Optimising the treatment of patients with long bone metastases

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Chapter 5

Trends in surgical treatment of pathologic fractures of the long bones advocate the use of prognostic models to identify patients who benefit from centralized care

Based on a questionnaire among members of the Dutch Orthopaedic Society and EMSOS

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Abstract

Aim

The aim of this study was to assess the current trends in the estimation of survival and the preferred forms of treatment of pathological fractures among national and international general and oncological orthopaedic surgeons, and to explore whether improvements in the management of these patients could be identified in this way.

Methods

All members of the Dutch Orthopaedic Society (DOS) and European Musculoskeletal Oncology Society (EMSOS) were invited to complete a web-based questionnaire containing 12 cases.

Results

A total of 96 (10.1%; groups 1 and 2) of 948 members of the DOS and 33 (18.1%; group 3) of 182 members of the EMSOS replied. The estimation of survival was accurate by more than 50% of all three groups, if the expected survival was short (<3 months) or long (>12 months). General orthopaedic surgeons preferred using an intramedullary nail for fractures of the humerus and femur, irrespective of the expected survival or the origin of primary tumour or the location of the fracture. Oncological orthopaedic surgeons recommended prosthetic reconstruction in patients with a long expected survival.

Discussion

Identifying patients who require centralised care, as opposed to those who can be adequately treated in a regional centre, can improve the management of patients with pathologic fractures. This differentiation should be based on the expected survival, the type and extent of the tumour, and the location of the fracture.

Introduction

The most common malignant bone tumours in adults are metastases.[1] The increased number of patients with cancer, due to the ageing population, and their increased survival due to continuously improving systemic treatments, have increased the number of patients with bone metastases.[2] Although primary bone tumours are usually treated by specialized oncological orthopaedic surgeons, pathological fractures caused by metastases are generally treated by all orthopaedic surgeons, and in some countries also by trauma surgeons. Some hospitals may have protocols that assign the care of these fractures to a certain specialist, but generally treatment is performed by whomever the patient is referred to. It is not known whether this has an adverse effect on the standard of care, but it can be hypothesized that the frequent routine treatment of pathologic fractures leads to an increased understanding of these fractures, which may improve their management. In an attempt to optimize the care of these patients, there may be room for improvement in the current systems, in which pathologic fractures are treated by too many surgeons with only some experience in the fixation of pathologic fractures.

The aim of this study was to assess the current trends in the estimation of survival and preferred treatment among national and international general and oncological orthopaedic surgeons to explore whether areas of improvement in the care of patients with a pathologic fracture might be identified.

Methods

All members of the Dutch Orthopaedic Society (DOS) and European Musculoskeletal Oncology Society (EMSOS) were invited by email to participate in an anonymous web-based questionnaire (enclosed at the end of this chapter), followed by a reminder email five weeks later. Dutch oncological orthopaedic surgeons were approached through the EMSOS. The first section of the survey covered the demographics of the surgeons. The second section dealt with the estimation of survival and which factors surgeons considered of influence. The third section consisted of 12 clinical cases including actual and impending fractures of the humerus and femur. All answers were multiple choice. The cases were based on patients who had been treated by the authors to reflect daily practise. Six cases were described as the patients had presented; subsequently, one aspect of each case, such as the age of the patient or the number of bony metastases, was altered to establish the paired cases, leading to a total of 12 cases.

Descriptive statistics were applied for the outcomes of the questionnaire.

Table 5.1 Demographics of respondents of the questionnaire

	Group 1 *n (%)*	*Group 2* *n (%)*	*Group 3* *n (%)*
Total respondents	50	46	33
Experience			
Resident	15 (30)	13 (28)	0
≤ 5 years	5 (10)	8 (17)	5 (15)
6 – 10 years	11 (22)	13 (28)	10 (30)
11 – 20 years	14 (28)	6 (13)	7 (21)
> 20 years	5 (10)	6 (13)	11 (33)
Frequency of pathologic fracture treatment			
> 2 times per month	0	2 (4)	17 (52)
1 – 2 times per month	0	15 (33)	11 (33)
1 – 2 times per 3 months	0	29 (63)	5 (15)
1 – 2 times per 6 months	29 (58)	0	0
1 – 2 times per year	21 (42)	0	0
Subspecialty*			
Hip/knee	21 (42)	18 (39)	13 (39)
Arthroplasty	17 (34)	15 (33)	15 (45)
General orthopaedics	10 (20)	12 (26)	13 (39)
Traumatology	10 (20)	15 (36)	6 (18)
Upper extremity	13 (26)	6 (14)	6 (18)
Foot/ankle	3 (6)	7 (15)	2 (6)
Paediatrics	4 (8)	6 (14)	3 (9)
Oncology	0	3 (7)	33 (100)
Sports	9 (18)	1 (2)	2 (6)
Spine	3 (6)	9 (20)	1 (3)
In training	15 (30)	13 (28)	0

*Respondents (excl. residents) can have more than one subspeciality.

