

Surgical Treatment of Bone Metastases in Patients With Breast Cancer

Hans Roland Dürr, MD;* *Peter Ernst Müller, MD*;*
*Thomas Lenz, MD**;* *Andrea Baur, MD†;* *Volkmar Jansson, MD*;*
*and Hans Jürgen Refior, MD***

In this retrospective study, the effect of surgical therapy on a series of 70 patients with breast cancer who were surgically treated for metastasis of the bone was evaluated. At presentation, 19 patients had one osseous lesion, 19 patients had multiple bone lesions, and 32 patients had additional visceral involvement. The surgical procedures included 60 palliative procedures, six radical resections, and four biopsies. In 14 surviving patients, the mean observation period was 35.6 ± 40.1 months. Of the six patients with radically resected solitary bone lesions, five patients had systemic progression of the disease develop. Of the 19 patients with presumably solitary bone lesions, five currently are free of tumor. Of the 19 patients with multiple bone lesions and initially no visceral tumor spread, only two are alive. Of the 32 patients with additional visceral metastases at surgery, four are alive with the disease. For the entire group, the survival rate was 59% after 1 year, 36% after 2

years, 13% after 5 years, and 7% after 10 years. The only two independent factors that were associated with survival were the extent of the disease and the duration of symptoms from bone metastasis. These findings suggest that in orthopaedic surgery in patients with bone metastases secondary to breast cancer, wide resection is not likely to be necessary. Patients with solitary bone lesions have a 39% chance of living 5 years.

From the *Department of Orthopedics and Orthopedic Surgery, Universität Rostock, Rostock, Germany; the **Department Orthopedics and Orthopedic Surgery, Ludwig-Maximilians-Universität München, Munich, Germany; and the †Institute of Radiology, Ludwig-Maximilians-University München, Munich, Germany.

This study was supported by the Curt-Bohnewand-Fund. Reprint requests to Hans Roland Dürr, MD, Orthopädische Klinik und Poliklinik, Universität Rostock, Ulmenstrasse 44/45, D-18055 Rostock, Germany.

Received: November 20, 2000.

Revised: February 16, 2001; May 21, 2001.

Accepted: June 27, 2001.

Because bone metastases are a common finding in patients with breast cancer, they are a major clinical concern. In a study of 587 patients with breast cancer, 405 (69%) had radiologic evidence of bone metastases.⁷ In autopsy studies, metastases in the skeleton occur at least as frequently as those in the lung.¹³ Significantly higher incidences are seen with steroid receptor-positive tumors and well-differentiated lesions.^{4,8} Approximately 50% of patients with metastatic bone disease have clinical symptoms develop, and 4% to 7% experience pathologic fractures of the long bones.^{9,16,17}

There are several well-known nonoperative treatment options for these lesions. However, patients with pathologic fractures require surgical intervention.^{1,5} These fractures respond more favorably to surgical treatment than do fractures secondary to primary tumors in other sites.¹⁵ However, some authors advocate total resections in selected patients with solitary or

multiple metastases from renal cell carcinoma.^{2,11} Strict patient selection is an important criterion regarding survival benefits and quality of life after surgical intervention. To evaluate prognostic factors on survival, a consecutive series of 70 patients with breast cancer who were surgically treated for metastasis to the bone in one institution were reviewed. Clinical behavior, surgical procedures, and treatment results were analyzed.

MATERIALS AND METHODS

Between January 1980 and September 1998, 70 consecutive patients (69 women, one man) with bone metastases secondary to breast cancer were treated surgically. Medical records and imaging procedures were reviewed for age, treatment of the primary tumor, time of appearance of bone and visceral metastases, clinical symptoms, surgical treatment, complications, and survival. Statistical analyses were done using the Cox regression for multivariate analysis, Kaplan-Meier life table analyses, and log-rank test for univariate analysis.

