001***
Arthroplasty	19 (24)	15 (18)	*0.342*
Shoulder and elbow	2 (2.6)	28 (34)	***<0.001***
General Orthopaedics	5 (6.4)	14 (17)	*0.052*
Hand and wrist	1 (1.3)	14 (17)	***0.001***
Foot and ankle	3 (3.8)	3 (3.6)	*0.999*
Spine	8 (10)	5 (6)	*0.391*
Sports	1 (1.3)	10 (12)	***0.010***
Paediatric	5 (6.4)	4 (4.8)	*0.739*
Other	2 (2.6)	1 (1.2)	*0.609*

bold font indicates a significant difference (two-tailed *p* value below 0.05). SD = standard deviation. - indicates not applicable. *Participants can have multiple subspecialties.

Fifty-three percent (SD±26%, 95% CI: 47 to 59) of orthopaedic oncologists recommended intramedullary nailing compared to 62% (SD±24%, 95% CI: 57 to 67) of other subspecialty surgeons (p = 0.023); endoprosthetic reconstruction was recommended by 8.8% (SD±9.8%, 95% CI: 6.6 to 11) of orthopaedic oncologists compared to 3.6% (SD±5.7%, 95% CI: 2.3 to 4.8) of other subspecialty surgeons (p < 0.001); and plate-screw fixation was recommended by 19% (SD±24%, 95% CI: 14 to 25) of orthopaedic oncologists compared to 9.5% (SD±16%, 95% CI: 5.9 to 13) of other subspecialty surgeons ($p = 0.003$). There was no difference in recommendation for nonoperative management between both groups.

Overall, intramedullary nailing was the most commonly recommended treatment (58%), followed by nonoperative management (22%), plate-screw fixation (14%), and endoprosthetic reconstruction (6.1%).

Interobserver agreement for recommending operative versus nonoperative management was poor among both orthopaedic oncologists (kappa: 0.23, 95% CI: 0.15 to 0.30, proportion of agreement: 76%) and other subspecialty surgeons (kappa: 0.25, 95% CI: 0.18 to 0.33, proportion of agreement: 72%) and did no differ between these groups ($p = 0.642$). When assessing interobserver agreement for recommending specific treatments, we found poor agreement among both orthopaedic oncologists (kappa: 0.16, 95% CI: 0.11 to 0.21, proportion of agreement: 46%) and other subspecialty surgeons (kappa: 0.19, 95% CI: 0.14 to 0.24, proportion of agreement: 56%) and again no difference between groups ($p = 0.369$).

Recommendation For Specific Treatment Based On Patient Characteristics

There were differences in recommendation for specific treatments based on tumor type, life expectancy, and anatomical location, but not fracture type (Table 2).

Among orthopaedic oncology surgeons, we found that plate-screw fixation was more often recommended for renal cell carcinoma (25%), as compared to breast (14%) and lung carcinoma (18%) ($p = 0.038$). Both endoprosthetic reconstruction (>3 months: 15%, <3 months: 2.7%, $p = 0.024$) and plate-screw fixation (>3 months: 24%, <3 months: 14%, $p = 0.004$) were more often recommended for patients who had a life expectancy over 3 months. Nonoperative management was rarely recommended in patients who were expected to live longer than 3 months (>3 months: 3.1%, <3 months: 35%, $p < 0.001$). Recommendation for a specific implant; intramedullary nailing (proximal: 38%, diaphyseal: 68%, $p < 0.001$), endoprosthetic reconstruction (proximal: 14%, diaphyseal: 3.3%, $p = 0.046$), and plate-screw fixation (proximal: 24%, diaphyseal: 15%, $p = 0.014$) also differed based on the anatomical location of the metastatic lesion (Table 2).

Among other subspecialty surgeons, we found that the decision for intramedullary nailing (>3 months: 73%, <3 months: 50%, $p = 0.011$), plate-screw fixation (>3 months: 14%, <3 months: 5.1%, $p < 0.001$), and nonoperative management (>3 months: 6.5%, <3 months: 43%, $p < 0.001$) differed based on life expectancy. Recommendation for a specific implant; intramedullary nailing (proximal: 49%, diaphyseal: 75%, $p = 0.003$), endoprosthetic reconstruction (proximal: 6.5%, diaphyseal: 0.6%, $p = 0.031$), and plate-screw fixation (proximal: 13%, diaphyseal: 5.6%, $p = 0.004$) also differed based on the anatomical location of the metastatic lesion (Table 2).