Respondents

Of the 948 members of the DOS who were approached, 96 (10.1%) completed the survey. Of the 182 members of the EMSOS who were approached, 33 (18.1%) replied. Respondents of the DOS were categorized into groups according to the frequency with which they treated pathologic fractures: once or twice every six months or less was classified as group 1 (52%; 50 of 96) and once or twice every three months or more was classified as group 2 (48%; 46 of 96). Respondents from the EMSOS were categorised as group 3. The demographics of the respondents are shown in table 5.1.

OPTIModel

The OPTIModel for the estimation of survival of patients with metastases of the long bones was used as the gold standard for the expected survival. These estimations were caterogized as: less than three months, three to six months, six to 12 months, and more than 12 months. This model is based on a large retrospective cohort and has been externally validated.[3]

Table 5.2 Prognostic factors for and methods to estimate survival according to respondents

	Group 1 *(n=50) (%)*	*Group 2* *(n=46) (%)*	*Group 3* *(n=33) (%)*
Prognostic factor[1]			
Primary tumour	48 (96)	45 (98)	28 (85)
Performance score	40 (80)	36 (78)	21 (64)
Visceral metastases	30 (60)	27 (58)	27 (82)
Brain metastases	24 (48)	33 (72)	22 (67)
Presence of other bone metastases	24 (48)	24 (52)	15 (45)
Age	15 (30)	19 (41)	13 (39)
Interval between primary tumour and metastasis	7 (14)	11 (24)	9 (27)
Number of other bone metastases	13 (26)	6 (13)	7 (21)
Actual fracture	8 (16)	4 (9)	7 (21)
Laboratory values	7 (14)	4 (9)	6 (18)
Pain	4 (8)	4 (9)	3 (9)
Gender	3 (6)	1 (2)	1 (3)
Survival estimation method[2]			
Ask oncologist	46 (92)	33 (72)	13 (39)
Tool/predictive model/nomogram	4 (8)	12 (26)	9 (27)
Own experience	0	1 (2)	9 (27)
Do not estimate survival	0	0	2 (6)

[1]Respondents were allowed to give a maximum of five answers. [2]Respondents could give one answer.

Results

What factors influence survival?

Respondents reported a mean of 4.6 factors (2 to 5) as being prognostic. The primary tumour was selected as a prognostic factor by 121 respondents (94%). An overview of the factors that were selected is shown in table 5.2.

How is survival estimated?

The methods of estimating survival are shown in table 5.2. A total of 79 respondents (82%) in groups 1 and 2 asked an oncologist for an estimation. This portion was smaller for group 3 (13/33; 39%). Almost one third of the latter group (9/33; 27%) based their estimate on their experience, while only one respondent in group 2 provided this answer. Prognostic models, tools, or nomograms were used by 25 (19%) respondents.

The estimation of survival for the cases

Respondents were asked to estimate survival in 11 cases (table 5.3). If a short survival of less than three months was expected according to the OPTIModel, the answers mainly corresponded in all groups (81%, 68%, and 79% for groups 1, 2, and 3, respectively). An effect of age was observed; the answers were more unequivocal if the patient was older. Group 3 respondents answered most consistently for patients with a long expected survival (>12 months); the mean rate of correct answers was 80% (64 to 97). The non-expert, not-frequent group 1 was less consistent if a long survival was expected; the mean rates of correct answers was 52% (45 to 58), while the non-expert, frequent group 2 recognized a long survival quite reliably with a mean rate of 68.5% (59 to 76). The difference in the estimation of long survival was especially evident in two cases with a solitary metastasis of a renal cell carcinoma (case 3a and 4a). In these two cases, the non-expert groups less frequently recognised the long expected survival. In the other four cases with a long survival, the difference between the expert and non-expert groups was less evident. In these more common cases from daily practice, the difference in the estimation of survival was more apparent between those that treat these patients regularly or not (groups 1 and 2). It was also easier for respondents to estimate a long survival in younger patients, as in cases 1a and 6a. In the older patients, as in case 1b and 6b, respondents were more inclined to give a shorter prognosis. Likewise, more respondents estimated a short survival for an older patient as when comparing case 2a with 2b. The cases with an intermediate expected survival (three to six months or six to 12 months) had low rates of correspondence between the respondents of each group (37%, 52%, and 52% for group 1, 2, and 3, respectively). The variation of answers was especially evident in group 1; in the other groups, however, the percentages of 'correct' answers were also not high (up to 64%).