The mean age of the 70 patients was 56.8 years (range, 30.7–82.7 years) (Fig 1). The locations of the surgical procedures are shown in Figure 2. The most common locations of bone metastases secondary to breast cancer were the spine (29 patients) and the proximal femur (27 patients). All patients

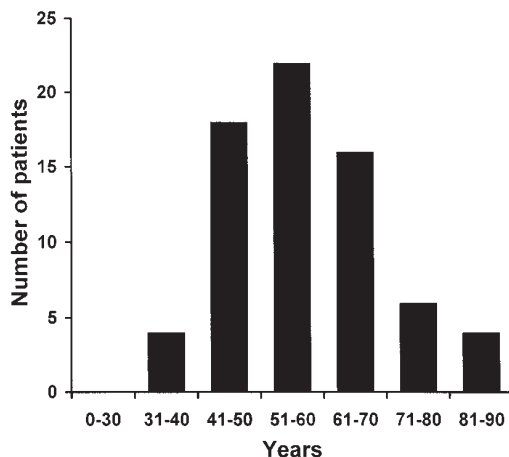


Fig 1. The distribution of age at the time of bone surgery in 70 patients with skeletal metastases secondary to breast cancer is shown.

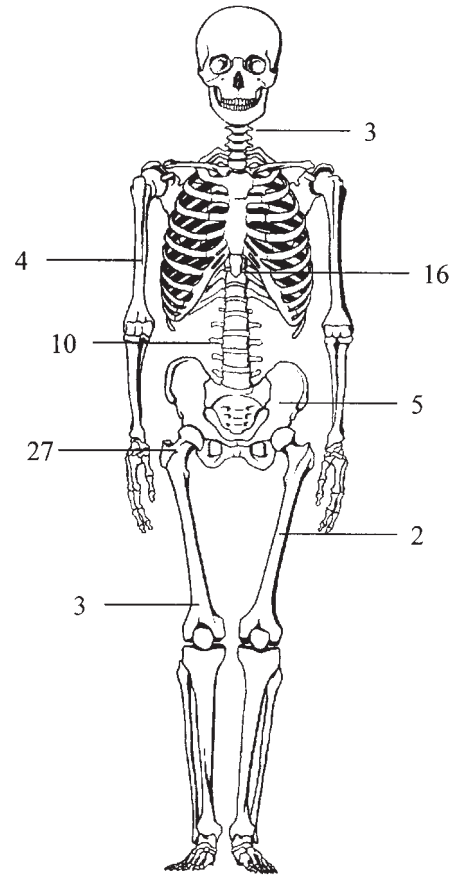


Fig 2. This drawing shows the locations of the lesions in 70 patients who had surgery because of bone metastases secondary to breast cancer.

presented with pain; 17 had a pathologic fracture of the spine, and 22 had a pathologic fracture of the extremities, including 15 fractures of the proximal femur. Ten patients had neurologic impairments because of spinal compression. Six patients had thoracic involvement, and the other four had lumbar compression. The mean duration of symptoms was 5.8 ± 8.9 months (median, 2.7 months; range, 0–41 months). In 15 (21%) patients, breast cancer was diagnosed as a result of symptoms caused by osseous metastases, and in four additional patients, bone metastases were evident at the time the primary diagnosis of breast cancer was made. At presentation, 19 patients had a solitary osseous lesion, 19 patients had multiple bone metastases (more than one lesion), and 32 patients had additional vis-

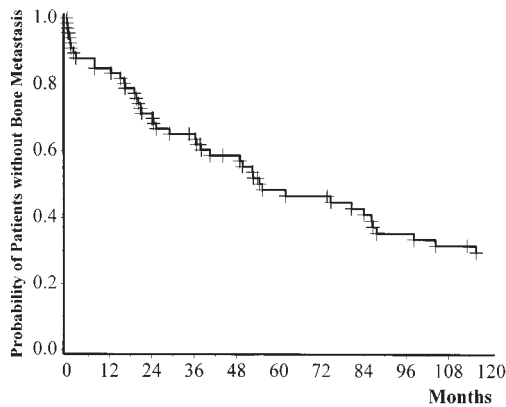


Fig 3. The times from diagnosis of breast cancer to bone metastasis surgery in 70 patients are shown.

ceral involvement. The time from diagnosis of breast cancer to bone metastasis surgery ranged from 0 to 29.8 years (mean, 5.9 ± 6 years; median, 4.3 years). Eighteen percent of the patients needed surgical therapy for bone metastases in the first year, 60% in the first 5 years, and 79% in the first 10 years. Fourteen patients had an interval longer than 10 years (Fig 3).