Table 2: Variation in management of metastatic humerus lesions based on case characteristics

	Group 1: Orthopaedic oncology surgeons							
	Intramedullary nail		**Endoprosthetic reconstruction**		**Plate-screw fixation**		**Nonoperative management**	
Tumor type	**Mean (±SD)**	***p* value**	**Mean (±SD)**	***p* value**	**Mean (±SD)**	***p* value**	**Mean (±SD)**	***p* value**
Breast carcinoma	54 (31)		9.0 (17)		14 (7.9)		23 (22)	
Renal cell carcinoma	47 (16)	*0.690*	14 (15)	*0.331*	25 (8.9)	**0.038**	13 (15)	*0.611*
Lung carcinoma	57 (16)		3.5 (4.8)		18 (8.1)		21 (21)	
Estimated life expectancy								
< 3 months	48 (20)	*0.303*	2.7 (4.8)	***0.024***	14 (8.1)	**0.004**	35 (15)	***<0.001***
> 3 months	58 (24)		15 (17)		24 (7.5)		3.1 (4.2)	
Fracture type								
Displaced Pathological fracture	53 (25)	*0.963*	11 (15)	*0.365*	20 (6.9)	*0.785*	16 (17)	*0.417*
Impending fracture	53 (20)		6.2 (12)		19 (11)		22 (22)	
Anatomical location								
Proximal	38 (20)	***<0.001***	14 (17)	***0.046***	24 (7.7)	**0.014**	24 (22)	*0.235*
Diaphysis	68 (12)		3.3 (4.5)		15 (8.7)		14 (16)	
	Group 2: Other subspecialty orthopaedic surgeons							
	Intramedullary nail		**Endoprosthetic reconstruction**		**Plate-screw fixation**		**Nonoperative management**	
Tumor type	**Mean (±SD)**	***p* value**	**Mean (±SD)**	***p* value**	**Mean (±SD)**	***p* value**	**Mean (±SD)**	***p* value**
Breast carcinoma	58 (29)		4.8 (11)		9.0 (7.1)		28 (25)	
Renal cell carcinoma	65 (20)	*0.848*	3.2 (4.4)	*0.823*	12 (8.5)	*0.493*	20 (21)	*0.781*
Lung carcinoma	63 (21)		2.7 (4.3)		7.7 (5.5)		27 (24)	
Estimated life expectancy								
< 3 months	50 (20)	**0.011**	1.0 (2.5)	*0.065*	5.1 (3.7)	***<0.001***	43 (16)	***<0.001***
> 3 months	73 (21)		6.1 (8.8)		14 (6.9)		6.5 (7.2)	
Fracture type								
Displaced Pathological fracture	64 (26)	*0.702*	5.0 (8.8)	*0.307*	9.1 (6.6)	*0.787*	22 (22)	*0.539*
Impending fracture	60 (21)		2.1 (4.0)		9.9 (7.7)		28 (24)	
Anatomical location								
Proximal	49 (22)	**0.003**	6.5 (8.8)	***0.031***	13 (7.6)	**0.004**	31 (25)	*0.175*
Diaphysis	75 (16)		0.60 (0.96)		5.6 (3.5)		19 (19)	

bold font indicates a significant difference (two-tailed *p* value below 0.05). The mean indicates the average percentage of surgeons recommending a specific treatment, SD = standard deviation.

Interobserver Agreement For Assessing Fracture Risk

The interobserver agreement for fracture risk estimation was poor among both orthopaedic oncologists (ICC: 0.053, 95% CI: 0.025 to 0.15) and other subspecialty surgeons (ICC: 0.042, 95% CI: 0.019 to 0.12) and did not differ between groups (p = 0.945).

DISCUSSION

Treatment of metastatic humeral lesions is a challenge and many factors are considered in surgical decision making. It is unclear to what extend tumor, patient, and surgeon characteristics influence the decision for surgical strategy. We found that orthopaedic oncology surgeons are less likely to choose intramedullary nailing, but more likely to use endoprosthetic reconstruction and plate-screw fixation as compared to colleagues that are not regularly involved in treatment of bone tumors. We also found that tumor type, life expectancy, and location of the fracture influence the decision for surgical strategy, but fracture type did not.