Treatment

In 12 cases, respondents were asked to choose the most appropriate treatment bearing in mind the location and the type of lesion (i.e. actual or impending fracture), as shown on a radiograph, and the expected survival. Six cases had comparable fractures of the proximal humerus. Table 5.4 shows the preferred form of treatment chosen by the respondents. If survival was expected to be short (less than three months or between three and six months) the choices did not differ much between the three groups. The most popular choice within each group was an intramedullary nail (62%, 48%, and 68%, for group 1, 2, and 3, respectively), although fixation with a plate, radiotherapy, and conservative therapy were also well-considered options. If survival was expected to be between six and 12 months, differences between the groups became clear: groups 1 and 2 were indecisive about the most appropriate option, with answers ranging between all options, while group 2 predominantly remained to have a preference for intramedullary nails. Group 3 also continued to consider nails or plates, but increasingly tended towards prosthetic reconstruction. If a survival of >12 months was expected, the difference between the groups was most evident: group 3 would treat almost every patient (90%) with a prosthesis, while groups 1 and 2 considered all surgical options, treating only approximately 50% to 60% with a prosthesis. Of the latter respondents, one third (33%) would use a conventional shoulder prosthesis as opposed to a tumour reconstruction, while most of group 3 (84/90; 93%) would use a tumour prosthesis.

Six other cases described patients with a fracture of the proximal femur. Responses of the appropriate treatment in relation to the estimated survival are shown in table 5.5. Approximately 20% of the respondents in all groups would choose conservative treatment if survival was less than three months. Most (60%-77%), however, preferred fixation with an intramedullary nail, despite the short survival. If survival was expected to be between three and six months, an intramedullary nail was the most preferred treatment for groups 1 and 2 (80%), while group 3 considered prosthetic reconstruction (61%). The latter respondents wavered between a hemiarthroplasty, a total hip arthroplasty or a modular tumour prosthesis. When the expected survival became longer, and especially >12 months, most (73%) of group 3 would choose a tumour prosthesis, while most (55%) of groups 1 and 2 preferred an intramedullary nail.

Discussion

In the future, surgeons should have more specific knowledge about the indications for treatment and the varying forms of treatment that are available for the increasing number of patients who will present with a pathological fracture, in order to ensure the best outcome. Many aspects of this treatment remain controversial.

Table 5.3 Survival estimations by respondent groups per case. For survival estimation answers there were four choices: <3 months, 3-6 months, 6-12 months, >12 months. Answers are presented as percentage within each respondent group per case. The second column (OPTIModel) states the expected survival according to the OPTIModel

		Group 1 (n=50)				*Group 2 (n=46)*				*Group 3 (n=33)*			
Estimated Survival (months)		*<3*	*3-6*	*6-12*	*>12*	*<3*	*3-6*	*6-12*	*>12*	*<3*	*3-6*	*6-12*	*>12*
	OPTIModel												
Case 1a	>12 months	0	8	38	54	0	7	17	76	0	0	18	82
Case 1b	>12 months	2	10	46	42	2	11	24	63	3	12	21	64
Case 6a	>12 months	0	8	37	55	0	0	28	72	0	6	15	79
Case 6b	>12 months	2	14	39	45	2	7	24	67	3	6	27	64
Case 3a	>12 months	2	10	30	58	2	9	30	59	0	0	6	94
Case 4a	>12 months	0	14	30	56	0	4	22	74	0	3	0	97
Case 4b	6-12 months	24	30	34	12	13	28	44	15	6	9	64	21
Case 5a	3-6 months	42	40	16	2	24	50	22	4	33	39	27	0
Case 5b	3-6 months	50	38	12	0	26	61	11	2	36	52	12	0
Case 2a	< 3 months	72	22	6	0	54	35	4	7	73	18	9	0
Case 2b	< 3 months	90	8	2	0	83	13	4	0	85	15	0	0

Table 5.4 Treatments of actual pathologic fractures of the humerus by survival estimation per respondent group; results of six cases (1a, 1b, 3a, 3b, 5a, 5b). The results are given as percentages within each survival estimation subgroup of each respondent group (e.g., <3 months, group 1). Totals of each subgroup (denominator) are reported in the last row.

