The Scandinavian Sarcoma Group skeletal metastasis register

Survival after surgery for bone metastases in the pelvis and extremities

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Introduction **The assessment of the prognosis for the individual patient is important for the choice of surgical treatment of skeletal metastases. In 1999 the Scandinavian Sarcoma Group (SSG) initiated the Skeletal Metastasis Register as a multicentric, prospective study to provide a scientific basis for treatment recommendations. To improve prognostication we analyzed the survival of patients with skeletal metastases surgically treated at 9 SSG centres.**

Patients and methods **460 patients with an average age of 64 years underwent 501 operations for non-spinal skeletal metastases. 7 % were operated for more than one metastasis. Carcinoma of the breast, prostate, kidney and lung were the dominating primary tumors.**

Results **The survival rate was 0.4 at 1 year, 0.3 at 2 years and 0.2 at 3 years. Univariate analysis showed that survival was related to bone localization, skeletal metastatic load, presence of visceral metastases, Karnofsky performance score, primary tumor type, presence of a complete pathological fracture and preoperative hemoglobin content. Multivariate regression analysis showed that pathological fracture, visceral metastases, haemoglobin content < 7 mmol/L and lung cancer were negative prognostic factors for survival. Myeloma was the sole positive prognostic factor for survival.**

During recent years, more attention has been directed towards improving palliative care for cancer patients with skeletal metastases. The aim of surgical treatment is to remove pain and maintain function for improved quality of life. Current operative treatment recommendations are mainly based on retrospective studies of single institutions (Yazawa et al. 1990, Bono et al. 1991, Yamashita et al. 1993, Smith et al. 1997, Dürr et al. 1998 and 2002, Wedin et al. 1999), but these patient series are often small and collected during a long period of time. Most studies deal with either bone metastasis in the spine or bone metastasis in the extremities due to differences in morbidity and treatment. SSG has since 1986 maintained a sarcoma register and in 1999 the Skeletal Metastasis Register was started with prospective registration of patients operated for skeletal metastases in the long bones and pelvis. In this first report we analyse possible prognostic factors affecting survival in a group of patients surgically treated in 9 SSG centres (Table 1).

Patients and methods

Criteria for inclusion were operation for bone metastases, myeloma or lymphoma in the extremities or pelvis. Between September, 1999 and

Table 1. Number of patients treated at 9 sarcoma centers

Sarcoma center	Number of treated patients
Stockholm, Sweden	149
Aarhus, Denmark	87
Tampere, Finland	53
Gothenburg, Sweden	50
DNR, Oslo, Norway	36
Bergen, Norway	30
Lund, Sweden	23
Ullevål, Oslo, Norway	16
Linköping, Sweden	16

March, 2003, 474 patients underwent 515 operations and were followed prospectively. 14 patients were excluded because of missing data. There were 253 (55%) women and 207 (45%) men with a median age of 64 (11–96) years. The patients were registrated at operation and followed until November 2003 or death. In patients treated for more than one metastasis, survival was assessed from the time of the first operation. Carcinoma of the breast, prostate, kidney and lung were the most common primary tumor (Table 2). 69% of the patients had more than one known bone metastasis at the time of the first surgical procedure and 32% had known visceral metastases. The indication for surgery was a complete pathological fracture in 71%, impending fracture in 18% and pain in 11%. The functional ability was assessed with the Karnofsky (1967) score as good, moderate or poor performance. Operations concerned femur in 62%, humerus in 18%, pelvis in 12% and other locations in 8%. 206 (45%) patients were treated with prosthetic procedures and 239 (52%) with internal fixation. 46 (10%) patients had complications, mainly wound infection or prosthetic dislocation. 7% of the patients had reoperation related to the first surgically treated bone metastasis.

Statistics

Survival rates after surgery were estimated with the Kaplan-Meier method. The univariate log-rank test was used to evaluate the prognostic significance of individual factors. The Cox multiple regression analysis was used to asses the prognostic influence of different clinical features for 1-year survival.

Results

348/460 (76%) patients have died. 19% of the patients died within the first 6 weeks after operation and 44% within the first 6 months. The 1-year survival rate for the 460 patients was 0.39 (Figure 1). Age at surgery, sex and operation method was not related to survival.

Univariate analysis showed that 1-year survival was related to bone localization, skeletal metastatic load, presence of visceral metastases, Karnofsky performance score, primary tumor, presence of pathological fracture and preoperative hemoglobin content (Table 2). Patients with a solitary skeletal metastasis had the highest survival rate while patients with visceral metastases had the lowest. Patients with myeloma, lymphoma, and breast or kidney cancer had high survival rates at 1 year, while those with prostate, lung or unknown cancer had the lowest.

