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ORIGINAL ARTICLE

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Surgery of skeletal metastases

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Abstract During a period of 5 years, 74 female and 27 male patients with an average age of 63.3 years underwent a total of 117 operations for the management of impending (*n*=41) or already existing (*n*=76) pathologic fractures due to osseous metastases. The average stay in hospital was 17.8 days, and the average postoperative survival 15.8 months. The patients whose limbs were stabilized as a preventive measure were discharged 1.5 days earlier and survived surgery 5.9 months longer than the patients with pathologic fractures. The large percentage of female patients is due to the predominant role of mammary cancer (50%) and the comparatively long survival of patients after a primary diagnosis of this type of carcinoma. The other diagnoses involved were (in order of frequency): bronchial carcinoma (11%), hypernephroma (8%) and non-Hodgkin's lymphoma (8%). The metastases were mainly located at the proximal end or shaft of the femur (59.8%) and in the humerus (18.8%) so that in the majority of cases it was possible to implant weight-bearing prostheses or at least achieve enough stability to allow non-weight-bearing physiotherapy and thus early remobilization. The rate of systemic complications (excluding fatalities) was 14.5%. Local complications in the operated area occurred in 24.8% of cases. As a result, revision surgery was necessary in 10 cases (8.5%), and the fatality rate in hospital (6 weeks) was 7.9%. In view of the advanced stage of the disease in most of the patients, some of them with polypathia, we see these results as a basis for the generous indication for preventive stabilization of osseous metastases. Except in some cases, the primary intention of this therapy is not to cure the disease or prolong life but to improve the quality of life remaining for these patients while keeping their stay in hospital as short as possible and the rate of complications at an acceptable level.

Keywords Osseous metastases · Pathologic fractures · Surgical therapy

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Introduction

Skeletal metastases are the result of hematogenous dissemination of cancer cells and the most frequent manifestation of tumours in the skeletal system. Solitary metastases are found in only about 5% of cases. As well as the filtering organs lung and liver, the skeletal system is one of the most frequent localizations of distant metastases of malignant tumours. This organotropism is explained by the drainage routes of the tumors, the large blood supply specific to this organ, and also by chemotactic factors and other, still partly speculative relationships between the medullary, bone and tumour cells [7, 11, 15, 16].

Increasingly differentiated diagnostic methods make it possible to detect metastases earlier than ever before. At the same time, improved methods of treatment lead to prolonged life expectancy accompanied by a rising incidence of bone metastases which are prone to fracture. The average life expectancy, however, is not determined by the treatment of the metastases, but by the nature of the primary tumour. The purpose of surgical therapy, therefore – with a few exceptions – is palliative, and the aim is to improve the quality of life remaining for the patient [9, 10, 13, 33] by:

- relieving pain
- preserving the function of the affected part of the skeleton
- preventing complications
- shortening the time spent in hospital,
- possibly facilitating care of the patient.

The choice of surgical procedure depends on the localization, number and size of the metastases, and the type of primary tumour and its malignancy. A retrospective analysis of 101 patients with bone metastases or pathological fractures was carried out in the Department of Traumatology and Reconstructive Surgery of the University Hospital Hamburg-Eppendorf (UKE) to investigate the possibilities open to the surgeon. The still surviving patients came for follow-up examination 6–12 months after the operation.

Patients and methods

During a 5-year period (1995–1999) 101 patients with bone metastases underwent 117 operations. Of these, 76 operations were performed to treat pathologic fractures, and 41 were performed in cases with impending fracture. Six patients were operated on twice during one stay in hospital, a further 6 underwent two operations during two stays in hospital, and 2 patients underwent three operations during three stays in hospital. Of the patients 50% had mammary cancer, 11% bronchial carcinoma, 8% renal cell cancer and 8% non-Hodgkin's lymphomas. Carcinoma of the colorectum and female genital tract and metastases from a primary tumour unknown at the time of surgery were each diagnosed in 5% of cases. Of the primary tumours 2% were prostatic carcinomas and another 2% melanomas. Carcinomas of the thyroid, stomach, urothelium and floor of the mouth accounted for skeletal metastases in 1% of the patients.

A standardized questionnaire was used to evaluate the patients' medical records. The data obtained from telephone interviews with patients were also classified by means of a standard questionnaire modified according to Enneking [6].