	Group 1				*Group 2*				*Group 3*			
Estimated Survival[1]	*<3*	*3-6*	*6-12*	*>12*	*<3*	*3-6*	*6-12*	*>12*	*<3*	*3-6*	*6-12*	*>12*
Conservative	13	3	2	0	21	4	0	0	15	0	2	1
Radiotherapy	12	13	15	12	3	5	6	4	19	16	7	1
Nail	68	67	41	24	48	68	55	26	62	51	38	2
Plate	7	7	11	12	24	15	21	9	4	30	24	5
Shoulder prosthesis	0	4	15	12	0	4	13	25	0	0	0	6
Tumour prosthesis	0	7	15	39	3	5	5	36	0	2	29	84
Total responses	60	72	85	83	29	82	62	100	26	43	45	82

Table 5.5 Treatments of actual pathologic fractures of the proximal femur by survival estimation per respondent group; results of six cases (2a, 3b, 4a, 4b, 6a, 6b). The results are given as percentages within each survival estimation subgroup of each respondent group (e.g., <3 months, group 1). Totals of each subgroup (denominator) are reported in the last row.

	Group 1				*Group 2*				*Group 3*			
Estimated Survival[1]	*<3*	*3-6*	*6-12*	*>12*	*<3*	*3-6*	*6-12*	*>12*	*<3*	*3-6*	*6-12*	*>12*
Conservative	18	0	0	0	19	3	0	0	22	0	0	0
Radiotherapy	0	0	0	0	1	0	0	0	0	0	0	0
Nail	70	81	63	55	77	80	76	54	60	39	11	14
Hemi	9	10	23	1	1	3	10	3	5	11	21	5
THP	2	6	1	11	1	3	14	14	2	11	8	8
Tumour prosthesis	1	2	12	33	0	13	0	30	13	39	61	73
Total responses	94	48	73	83	70	40	58	108	55	18	38	86

THP: total hip prosthesis

We should, however, wonder whether it is feasible for all surgeons currently managing these fractures, to remain up to date in this area. Should the treatment of pathologic fractures become a sub-speciality and should patients with these fractures be referred to such specialists? In order to assess whether these ideas are worth exploring, we designed a study based on a questionnaire to evaluate current similarities and differences in treatment between orthopaedic surgeons who treat pathologic fractures infrequently (group 1) or frequently (group 2), and those who specialize in oncology (group 3).

This study has limitations. First, the response rate of the questionnaire was low. The method of distribution of the questionnaire, by email, carries the risk of not reaching all the intended recipients. Although email lists of both societies were used, we do not know whether the email reached and was read by its recipient.

The low response rate might also be due to a low interest in pathologic fractures, compared with general orthopaedic problems, such as arthroplasty or traumatic fractures. Second, there might have been response bias among the respondents. Third, the groups of respondents were not completely comparable, as, for instance, group 3 did not contain residents. The distribution of experience is thus less broad in group 3 than in the other groups. This could affect the interpretation of the results as the differences could be attributed to the extent of experience. However, in the Netherlands, all residents receive training in orthopaedic oncology. It thus may have been that the residents who responded to the questionnaire were those with an interest in oncology after their oncology internship. Despite not having completed their training, these residents might have more knowledge about pathologic fractures and treat them more often than orthopaedic surgeons with extensive experience. This issue remains debatable, but it was clearly appropriate to include residents in the general orthopaedic categories in this exploratory study. Fourth, with regard to the survival estimation, the fact that the questionnaire was only sent to surgeons can be regarded a limitiation. In the light of the results of the question on how survival is estimated, to which many respondents replied that they ask the opinion of the medical oncologist, it could be that medical oncologists should have been included in the study. Although it would be interesting to compare the estimations of medical oncologists, orthopaedic surgeons, and prognostic models, this was not the aim of the study. Fifth, despite aiming to present varying cases, few fitted into the "intermediate" survival groups (three to six months, six to 12 months) compared with those with a long survival (>12 months). A more equal distribution among survival groups would have provided more insight into this difficult group, regarding both the estimate of survival and preferred treatment. Finally, in order to encourage completion of the questionnaire, the descriptions of the cases were based on real clinical cases and the replacement of clinical variables in the paired cases was limited to one variable, either age of the patients or number of metastases. Although there were three comparable cases with fractures of the proximal humerus and femur each, this is not a great number of comparable cases. As a result of these limitations, the outcomes of this study should be interpreted with care. The conclusions should be regarded as foundation for further research that should take these limitations into account.