This study has limitations. First, this study only assessed the decision for operative versus nonoperative management and specific implants, but did not assess adjuvants (e.g. radiation therapy). There is substantial variation in use of these adjuvants.[1] Difference in decision for a specific implant may stem from differences in local treatment of the metastasis (e.g. curettage or resection). Second, only 6.9% of those invited for the SORG and 20% of the members of the SOVG completed the survey. Furthermore, participants are a subgroup within the larger community of orthopaedic surgeons that treat metastatic humeral lesions. The majority of participants are Western orthopaedic surgeons and this might limit the studies' generalizability. In addition, when comparing baseline characteristics we found a difference in location of practice between both study groups. This might confound the association of subspecialty with the decision for implants. However, stratifying participants from North America and Europe demonstrated the same trends in use of implants when comparing orthopaedic oncologists and other subspecialty surgeons. In addition, years in practice and sex did not differ between both groups. We therefore feel that the difference in decision for a specific implant based on subspecialty training was not confounded by years in practice, sex, or location of practice. Third, the analyses of interobserver agreement might have been subject to the so-called "kappa paradox" because the kappa values were considerably lower than the observed proportion of agreement, especially in the decision for operative versus nonoperative management (e.g. the kappa among orthopaedic oncologists was 0.23 [poor agreement], while the overall observed proportion of agreement was 76%).[8,9] The kappa paradox describes that if the prevalence of an outcome is low, it causes an imbalance in the marginal totals, generating a low kappa.[8] This might have been the case in calculating the kappa values in our study and we therefore also presented the observed proportions of agreement. We see this as a minor limitation as a comparison of kappa values or observed proportions of agreement did not result in a difference in interobserver agreement.

Our finding that orthopaedic oncology surgeons recommend endoprosthetic reconstruction and plate-screw fixation more often, and less commonly recommend intramedullary nailing as compared to other subspecialty surgeons probably has its root in their training. Orthopaedic oncologists are trained in the treatment of bone and soft tissue neoplasms, developmental dysplasias, tumor-like conditions, and major skeletal defects.[12] As such, they might be more comfortable with creating a bony defect by resection of a metastatic lesion and subsequently reconstructing this defect using a prosthesis or plate-screw fixation with cement augmentation or allograft to fill the defect. In addition, they might be more aware of options for adjuvant treatment than other subspecialists and therefore base their decision for an implant on its combination with adjuvant treatment. Furthermore, orthopaedic oncologists might be more often confronted with the local complications of surgical management (such as tumor progression) and therefore be more inclined to treat metastatic lesions aggressively. It would be interesting to compare surgical and oncological outcomes between orthopaedic oncologists and orthopaedic surgeons not regularly involved in treatment of bone tumors as their surgical decision making differs.

We also studied the impact of commonly cited patient and tumor factors that are considered in surgical decision making and found that estimated life expectancy is a strong

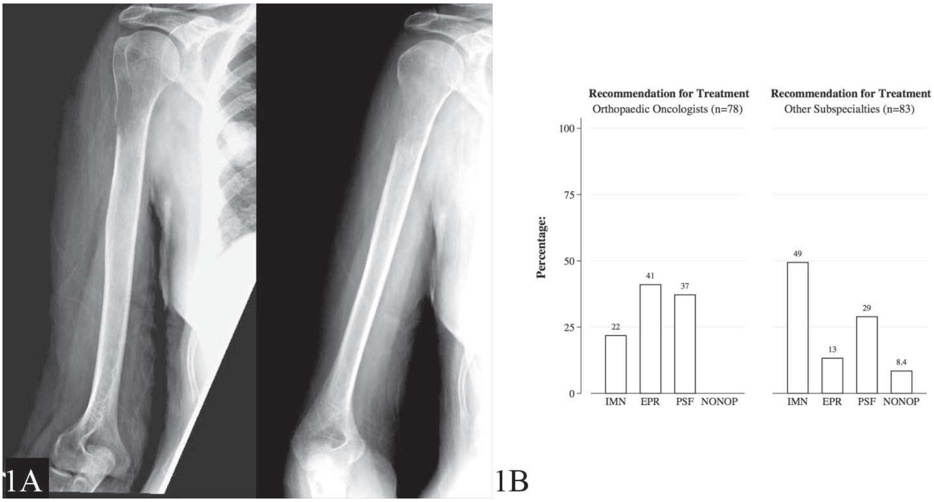
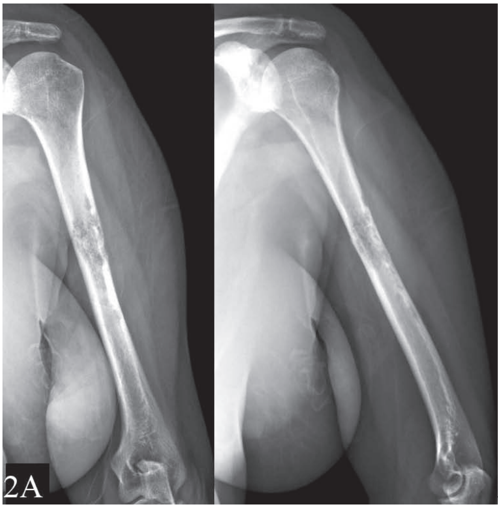
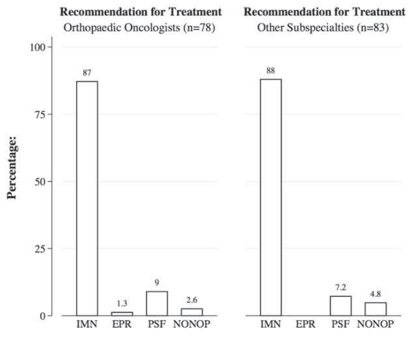