The date of death of the 62 already deceased patients was ascertained from the patients' family doctor or the central registration office. The periods between primary diagnosis, operation date and date of death were necessary for the evaluation of the data according to the Kaplan-Meier method. All clinically relevant data were evaluated using a statistics programme. Analysis of qualitative parameters for the survival periods was carried out by using the log-rank test and with regard to the duration of the patients' stay in hospital using the Wilcoxon-Mann-Whitney test. The significance level chosen for both test methods was p=0.05.

Results

Age and gender

The average age of the patients was 63.3 years (range 31–92 years). The majority were in their sixth or seventh decade. The patients were predominantly female (73.3%) with only 26.7% males (Fig. 1).

Period between primary tumour and metastasis

The period of time that elapsed between diagnosis of the primary tumor and evidence of osteolysis or pathologic fracture was 48.3 months on average. In the 1st year after diagnosis of the primary tumour, osseous metastases were diagnosed in 29 patients, and in the 2nd year in 14. From the 13th year on after primary tumour diagnosis, osseous metastases were detected in 15 further patients (Fig. 2). The average intervals between diagnosis of the three most frequent primary tumours and the first osseous metastasis/operation were: mammary cancer 62.8/80 months, hypernephroma 9.1/27.8 months, bronchial carcinoma 3.5/5.9 months. The average periods between manifestation of the first clinical symptoms of the metastasis and stabilization by surgery were: mammary cancer 17.2 months, renal cell cancer 18.7 months, bronchial carcinoma 2.5 months.

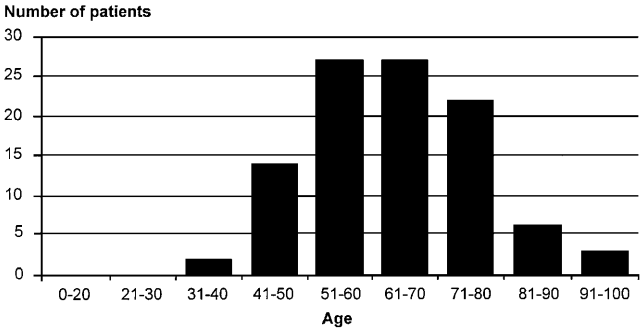

Fig. 1 Age distribution of patients (n=101)

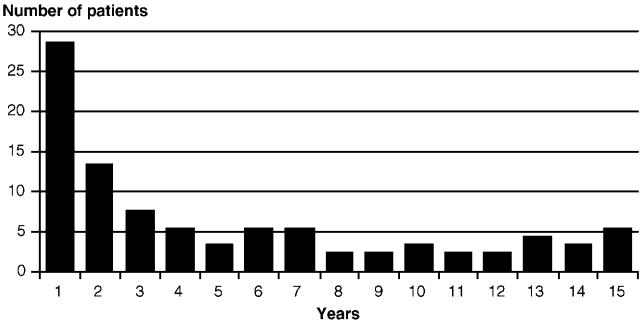

Fig. 2 Period between primary tumour diagnosis andthe first osseous metastasis (n=101)

Diagnostics and distribution of skeletal metastases

In 35 patients local pain and tumour follow-up led to the diagnosis of an osseous metastasis prior to fracture. In 66 cases pathologic fractures had already occurred, some of them accompanied by deformity or neurological symptoms. Of the 117 operations, 41 (35%) were preventive measures and 76 (65%) were performed to treat the pathological fractures. In the previous 5-year period, the corresponding figures were 40% (preventive measures) and 60% (pathologic fractures).

In addition to anamnesis and clinical examination, standard radiography (Fig. 3) was the most important of the various methods of examination.

Bone scanning was very helpful, particularly in detecting cases for preventive stabilization. Computed tomography or magnetic resonance imaging were only necessary when adjoining structures (e.g. the spinal column) or the extent of soft-tissue involvement determined the therapeutic procedure. The surgically treated metastases were localized throughout the skeleton (Table 1, Fig. 4):