The palliative intent of the treatment of pathologic fractures aims for a "once-in-a-lifetime fixation" and the correct estimation of survival is important in order to prevent over treatment in patients with a short survival, and undertreatment in those with a long survival. The results show that in most cases the estimation of survival of most respondents in each group was in accordance with the

estimation of the OPTIModel, but number of correct estimations differed greatly. Overall, the mean proportions of respondents estimating the correct survival were 53%, 64%, and 72% for groups 1, 2, and 3, respectively. The highest correct rates in group 1 were for the cases with a short estimated survival, while group 3 scored best on the cases with a solitary kidney metastasis. The long survival of the latter cases was not recognised by as many respondents in the other two groups, possibly indicating that recent studies showing a favourable outcome for patients with solitary kidney metastases[4] are less known among general orthopaedic surgeons. It is interesting to note that all three groups had difficulty with the cases with an intermediate survival. This, together with the good short-term estimations by group 1, might be due to the so-called "horizon effect", which suggests that clinicians are more accurate when recognising a shorter survival than a longer survival, similar to that recognized in weather forecasting.[5] The relatively good estimations for patients with a long estimated survival, especially respondents in groups 2 or 3, however, shows a trend opposite to the "horizon-effect". These differences cannot be explained. However, based on the answers respondents gave to the question "*how do you estimate survival?*" we can conclude that the non-experts consult an oncologist more frequently and are probably less used to estimating survival in general, compared with the oncological orthopaedic surgeons, who are more frequently confronted with this question when treating primary bone tumours.

The results show an influence of the age of the patient in all three groups. More respondents identified a long survival if the patient was younger, and a short survival if the patient was older. Thus, while few respondents identified age as prognostic factor for survival in the first question, it might play a role subconsciously. It may simply reflect human nature in that death is easier to accept when it occurs at an older age. However, no prognostic studies for survival after a pathologic fracture have shown an effect of age.[3,6-8] Surgeons should be aware of the subliminal effect of age and not let their estimations of survival be biased by it.

The results dealing with the estimation of survival cannot be compared with other studies, because to our knowledge no other questionnaires dealing with pathologic fractures asked respondents to give an estimation of survival.[9-11] One could discuss whether these results agree or disagree with those of studies that report that estimation of survival by physicians is frequently inaccurate.[5,12] Depending on the interpretation of the rate of correct estimation in this study, is a correct estimation of 60% accurate or is it too inaccurate? This is a difficult question to answer. The answer partly depends on the amount of influence of the expected survival on the choice of treatment. Also, although the OPTIModel

is a validated tool, its estimation of survival cannot be 100% correct. 'Correct' estimation in the context of this study should therefore be interpreted with caution, for we will never have a 100% correct estimation. Finally, it is not known whether some respondents already used a prognostic model to estimate survival for the cases in the questionnaire. If that is the case, the true estimations based on ones' experience might be even less correct, for the results might be biased by 'correct' estimations by models. Nonetheless, we believe that an overall rate of 'correct' estimations of 63% would suggest that prognostic tools should be used. The most benefit can be gained for the mid-term estimations. The use of a prognostic model would lead to more accurate estimation in the approximately 25% who estimated survival incorrectly in cases with an evidently short or long survival.

Respondents were asked to choose the most appropriate treatment for 12 cases, taking the estimated survival into account. For fractures of both the humerus and femur, most general orthopaedic surgeons would treat the fracture with an intramedullary nail, irrespective of the expected survival. Oncological orthopaedic surgeons, however, preferred to use a prosthesis if expected survival was >12 months. The percentage of oncological surgeons who recommended a prosthetic reconstruction for cases with a long expected survival was approximately twice that of general orthopaedic surgeons. This is in accordance with a previously performed survey by Janssen et al. regarding fractures of the humerus.[11] The fact that oncological surgeons are more comfortable with prosthetic reconstruction is not surprising, as their expertise lies in this field. However, the answers regarding resection and prosthetic reconstruction included the option to refer a patient for such treatment. The answers of general surgeons thus do not reflex the fact that they uncommonly perform this procedure, but that they less frequently recognise the need for such an implant. Many recent studies, however, have shown that prosthetic reconstruction is preferable to an intramedullary nail, especially if a long survival is expected.[13-16] The difference in this study is important for these patients, as currently their chance of receiving what is regarded as most appropriate treatment depends on the surgeon to whom they are referred. This trend should be further evaluated on a broader scale and by country, in order to further improve care. Should all orthopaedic surgeons be better educated, or should the care of certain patients be assigned to those with oncological training? Both are probably not feasible. The first because accumulating detailed knowledge is only regarded as worthwhile if the knowledge can be applied regularly. The second because of the incidence of pathologic fractures and the limited number of oncological orthopaedic surgeons in a region. Additionally, many of the pathologic fractures are excellently treated by general orthopaedic

surgeons and do not require specialized care. The most important issue is the selection of those patients who need centralized, specialized care. In order to aid that selection, a digital application can be used. The OPTIModel provides insight into both the expected survival, based on a recently published prognostic model,[3] and possible forms of treatment as suggested by experts in the field using the OPTIModel app, available in app stores and on www.optimal-study.nl/tool. The use of such a supportive tool can help differentiate patients with a short survival who are adequately treated with an intramedullary nail in a regional hospital from patients with a long expected survival who need referral to a specialized centre for prosthetic reconstruction.