Surgical therapy in the 70 patients varied greatly depending on the tumor sites, the extent of the disease, the patient's general status, and the followup period. Indications for treatment were impending

fractures or fractures of the long bones, otherwise untreatable pain and instability, and spinal compression because of tumor. Incisional biopsy was done in four patients. In one patient resection of the proximal humerus without reconstruction was done. In 29 patients with involvement of the spine, 11 were treated with only dorsal decompression, in 15 patients additional dorsal instrumentation was used, and in three patients a partial vertebral resection was done. In 15 patients, resection of the tumor and implantation of a tumor endoprosthesis was done. Seven patients received a standard hip arthroplasty, and one patient received a semiconstrained knee endoprosthesis. In 12 patients, an intralesional resection with cementation and instrumentation was done. In one patient, an acetabular resection and reconstruction with a custom-made endoprosthesis was done (Fig 4). In six patients with solitary bone lesions without additional visceral tumor spread, a wide total tumor resection was done. In 60 patients, a palliative intralesional or marginal procedure was done, whereas in four patients, only a biopsy was done. Adjuvant radiation was administered in 55 patients, with 13 patients treated preoperatively. In these 13 patients, eight had a pathologic fracture develop at the femur, and two had a neurologic complication develop because of a vertebral fracture despite radiation therapy. Chemotherapy was used in 29 patients; in nine of these patients, the chemotherapy was given before surgery.

Fifty-eight (83%) patients have died of their disease. In the 12 surviving patients, the mean ob-

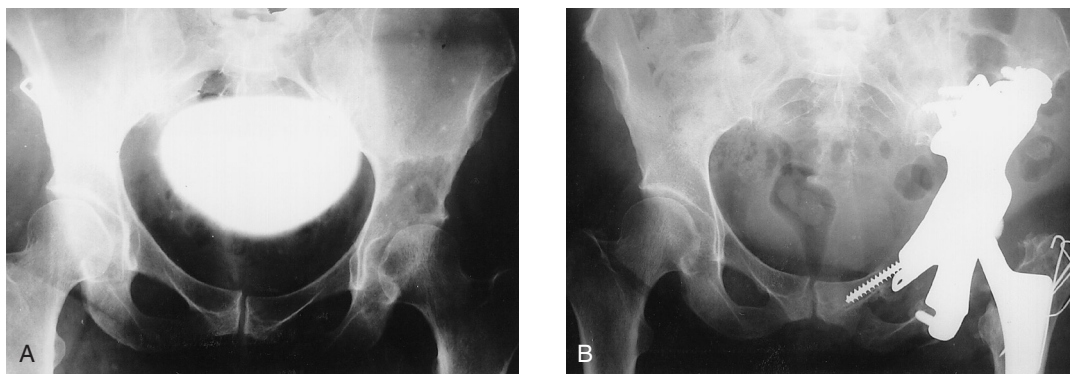


Fig 4A–B. (A) The radiograph of the pelvis of a 42-year-old patient shows an osteolytic metastatic lesion 2 years after primary diagnosis of breast cancer in the left acetabular region. At that time the patient did not have additional tumor spread. (B) The radiograph of the pelvis of the same patient 2 years after acetabular resection shows the reconstruction with an individual implant. The patient had additional bone, liver, and pulmonary metastases develop but is alive 58 months after surgery.

ervation period was 41.6 ± 40.4 months (range, 2–131 months; median, 34.5 months). Three patients have been observed for less than 12 months.