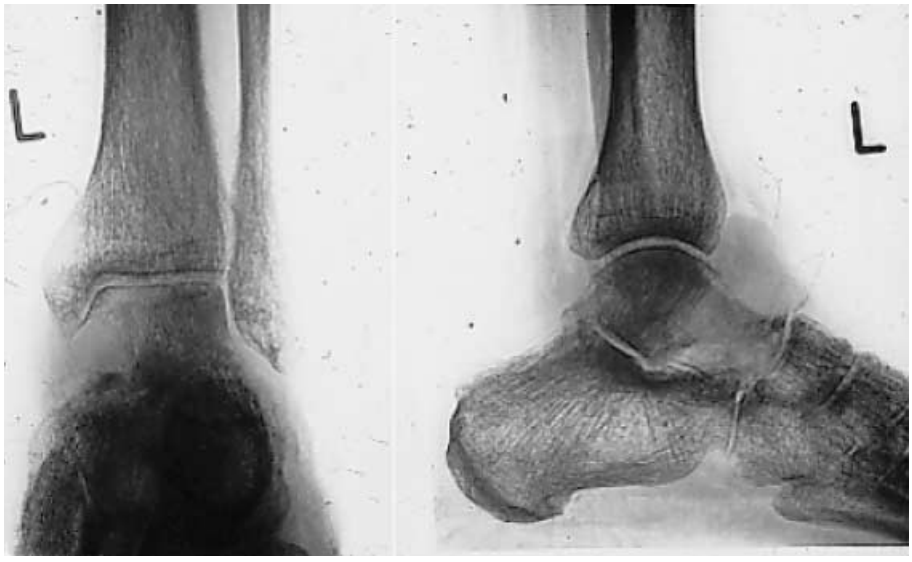

Fig. 3 Standard radiograph of calcaneus, lateral view: solitary colon carcinoma metastasis

Table 1 Localization of pathologic fractures and potential fractures due to osteolysis (*n*=117 operations)

Section of skeleton	Number	Percentage
Femur	70	59.8
Humerus	22	18.8
Spinal column	12	10.2
Pelvis	7	5.9
Clavicula	2	1.7
Tibia	1	0.9
Calcaneus	1	0.9
Ulna	1	0.9
Ribs	1	0.9
Total	117	100

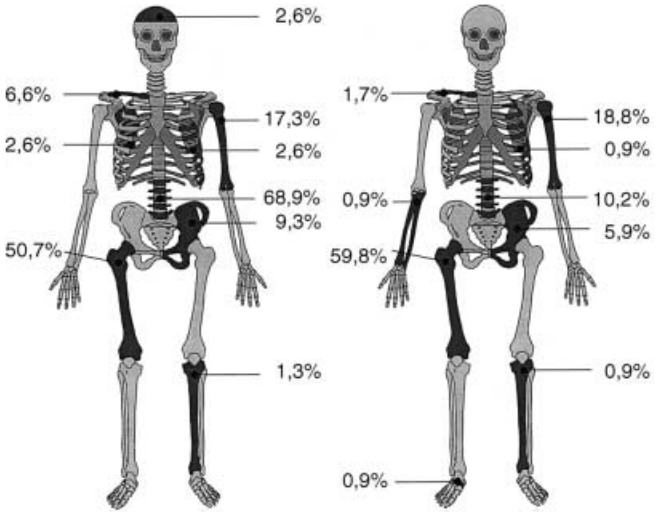

Fig. 4a,b Distribution of osseous metastses in the skeleton (according to Hecht, **a**) and in our patient group (**b**)

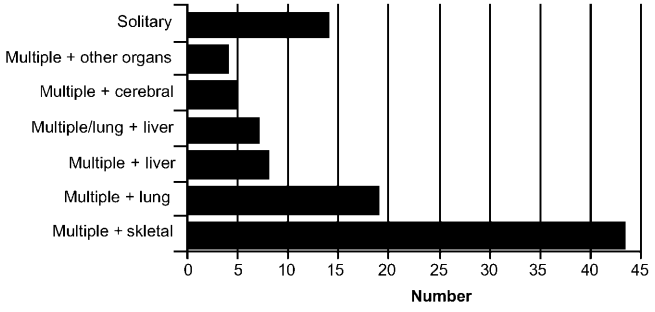

Fig. 5 Distribution pattern of the metastases (*n*=101)

Metastatic form

Of 101 patients 86 (85.1%) had metastases in a number of different organs, i.e. more than one localisation independent of the originally affected organ system. In 15 cases only solitary osseous metastases were detected at the time of diagnosis (Fig. 5).

Surgical procedure

Of the operations 15% were compound osteosyntheses, and in 33% intramedullary nails were used. In the previous reference period (1990–1994), the percentage of compound osteosyntheses performed was about 27%, and the percentage of intramedullary nail procedures about 20%. As far as the long bones were concerned, therefore, there was a marked trend towards intramedullary stabilization. The percentage of endoprosthetic procedures also increased, rising to 26% in comparison with 19% in the previous reference period (Fig. 6).