This study focused on a different aspect than most studies that aim to improve the treatment of patients with a pathologic fracture. While asking detailed questions about treatment in the questionnaire, the conclusions were used to evaluate how the care can be improved on a more general scale. Based on the results, patients might benefit if there were better differentiation between those who are adequately treated in a regional centre and those who require referral for specialist care. This differentiation should be based on expected survival, the location of the fracture and the type of fracture (impending or actual). Digital applications can help match patients to the most appropriate treatment.

References

1. Freeman AK, Sumathi VP, Jeys L. Metastatic tumours of bone. *Surgery (Oxford) 2015;33-1:34-9.*

2. Ratasvuori M, Wedin R, Keller J, Nottrott M, Zaikova O, Bergh P, Kalen A, Nilsson J, Jonsson H, Laitinen M. Insight opinion to surgically treated metastatic bone disease: Scandinavian Sarcoma Group Skeletal Metastasis Registry report of 1195 operated skeletal metastasis. *Surg Oncol 2013;22-2:132-8.*

3. Willeumier JJ, van der Linden YM, van der Wal C, Jutte PC, van der Velden JM, Smolle MA, van der Zwaal P, Koper P, Bakri L, de Pree I, Leithner A, Fiocco M, Dijkstra PDS. An Easy-to-Use Prognostic Model for Survival Estimation for Patients with Symptomatic Long Bone Metastases. *J Bone Joint Surg Am 2018;100-3:196-204.*

4. Ratasvuori M, Wedin R, Hansen BH, Keller J, Trovik C, Zaikova O, Bergh P, Kalen A, Laitinen M. Prognostic role of en-bloc resection and late onset of bone metastasis in patients with bone-seeking carcinomas of the kidney, breast, lung, and prostate: SSG study on 672 operated skeletal metastases. *J Surg Oncol 2014.*

5. Chow E, Harth T, Hruby G, Finkelstein J, Wu J, Danjoux C. How Accurate are Physicians' Clinical Predictions of Survival and the Available Prognostic Tools in Estimating Survival Times in Terminally Ill Cancer Patients? A Systematic Review. *Clinical Oncology 2001;13-3:209-18.*

6. Forsberg JA, Eberhardt J, Boland PJ, Wedin R, Healey JH. Estimating survival in patients with operable skeletal metastases: an application of a bayesian belief network. *PLoS One 2011;6-5:e19956.*

7. Katagiri H, Okada R, Takagi T, Takahashi M, Murata H, Harada H, Nishimura T, Asakura H, Ogawa H. New prognostic factors and scoring system for patients with skeletal metastasis. *Cancer Med 2014.*

8. Westhoff PG, de Graeff A, Monninkhof EM, Bollen L, Dijkstra SP, van der Steen-Banasik EM, van Vulpen M, Leer JW, Marijnen CA, van der Linden YM, Dutch Bone Metastasis Study G. An easy tool to predict survival in patients receiving radiation therapy for painful bone metastases. *Int J Radiat Oncol Biol Phys 2014;90-4:739-47.*

9. Steensma M, Healey JH. Trends in the surgical treatment of pathologic proximal femur fractures among Musculoskeletal Tumor Society members. *Clin Orthop Relat Res 2013;471-6:2000-6.*

10. Araki N, Chuman H, Matsunobu T, Tanaka K, Katagiri H, Kunisada T, Hiruma T, Hiraga H, Morioka H, Hatano H, Asanuma K, Nishida Y, Hiraoka K, Okamoto T, Abe S, Watanuki M, Morii T, Sugiura H, Yoshida Y, Ohno T, Outani H, Yokoyama K, Shimose S, Fukuda H, Iwamoto Y. Factors associated with the decision of operative procedure for proximal femoral bone metastasis: Questionnaire survey to institutions participating the Bone and Soft Tissue Tumor Study Group of the Japan Clinical Oncology Group. *J Orthop Sci 2017.*

11. Janssen SJ, Bramer JAM, Guitton TG, Hornicek FJ, Schwab JH. Management of Metastatic Humeral Fractures: variations according to orthopedic subspecialty, tumor characteristics. *Orthop Traumatol Surg Res 2017.*

12. White N, Reid F, Harris A, Harries P, Stone P. A Systematic Review of Predictions of Survival in Palliative Care: How Accurate Are Clinicians and Who Are the Experts? *PLoS One 2016;11-8:e0161407.*

13. Harvey N, Ahlmann ER, Allison DC, Wang L, Menendez LR. Endoprostheses last longer than intramedullary devices in proximal femur metastases. *Clin Orthop Relat Res 2012;470-3:684-91.*