RESULTS

Fourteen (20%) patients had complications associated with the surgical treatments. These complications included pulmonary dysfunction in four patients, cardiac insufficiency in three patients, neurologic impairments in two patients, postoperative bleeding in two patients, multiorgan failure in one patient, deep infection in one patient, severe thromboembolic event in one patient, pseudarthrosis in one patient, and failure of osteosynthesis in two patients. In these 14 patients, three (21%) received chemotherapy, radiotherapy, or both before surgery, compared with 11 (16%) in the whole study group, indicating that nonsurgical pretreatment did not significantly affect the rate of complications. Six (8.6%) patients died within the first 30 days after surgery.

No patient had local recurrence or local tumor progression. Of the six patients with radically resected solitary bone lesions, four died because of progression of the disease, one is alive with progressive visceral and osseous metastases, and one 61-year-old patient is free of disease 10.9 years after resection of the proximal femur. Of the 19 patients with presumably solitary bone lesions, 12 (63%) died because of progression of disease, three have progressive disease, and four are free of tumor, three of them more than 5 years after surgery. The 5-year survival rate in this group is 39%. Of the 19 patients with multiple bone lesions with initially no visceral tumor spread, 17 (89%) died because of progression of the disease, and two patients are alive 2 and 16 months after surgery. Of the 32 patients with additional visceral metastases at surgery, 29 (91%) are deceased and three are alive with disease, all with less than 12 months followup.

For the entire group, the survival rate was 59% after 1 year, 36% after 2 years, 13% after 5 years, and 7% after 10 years (Fig 5). The most significant predictive factors for survival were

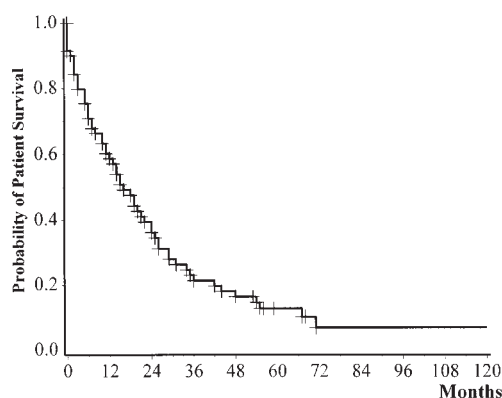


Fig 5. This graph shows the overall survival of 70 patients who were treated surgically for bone metastasis secondary to breast cancer.

the involvement of multiple bones and visceral tumor spread (Fig 6). The patient's age and the amount of time between diagnosis of the breast cancer and surgical intervention were not significantly associated with survival. Regarding the location of the osseous metastases, no difference in survival was seen in extremity or trunk lesions, even after adjusting for solitary or multiple involvement. Chemotherapy did not influence survival, whereas the patients who had chemotherapy before surgery showed a sig-

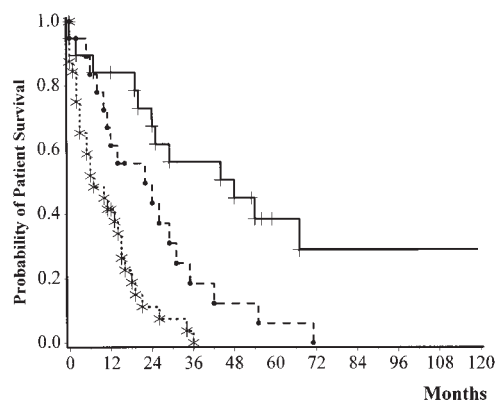


Fig 6. The overall survival of 19 patients with solitary bone metastases (+), 19 patients with multiple osseous involvement (•), and 32 patients with additional visceral metastasis (*) ($p = 0.0001$) is shown.