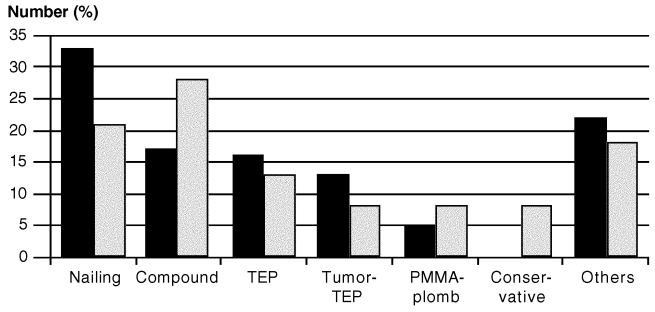

Fig. 6 Therapy procedure in the current (*black*, *left*) and the previous (*shaded*, *right*) 5-year reference period (n=237)

Blood units used

The average amount of banked blood used per operation was between 3 (DHS) and 8.2 units of packed red cells (condylar screw). The number of units used was low not only for dynamic hip screw (DHS) operations, but also for compound osteosyntheses (3.3 units per operation) and/or the various medullary nail procedures (4.5 units per operation). This was mainly due to haemostasis after insertion of polymethylmethacrylate (PMMA) during the compound osteosynthesis procedure and the low operational trauma during intramedullary nail procedures as well as the relatively short operating times.

Duration of hospitalization

The average duration of the patients' stay in hospital was 17.8 days. Six patients underwent two operations during one stay, and 10 were re-admitted for a second operation during a second stay (n=111). The majority of patients were discharged from hospital between the 8th and 14th postoperative day (Fig. 7).

The average hospitalization stay of the patients who underwent preventive surgery was 16.8 days, and of patients with pathologic fractures 18.3 days (p=0.134). After intramedullary nail operations the postoperative stay in hospital was 16.6 days, which lay between 15.9 days after preventive surgery and 17.3 days after surgery for pathologic fractures.

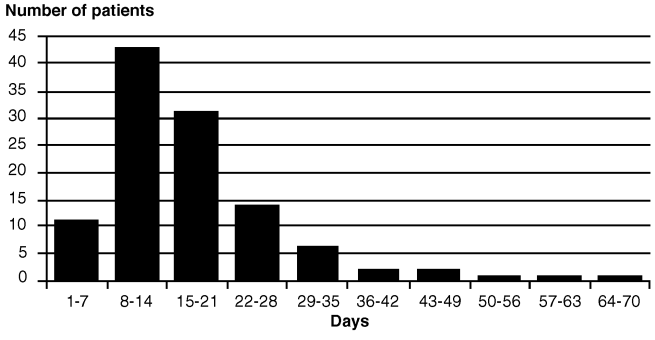

Fig. 7 Duration of hospitalization (n=111)

Functional results

On the day of discharge, 68 patients with endoprostheses or osteosyntheses of the lower extremities (n=79) were capable of full (51, 64.6%) or partial (17, 21.5%) weight-bearing. Nine patients (11.4%) were not allowed to bear weight for several weeks, and in 2 patients (2.5%) the most that could be achieved was a stable position for the limb due to multiple osseous metastases. In the upper extremity (n=23) 22 metastases or pathologic fractures of the humerus were treated. In 1 case the ulna was affected. Five patients (21.7%) regained full use of the operated arm by the day of discharge. Sixteen patients (69.6%) achieved limited use of the arm with stability during physiotherapy which allowed them to perform certain activities independently, e.g. personal hygiene. In 2 patients (8.7%) it was only possible to achieve a stable position for the limb (Table 2).

After osteosynthesis procedures in the spinal column (n=12), 10 patients were mobilized with full weight-bearing. Due to an incomplete transverse syndrome 1 patient was capable of partial weight-bearing only, and another patient died on the 2nd postoperative day as a result of a fulminant pulmonary embolism.

Pain relief

After 54% of the operations, it was possible to reduce the patients' need for analgesics. In 33% the use of painkilling medication was unchanged in comparison with the preop-

Table 2 Functional results of the lower and upper extremities

	Patients (n)	Patients (%)
Lower extremity (n=79)		
Full weight-bearing	51	64.6
Partial weight-bearing	17	21.5
No weight-bearing	9	11.4
Stable position	2	2.5
Total	79	100
Upper extremity (n=23)		
Full use of arm	5	21.7
Limited use of arm	16	69.6
Stable position	2	8.7
Total	23	100

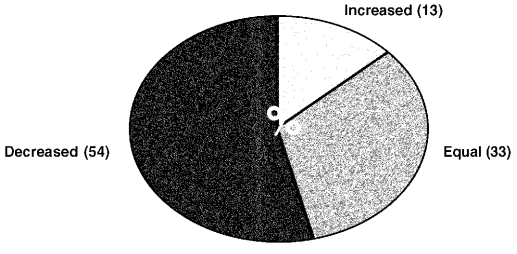

Fig. 8 Postoperative intake of analgesics

erative period, and in 13% there was an increase in intake (Fig. 8).