14. Errani C, Mavrogenis AF, Cevolani L, Spinelli S, Piccioli A, Maccauro G, Baldini N, Donati D. Treatment for long bone metastases based on a systematic literature review. *Eur J Orthop Surg Traumatol 2016.*

15. Di Martino A, Martinelli N, Loppini M, Piccioli A, Denaro V. Is endoprosthesis safer than internal fixation for metastatic disease of the proximal femur? A systematic review. *Injury 2017;48:S48-S54.*

16. Yu Z, Xiong Y, Shi R, Min L, Zhang W, Liu H, Fang X, Tu C, Duan H. Surgical management of metastatic lesions of the proximal femur with pathological fractures using intramedullary nailing or endoprosthetic replacement. *Molecular and Clinical Oncology 2017.*

Questionnaire

General questions

How many years have you been working as a (consultant) orthopaedic surgeon?

- Resident
- Less than 5 years
- 6 – 10 years
- 11 – 20 years
- More than 20 years

How often do you treat patients with a pathologic fracture?

- More than 2 times per month
- 1 – 2 times per month
- 1 – 2 times per 3 months
- 1 – 2 times per half year
- 1 – 2 times per year
- (almost) never

Other subspeciality interests: *check all that apply*

- General orthopaedics
- Joint reconstruction
- Hip/knee
- Foot/ankle
- Upper extremity
- Spine
- Sport orthopaedics
- Paediatric orthopaedics
- Traumatology

Survival estimation

Which factors do you regard as influencers of the remaining survival when patients present with an actual or impending pathologic fracture? *select at most 5 answers*

- ◊ Age
- ◊ Gender
- ◊ Primary tumour
- ◊ Presence of other bone metastases
- ◊ Number of other bone metastases
- ◊ Presence of brain metastases
- ◊ Presence of visceral metastases
- ◊ General health / performance status
- ◊ Pain
- ◊ Interval between diagnosis of primary tumour and diagnosis of pathologic fracture
- ◊ Actual fracture or impending fracture
- ◊ Blood values (e.g. Hb, leukocyte count, thrombocyte count, albumin, calcium, biliribine, LDH, CRP)

How do you estimate the remaining survival?

- Based on my own experience
- Using a tool/nomogram/model
- I ask the oncologist/radiotherapist
- I do not estimate the remaining survival

If using a tool/nomogram/model, please state which one is used:

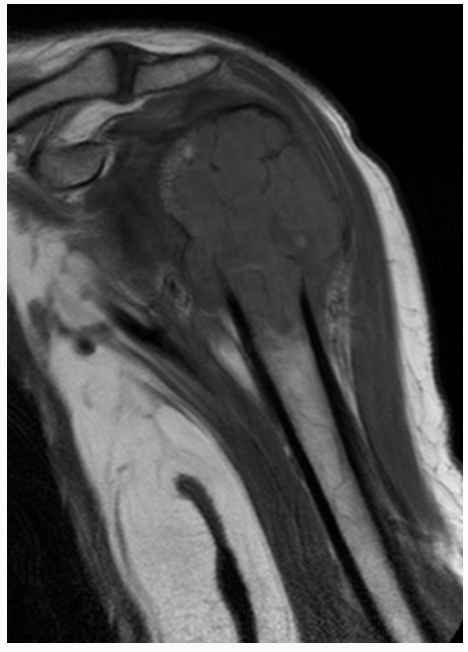
_____

Case 1

1A. A 35-year-old woman presents with a pathologic fracture of the proximal humerus caused by a breast cancer (ER/PR+, HER2-) metastasis. There are no brain or lung metastases, but eight other bone metastases (located in spine, pelvis and femurs) are present. The other bone metastases give no complaints and the patient is able to continue her daily living. Her left arm is now however causing continuous pain.

1B. A 70-year-old woman presents with a pathologic fracture of the proximal humerus caused by a breast cancer (ER/PR+, HER2-) metastasis. There are no brain or lung metastases, but eight other bone metastases (located in spine, pelvis and femurs) are present. The other bone metastases give no complaints and the patient is able to continue her daily living. Her left arm is now however causing continuous pain.

See the X-ray and MRI image below for more information. Distally in the humerus no other lesions are present.



Case 2

2A. A 32-year-old man presents with a subtrochanteric pathologic fracture caused by lung carcinoma (EGFR negative). The disease has spread diffusely throughout the lungs and skeleton. Brain metastases are suspected because of significant changes in the behaviour of the patient. He has been bedridden since several weeks due to the pain in the hip.

2B. A 70-year-old man presents with a subtrochanteric pathologic fracture caused by lung carcinoma (EGFR negative). The disease has spread diffusely throughout the lungs and skeleton. Brain metastases are suspected because of significant changes in the behaviour of the patient. He has been bedridden since several weeks due to the pain in the hip.