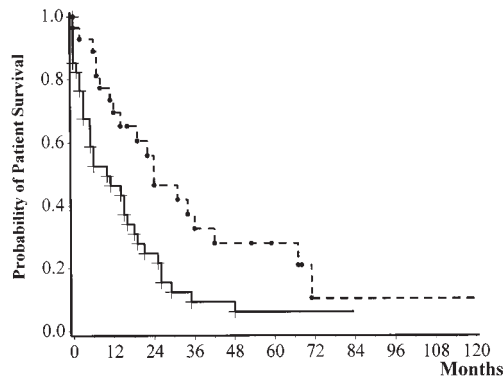


Fig 7. The survival in 34 patients who had surgery of bone metastases with clinical symptoms lasting less than 3 months (*) and 28 patients with symptoms lasting more than 3 months (+) ($p = 0.0081$) is shown.

nificantly worse prognosis than did patients who received chemotherapy after surgery. Patients who had clinical symptoms of bone metastases for less than 3 months showed a significantly poorer prognostic outcome than did patients with a longer period of symptoms (Fig 7). Thus, the only two independent factors associated with survival were the extent of the disease and the duration of symptoms attributable to bone metastasis (Table 1).

DISCUSSION

The survival rate of patients with skeletal metastases from breast cancer is more favorable than the survival rate of patients with

bone metastases secondary to other cancers.^{3,12} It is clear from the current study and others that patients with breast cancer with bone lesions and additional visceral metastasis have a poorer prognosis than do patients with only bone lesions.⁸ Regarding the anatomic location of the bone lesions, a study of 82 patients reported that a significantly higher proportion of patients with lesions above the lumbosacral junction showed visceral tumor spread compared with patients with lesions below the lumbosacral junction.¹⁹ In the current study, visceral tumor spread was distributed evenly among all bone locations. The overall osseous tumor load was a strong significant factor of survival; patients with solitary bone lesions had better survival rates than did patients with multiple lesions. However, the extent of osseous metastasis (solitary or multiple) is prognostically significant only in patients who survive at least 2 years (such as patients with renal cell carcinoma).^{2,11,12}

The age of the patients and the time between diagnosis of the primary disease and bone surgery did not influence survival in this group of patients, a finding that is consistent with the literature.¹⁴ The only additional prognostic factor for survival independent of metastatic spread was the duration of symptoms. Patients who had symptoms less than 3 months seemed to have more aggressive tumors and thus a poorer overall prognosis.

One of the aims of this study was to determine whether radical resection of metastatic bone lesions in patients with breast cancer

TABLE 1. Multivariate Analysis of Presumed Factors on Survival in 70 Patients Treated Surgically for Bone Metastases Secondary to Breast Cancer

| Factor | Parameter | Standard Error | Risk Ratio | p Value |
|---------------------------|-----------|----------------|------------|---------|
| Tumor spread ⁺ | 0.881 | 0.215 | 2.41 | 0.0001 |
| Symptoms [#] | -0.700 | 0.319 | 0.50 | 0.0283 |
| Latency [*] | 0.195 | 0.167 | 1.22 | 0.2468 |
| Age | 0.007 | 0.014 | 1.01 | 0.6193 |
| Location [§] | 0.041 | 0.328 | 1.04 | 0.9007 |
| Fracture | 0.287 | 0.328 | 1.33 | 0.3814 |

⁺ = solitary osseous, multiple osseous, visceral; [#] ≤ 3 months, > 3 months; ^{*} = Initial, ≤ 12 months, > 12 months; [§] = trunk, extremities.