Complications and fatality rate

General, systemic complications (non-fatal) occurred in 17 of the 117 cases (14.5%) (Table 3).

A total of 29 local complications (24.8%) occurred (Table 4), making 10 revisions (8.5%) necessary (Table 5).

Of the 101 patients 46 underwent additional radiotherapy, and 39 patients additional chemotherapy. In 17 cases a combined radio- and chemotherapy was carried out, and 32 patients received endocrinotherapy (Table 6).

The seven dislocations occurred in 3 patients, 1 of them with fivefold dislocation. The two nerve lesions involved the femoral nerve after implantation of a special tumour total endoprothesis and the radial nerve after plate osteosynthesis of the humerus. The screw perforation, splenic rupture, pleural effusion and pleural empyema all occurred after anterior stabilization of extensive vertebral metastases.

The revision operations included two implantations of a total hip prosthesis following complications with a medullary nail, exchange of a prosthesis stem and an acetabular cup, and exchange of a standard prosthesis for a special tumour total prosthesis. In 1 case Palacos cement which had protruded close to the knee joint had to be removed as it threatened to narrow the retropatellar space.

Eight of 101 patients (7.9%) died while still in hospital. Two patients died of fulminant pulmonary embolism, 1 of two-stage splenic rupture (see above), while the remainder had clinical symptoms of cardiovascular failure as a result of tumour-related poor general health.

Table 3 General complications (n=17)

	Number
Pneumonia	6
Venous thrombosis in the legs	4
Pulmonary embolism	3
Temporary renal insufficiency	1
Renal failure	1
Addisonian crisis	1
Paraparesis (meningitis carcinomatosa)	1

Table 4 Local complications (n=29)

	Number
Dislocation of joint prosthesis	7
Deep wound infection	3
Haematoma	3
Material fracture	3
Superficial wound infection	2
Nerve lesion	2
Intraoperative femur fracture	2
Protrusion of Palacos	1
Perforation by screw	1
Other forms of disturbed wound healing	1
Pleural effusion	1
Pleural empyema	1
Two-stage splenic rupture	1
Fracture following screw osteosynthesis	1

Table 5 Revision operations (n=10)

	Number
Prosthesis exchange, prosthesis implantation	3
Exchange of osteosynthetic material	3
Insertion of polymethylmethacrylate pellets	2
Removal of Palacos	1
Exchange of acetabular component	1

Table 6 Supplementary radio- and chemotherapy

	Number
Radiotherapy	46
Radiation of operated region	15
Radiation of other skeletal sections	17
Combined radiation of operated region and other skeleton sections	14
Chemotherapy	39
Preoperative	24
Postoperative	9
Pre- and postoperative	6

Survival

The survival period after diagnosis of the primary tumor was 71 months on average, ranging from 258 months (mammary cancer) to 1 month (plasma cell tumour). Of the patients in this study, the mammary cancer patients survived longest with 95 months on average, followed by the patients with hypernephroma (47 months) and bronchial carcinoma (18 months) (Fig. 9).

The average postoperative survival (means of survival periods of deceased patients) was 15.8 months. It was much lower for patients with pathologic fractures (10.3 months) than for patients after preventive stabilization (16.2 months) (p=0.19). The mammary cancer patients had an average postoperative survival of 16.8 months. The bronchial car-

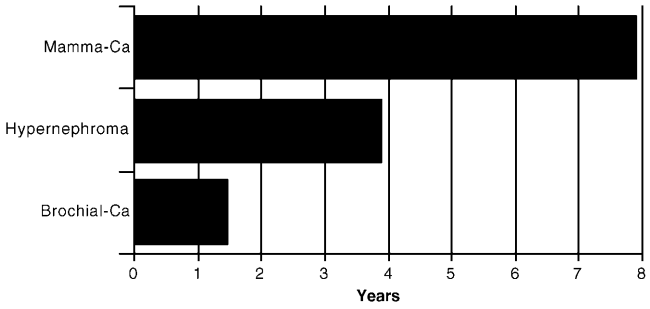

Fig. 9 Average survival (means of survival periods) after diagnosis of primary tumour