Figure 1A: An example of a case that demonstrated much variability in recommendation for treatment (Case 5B). Case description: A 59-year-old female has activity related pain in her arm. The patient has widely metastatic renal cell carcinoma. The patient walks with a walker, and has not had radiotherapy. The estimated life expectancy is more than 3 months.

Figure 1B: Bar graphs demonstrating the treatment recommendations among orthopaedic oncology surgeons (left) and other subspecialty surgeons (right) for the case presented in Figure 1A.

driver of recommending operative versus nonoperative management; operative treatment was recommended for almost all patients with more than 3 months life expectancy, while nonoperative management was recommended for over one-third of those with life expectancy less than 3 months. The strong influence of life expectancy on decision making emphasizes the need for an accurate method to estimate survival.[13] Tumor type, life expectancy, and anatomical location influences the decision for a specific implant. For example, intramedullary nailing was most commonly recommended for metastatic lesions located in the diaphysis, while endoprosthetic reconstruction and plate-screw fixation were more commonly recommended for proximal metastatic lesions. Trends in how these factors influence decision making were comparable between orthopaedic oncologists and other subspecialty surgeons. Some specific cases demonstrated more variability in recommendation for treatment (Figure 1) than others (Figure 2); participants seemed to be more likeminded when choosing treatment for diaphyseal lesions as compared to proximal lesions. Our findings can help to create guidelines by reaching consensus; this might reduce variation, improve quality of care, and decrease costs.[14,15] However, our findings do not imply that one approach is superior to another. Studies that directly compare outcomes between different treatments, preferably in a prospective experimental study design, are needed. Especially the areas that demonstrated most controversy (e.g. Figure 1) benefit from further comparative study.





2B

Figure 2A: An example of a case that demonstrated little variability in recommendation for treatment (Case 3B). Case description: A 62-year-old female has activity related pain in her arm. The patient has widely metastatic breast carcinoma. The patient walks with a walker, and has not had radiotherapy. The estimated life expectancy is more than 3 months.

Figure 2B: Bar graphs demonstrating the treatment recommendations among orthopaedic oncology surgeons (left) and other subspecialty surgeons (right) for the case presented in Figure 2A.

The interobserver agreement for assessment of fracture risk was poor. Fracture risk is an important factor in deciding whether to treat an impending fracture surgically or not. However, the accuracy of current classification systems (e.g. the Mirels classification; including the site, lesion type, size of the lesion, and pain) in predicting the risk of fracture is relatively poor.[16-18] A Mirels score of 9 or higher is commonly used as a cut off for recommending prophylactic fixation. New techniques, such as finite element analyses and CT-based rigidity analysis demonstrate promising results.[19-21] Including data from such techniques might improve fracture risk estimation.[22]

In conclusion, subspecialty training and patient and tumor characteristics influence the decision for surgical management and the decision for a specific implant in metastatic humeral lesions. Our findings can be used when developing guidelines and demonstrate where additional comparative study is most needed. It could be valuable to discuss metastatic humeral lesions cases preoperatively in a team with an orthopaedic oncologist because of their expertise in reconstructing major skeletal defects and knowledge about adjuvant treatments.

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