Multivariate regression analysis was based on the clinical factors found to be prognostic for 1-year survival at univariate analysis. The analysis selected pathological fracture, presence of visceral metastasis, hemoglobin < 7 mmol/L and lung cancer as independent negative prognostic factors for survival. Myeloma was a positive prognostic factor (Table 3). Excluding preoperative hemoglobin content from the multivariate analysis, good Karnofsky score was a positive factor ($p = 0.003$).

Discussion

In most studies of metastatic bone disease, including our, the prognosis is poor, 1-year survival is 0.30 to 0.54; in our study 0.39 (Bono et al. 1991, Bauer et al. 1995, Dürr et al. 1998, Bohm et al. 2002). The differences can be explained by patient selection, type of primary tumor and indications for surgery.

Operation of a pathological fracture in the femur gives immediate reduction in pain, facilitates patient nursing and reestablishes walking function. Patients operated for bone metastases of the pelvis, almost exclusively the acetabular area, had a tendency of longer survival than those operated for metastases in the femur. Such patients are selected since they pose less urgent demands for surgical

Table 2. Univariate analysis of 1-year survival rates according to various clinical factors in the 460 operated patients

Factors	Number of patients	Survival rate	P-value
Age at surgery:	0–65 229	(50%)	0.44
>65	231 (50%)	0.34	
Sex: Female	253 (55%)	0.44	
Male	207 (45%)	0.33	
Metastatic load			
Solitary skeletal	95 (21%)	0.53	<0.001
Multiple skeletal	317 (69%)	0.36	
Unknown skeletal	48 (10%)	0.33	
No visceral metastasis	225 (49%)	0.46	
Visceral metastases	146 (32%)	0.27	<0.001
Unknown visceral	89 (19%)	0.43	
Primary tumor			
Myeloma	32 (7%)	0.65	0.002
Lymphoma	14 (3%)	0.50	
Breast	142 (31%)	0.50	
Kidney	56 (12%)	0.43	
Others	60 (13%)	0.34	
Prostate	70 (15%)	0.26	0.02
Lung	49 (11%)	0.24	0.009
Unknown	37 (8%)	0.17	<0.001
Pathologic fracture			
No	133 (29%)	0.47	0.007
Yes	327 (71%)	0.36	
Localisation			
Others	18 (4%)	0.72	0.01
Tibia	20 (4%)	0.50	
Pelvis	53 (12%)	0.49	
Femur	285 (62%)	0.36	
Humerus	84 (18%)	0.34	
Karnofsky score			
Good	84 (18%)	0.55	0.002
Moderate	263 (57%)	0.38	
Poor	108 (24%)	0.25	0.002
Unknown	5 (1%)		
Operation method			
Internal fixation	239 (52%)	0.41	
Prosthesis	207 (45%)	0.33	
Other	14 (3%)		
Hemoglobin preoperative			
<7 mmol/l	118 (26%)	0.22	<0.001
≥7 mmol/l	154 (33%)	0.50	
Unknown	188 (41%)	0.41	

Table 3. Multivariate analysis of prognostic factors for survival

Factors	Coefficient	SD	p-value
Negative			
Pathologic fracture	0.20	0.09	0.03
Visceral metastases	0.35	0.17	0.04
Hemoglobin <7mmol/L	0.50	0.16	0.002
Lung cancer	0.66	0.26	0.01
Positive			
Myeloma	-0.95	0.40	0.02

treatment than patients with a pathological fracture in femur (Table 2).

It has been found that patients with myeloma, lymphoma, kidney and breast cancer have a better prognosis (Smith et al. 1992, Bauer et al. 1995, Althausen et al. 1997, Dürr et al. 1997, 1998, 1999 2002), but in our series only myeloma was statistically significant in the univariate as well as the multivariate analysis. Our study support previous findings that lung cancer patients have a poor prognosis (Bauer et al. 1995, Dürr 1998). Prostate cancer has earlier been found to be either a positive (Bohm et al. 2002) or negative prognostic factor (Bauer et al. 1995). The reason may be that a higher proportion of hormone-refractory patients leads to lower survival rates. In our study prostate cancer was a negative prognostic factor in the univariate analysis, but not in the multivariate analysis.

Our study confirms that a complete pathological fracture and known visceral metastases are independent negative prognostic factors. (Bauer et al. 1995, Rex et al. 2000, Bohm et al. 2002, Dürr et al. 2002). Solitary skeletal metastasis was a positive prognostic factor in the univariate analysis, but was not an independent factor in the multivariate analysis as in the series of Bauer et al. (1995).