See the X-ray below. Further distally in the femur there are no lesions.

Case 3

3A. A 68-year-old woman has a fracture of the humerus shaft caused by a solitary metastasis of a renal cell carcinoma. There are no visceral metastases and the primary tumour has been resected. The arm is very painful (despite pain medication: paracetamol 4g/day and fentanyl transdermal patch 50µg/3 days) and the patient is unable to use her arm.

3B. A 68-year-old woman has a fracture of the humerus shaft caused by a metastasis of a renal cell carcinoma. Multiple other bone metastases are present in the spine and pelvis. There are no visceral metastases and the primary tumour has been resected. The arm is very painful (despite pain medication: paracetamol 4g/day and fentanyl transdermal patch 50µg/3 days) and the patient is unable to use her arm.

See the X-ray below and a transverse slice of the CT.

Case 4

4A. A 40-year-old man presents with an intertrochanteric fracture caused by a solitary metastasis of a renal cell carcinoma. There are no visceral metastases and the primary tumour has been resected. The hip is painful and limits the walking ability of the patient. Otherwise the patient is able to lead his life relatively normal.

4B. A 40-year-old man presents with an intertrochanteric fracture caused by a metastasis of a renal cell carcinoma. Multiple bone metastases (>10) are present throughout the entire skeleton. There are no visceral metastases and the primary tumour has been resected. The hip is painful and limits the walking ability of the patient. Otherwise the patient is able to lead his life relatively normal.

See the X-ray below.

Case 5

5A. A 38-year-old man presents with a fracture of the proximal humerus shaft caused by a lung carcinoma (EGFR negative) metastasis. Throughout the mediastinum multiple enlarged lymph nodes have been detected as well as multiple bone metastases (>20) in the entire skeleton. The liver shows several lesions suspect for metastases. Until the current fracture the patient was able to perform his daily activities, however his condition is deteriorating slowly. With a walker he is able to walk 100 meters. The patient has had radiotherapy for several painful spine metastases, with good effect.

5B. A 75-year-old man presents with a fracture of the proximal humerus shaft caused by a lung carcinoma (EGFR negative) metastasis. Throughout the mediastinum multiple enlarged lymph nodes have been detected as well as multiple bone metastases (>20) in the entire skeleton. The liver shows several lesions suspect for metastases. Until the current fracture the patient was able to perform his daily activities, however his condition is deteriorating slowly. With a walker he is able to walk 100 meters. The patient has had radiotherapy for several painful spine metastases, with good effect.

See the X-ray below.

Case 6

6A. A 42-year-old woman presents with a subtrochanteric fracture based on breast cancer (ER+/PR+, Her2-). There are no lung, liver, or brain metastases, but there are other bone metastases present in her pelvis and left femur. The patient is still very active and did not feel limited by her disease until this fracture occurred.

6B. A 72-year-old woman presents with a subtrochanteric fracture based on breast cancer (ER+/PR+, Her2-). There are no lung, liver, or brain metastases, but there are other bone metastases present in her pelvis and left femur. The patient is still very active and did not feel limited by her disease until this fracture occurred.

See the X-ray below. Further distally in the femur there are no lesions.

Questions for case 1A and 1B | case 3A and 3B | case 5A and 5B

What is your estimation of the remaining survival?

- Less than 3 months
- 3 to 6 months
- 6 to 12 months
- more than 12 months

What would your treatment of this patient be (based on the estimated survival)?

- Plate fixation with cement
- Plate fixation without cement
- Intramedullary nail fixation with cement
- Intramedullary nail fixation without cement
- Shoulder prosthesis
- (refer patient for a) (modular) tumour prosthesis after en bloc resection with free margins
- (refer patient for a) (modular) tumour prosthesis after intralesional resection
- Radiotherapy
- Conservative; pain medication

Questions for case 2A and 2B | case 4A and 4B | case 6A and 6B

What is your estimation of the remaining survival?

- Less than 3 months
- 3 to 6 months
- 6 to 12 months
- more than 12 months

What would your treatment of this patient be (based on the estimated survival)?

- Intramedullary nail fixation with cement in the collum
- Intramedullary nail fixation with cement in the shaft
- Intramedullary nail fixation with cement to fill the lesion
- Intramedullary nail fixation with cement in the collum and to fill the lesion
- Intramedullary nail fixation without cement
- Hemiarthroplasty
- Total hip arthroplasty

- (refer patient for a) (modular) proximal femur tumour prosthesis after en bloc resection with free margins
- (refer patient for a) (modular) proximal femur tumour prosthesis after intralesional resection
- Radiotherapy
- Conservative; pain medication