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Published in:
Acta Orthopaedica Scandinavica. Supplementum

DOI:
10.1080/00016470410001708270

2004

Link to publication

Citation for published version (APA):
Hansen, B. H., Keller, J., Laitinen, M., Berg, P., Skjeldal, S., Trovik, C., Nilsson, J. E., Walloe, A., Kalén, A., & Wedin, R. (2004). The Scandinavian Sarcoma Group skeletal metastasis register: Survival after surgery for bone metastases in the pelvis and extremities. *Acta Orthopaedica Scandinavica. Supplementum*, *75*(Supplement 311), 11-15. https://doi.org/10.1080/00016470410001708270

Total number of authors:
10

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Download date: 12. Oct. 2024

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 patients	Number of treated
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				
0–7 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-

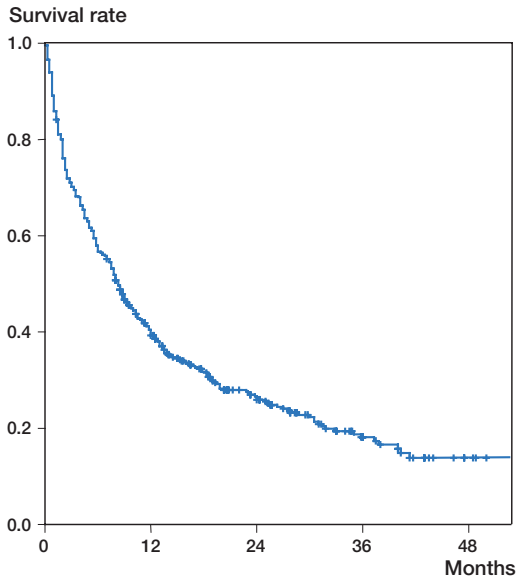

Figure 1. Survival rate for the whole series of 460 patients was 0.39 at 1 year, 0.26 at 2 years and 0.18 at 3 years.

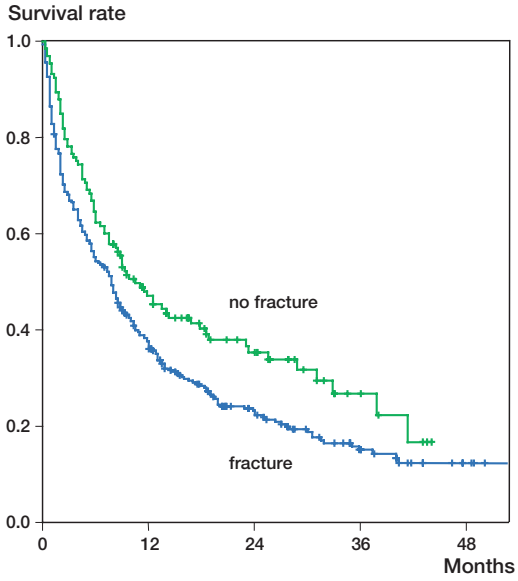

Figure 2. 1-year survival rate for pathologic fracture was 0.36 and 0.47 for no fracture. p = 0.007.

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

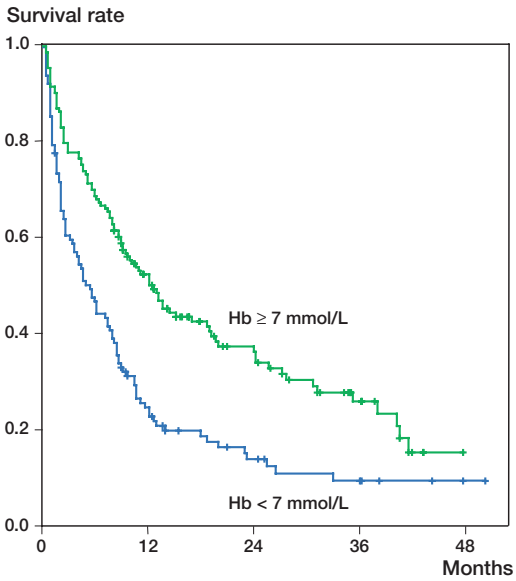

Figure 3. 1-year survival rate for hemoglobin < 7 mmol/L was 0.22 and 0.50 for hemoglobin ≥7 mmol/L. p < 0.001.

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.

Evy Nilsson at the Scandinavian Sarcoma Group Secretariat in Lund, Sweden helped with collection of the clinical data.

Althausen P, Althausen A, Jennings LC, et al. Prognostic factors and surgical treatment of osseous metastases secondary to renal cell carcinoma. Cancer1997; 80: 1103-9.

Bauer HFC, Wedin R. Survival after surgery for spinal and extremity metastases. Prognostication in 241 patients. Acta Orthop Scand 1995; 66: 143-6.

Bohm P, Huber J. The surgical treatment of bony metastases of the spine and limbs. J Bone Joint Surg Br 2002; 84(4): 521-9.

Bono B, Cazzaniga P, Zurrida SM, et al. Palliative surgery of metastatic bone disease: a review of 83 cases. Eur J Cancer 1991; 27(5): 556-8.

Durr HR, Refior HJ. Prognosis of skeletal metastases. Orthopade 1998; 27(5): 294-300.

Durr HR, Huhne JH, Hagena FW, et al. Surgical treatment for myeloma of the bone. A retrospective analysis of 22 cases. Arch Orthop Trauma Surg 1997; 116(8): 463-9.

Durr HR, Maier M, Pfaler M, et al. Surgical treatment of osseous metastases in patients with renal cell carcinoma. Clin Orthop 1999; 367: 283-90.

Durr HR, Muller PE, Lenz T, et al. Surgical treatment of bone metastases in patients with breast cancer. Clin Orthop 2002; 396: 191-6.

Karnofsky DA. Clinical evaluation of anticancer drugs. Gann Monogr 1967; 2: 223-31.

Matzkin H, Perito PE, Soloway MS. Prognostic factors in metastatic prostate cancer. Cancer 1993; 72(12suppl): 3788-92.

Rex A, Marco W, Dhiren S, et al. Functional and oncological outcome of acetabular reconstruction for the treatment of metastatic disease. J Bone Joint Surg 2000; 82: 642.

Smith EM, Kursh ED, Makley J, et al. Treatment of osseuos metastases secondary to renal cell carcinoma. J Urol 1992; 148(3): 784-7.

Tokuhashi Y, Kawano H, Toriyama S. Score assessment of metastatic bone tumour for operative treatment. In: Langlais F, Tomeno B eds. Limb salvage- major reconstructions in oncologic and nontumoral conditions. Berlin Heidelberg: Springer Verlag, 1991; 725-32

Yamashita K, Denno K, Ueda T et al. Prognostic significance of bone metastases in patients with metastatic prostate cancer. Cancer 1993; 71: 1297-1302.

Yazawa Y, Frassica FJ, Chao EY, Pritchard DJ, Sim FH, Shives TC. Metastatic bone disease. A study of the surgical treatment of pathological humeral and femoral fractures. Clin Orthop 1990; (251): 213-9.

Wedin R, Bauer HC, Wersäll P. Failures After Operation for Skeletal Metastatic Lesions of Long Bones. Clin Orthop 1999; 358: 128-39.