Only few authors have addressed performance and general health as prognostic factors. Patients with poor performance score have been shown to have a shorter survival as compared to patients with a good score (Tokuhashi 1991, Matzkin et al. 1993, Rex et al. 2000). In our study Karnofsky score was an independent factor first after excluding preoperative hemoglobin content from the multivarate analysis.

Hemoglobin has been used as a prognostic factor in metastatic prostate cancer (Matzkin et al. 1993). We found that preoperative anemia (< 7 mmol/L) was a strong negative prognostic factor in this heterogeneous group of cancer patients.

In the multivariate analysis we found the following negative factors: pathologi-

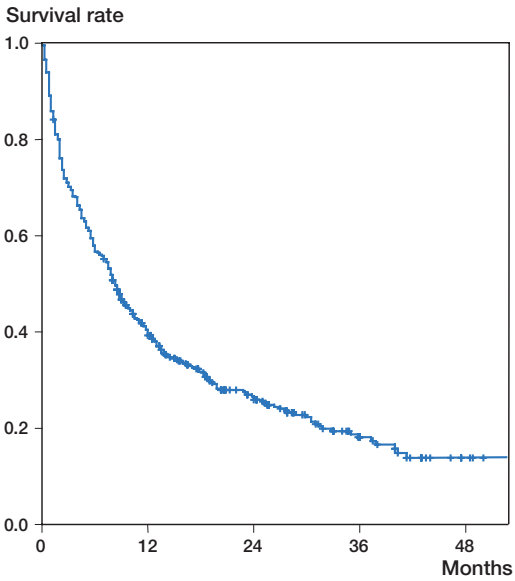

Figure 1. Survival rate for the whole series of 460 patients was 0.39 at 1 year, 0.26 at 2 years and 0.18 at 3 years.

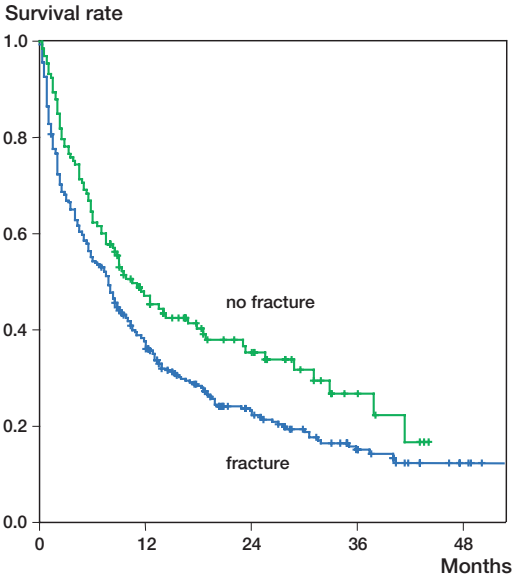

Figure 2. 1-year survival rate for pathologic fracture was 0.36 and 0.47 for no fracture. p = 0.007.

cal fracture, visceral metastasis, lung cancer, low hemoglobin and only one positive: myeloma. In the clinical practice it is of importance to identify patients with a very short survival and also patients with an exceptionally long survival. Most patients with 2 or 3 negative independent prognostic factors have an extremely short survival, whereas patients

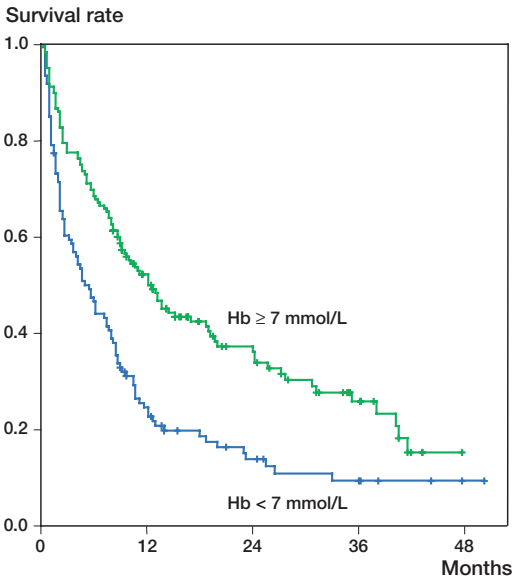

Figure 3. 1-year survival rate for hemoglobin < 7 mmol/L was 0.22 and 0.50 for hemoglobin ≥7 mmol/L. p < 0.001.

with no negative prognostic features may have a good prognosis. As a consequence, surgical procedures and reconstruction should be chosen that minimize the risk of long term failure in patients with a good prognosis and be as simple as possible in patients with a poor prognosis.

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