might lead to a significantly longer survival rate. Because only one of the six patients with a wide resected solitary bone lesion survived free of tumor for more than 5 years, whereas the other five patients had progressive disease develop, the data suggest that radical resections of bone lesions in patients with breast cancer do not significantly improve survival. Only three of 19 (16%) patients with initially solitary bone lesions survived free of tumor 5 years after surgery, in contrast to patients with renal cell carcinoma.^{2,11} Because local radiation results in sufficient local tumor control,⁵ especially after intralesional or marginal resection of the metastatic lesion, there seems to be no need for aggressive surgical treatment in these patients. However, as shown in the current study, radiotherapy alone did not prevent pathologic fracture or neurologic complications in numerous patients. Chemotherapy, hormone treatment, and more recently, bisphosphonates, also are effective therapies in bone lesions of breast cancer.^{6,10} However, one has to be aware that surgical reconstruction has to reflect the comparably long survival of this group of patients. In the current study, one of 12 reconstructions using osteosynthetic devices and cementation failed because of insufficient fixation, and one dorsal instrumentation at the spine had to be extended for the same reason. These findings are consistent with findings in another study also advocating endoprosthetic reconstruction instead of osteosynthetic devices in metastatic bone lesions, especially in patients who received radiation treatment before surgery.¹⁸ The current findings suggest that in orthopaedic surgery in patients with bone metastases secondary to breast cancer, wide resection is not likely to be necessary. Patients with solitary bone lesions have a 39% chance of living after 5 years. Orthopaedic surgery in these patients should be confined to patients whose impending or actual fractures or neurologic complications force surgical treatment.

References

1. Aaron AD: Treatment of metastatic adenocarcinoma of the pelvis and the extremities. *J Bone Joint Surg* 79A:917-932, 1997.
2. Althausen P, Althausen A, Jennings LC, et al: Prognostic factors and surgical treatment of osseous metastases secondary to renal cell carcinoma. *Cancer* 80:1103-1109, 1997.
3. Bauer HCF, Wedin R: Survival after surgery for spinal and extremity metastases: Prognostication in 241 patients. *Acta Orthop Scand* 66:143-146, 1995.
4. Campbell FC, Blamey RW, Elston CW, et al: Oestrogen-receptor status and sites of metastasis in breast cancer. *Br J Cancer* 44:456-459, 1981.
5. Cheng DS, Seitz CB, Eyre HJ: Nonoperative management of femoral, humeral, and acetabular metastases in patients with breast carcinoma. *Cancer* 45:1533-1537, 1980.
6. Clavel M: Management of breast cancer with bone metastases. *Bone* 12(Suppl 1):S11-S12, 1991.
7. Coleman RE, Rubens RD: Bone metastases and breast cancer. *Cancer Treat Rev* 12:251-270, 1985.
8. Coleman RE, Rubens RD: The clinical course of bone metastases from breast cancer. *Br J Cancer* 55:61-66, 1987.
9. Coran AG, Banks HH, Aliapoulios MA, et al: The management of pathologic fractures in patients with metastatic carcinoma of the breast. *Surg Gynecol Obstet* 127:1225-1230, 1968.
10. Diel IJ, Solomayer EF, Costa SD, et al: Reduction in new metastases in breast cancer with adjuvant clodronate treatment. *N Engl J Med* 339:357-363, 1998.
11. Dürr HR, Maier M, Pfahler M, et al: Surgical treatment of osseous metastases in patients with renal cell carcinoma. *Clin Orthop* 367:283-290, 1999.
12. Dürr HR, Refior HJ: Prognosis of skeletal metastases. *Orthopäde* 27:294-300, 1998.
13. Lee YT: Breast carcinoma: Pattern of metastasis at autopsy. *J Surg Oncol* 23:175-180, 1983.
14. Miller F, Whitehill R: Carcinoma of the breast metastatic to the skeleton. *Clin Orthop* 184:121-127, 1984.
15. Parrish F, Murray JA: Surgical treatment for secondary neoplastic fractures. *J Bone Joint Surg* 52A:665-686, 1970.
16. Schurman DJ, Amstutz HC: Orthopedic management of patients with metastatic carcinoma of the breast. *Surg Gynecol Obstet* 137:831-836, 1973.
17. Ulloa MA, Merchan EC: Prognostic factors for bone metastases in breast cancer. *Int Orthop* 17:60-63, 1993.
18. Wedin R, Bauer HCF, Wersäll P: Failures after operation for skeletal metastatic lesions of long bones. *Clin Orthop* 358:128-139, 1999.
19. Yamashita K, Ueda T, Komatsubara Y, et al: Breast cancer with bone-only metastases: Visceral metastases-free rate in relation to anatomic distribution of bone metastases. *Cancer* 68:634-637, 1991.