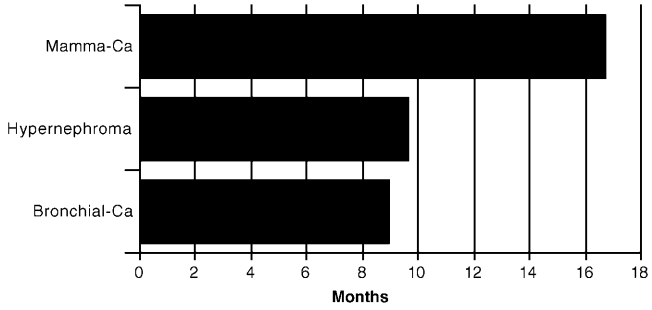

Fig. 10 Average postoperative survival for the three most frequent tumours

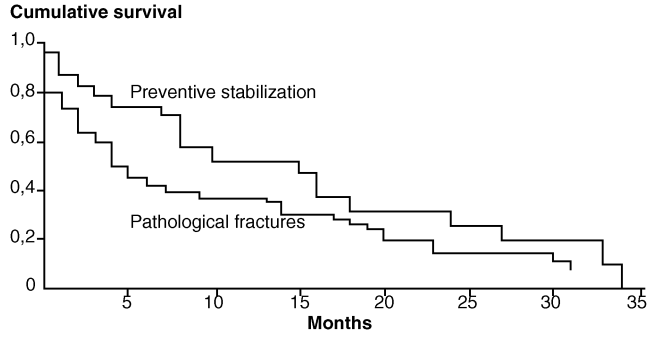

Fig. 11 Postoperative survival analysis according to Kaplan-Meier (n=101)

cinoma and hypernephroma patients had an average postoperative survival of 9.0 and 9.7 months, respectively (Fig. 10).

The survival curves according to Kaplan-Meier are shown in Fig. 11.

Follow-up results

Twelve of the 101 patients were followed-up after postoperative intervals ranging from 6 to 23 months. Of these, 8 had mammary cancer, while the 4 others had cancer of the rectum, prostate, stomach or bronchial carcinoma.

Subjective complaints

Six of the 12 patients reported no (n=4) or only slight pain in the affected skeletal section. Four patients reported tolerable pain which was mainly dependent on weight-bearing and/or the awareness of the presence of a foreign body. Only 2 patients experienced intermittent pain while at rest or during the night. When assessed together with the functional result (see below), mobility and the postoperative intake of analgesics, 5 patients considered the result of the operation to be good. Five were of the opinion that the result was satisfactory, 1 thought it was very good, and 1 thought it was poor.

Functional results

Seven patients (58.3%) did not require any orthopaedic aids. Five (41.7%) used a cane or two crutches. Three patients were no longer able to climb stairs due to their generally weak state of health. Five of the 9 remaining patients had no trouble climbing several flights of stairs without aid, while 4 patients needed the support of the banisters only or of the banisters and a cane. More differentiated functional tests were not carried out as the aim of the therapy of these 12 patients with advanced cancer was to allow them to return to their home environment.

Discussion

Constant improvement in the interdisciplinary treatment of malignant tumours has resulted in prolonged life expectancy on the one hand, but also in an increase in the incidence of osseous metastases and pathologic fractures on the other. Here, surgery is the main method of therapy, although it can only be of a palliative nature. The foremost aims are to preserve the function of the affected section of the skeleton, relieve pain and facilitate care of the patient while keeping hospitalization as short as possible. The procedure most frequently performed to achieve these aims is a stabilizing osteosynthesis in the lower extremities which allows full weight-bearing, and in the upper extremities a stabilizing osteosynthesis which at least allows certain everyday activities [7, 12, 14].

Since the indication for operation is largely determined by impending or already existing complications, the choice of surgical method and the right time for operation are currently the subjects of intense discussion. In our study the prognosis for the patient depends on the type of primary tumour and not on the therapy of the metastases. The average survival of our patients after diagnosis of mammary cancer was 7.9 years. Bronchial carcinoma patients, however, survived only 1.5 years on average after diagnosis.

Besides histology and clinical symptoms, the period that elapses between diagnosis of the primary tumour and manifestation of metastases is a useful factor in assessing the progress of the disease [10, 29, 33]. This is particularly important when planning large operations, as these should always be based on a sensible balance between the operative risk, operative trauma and duration of hospitalization on the one hand and the statistical life expectancy of the patient and the achievable improvement in quality of life on the other. This consideration can in some cases justify very extensive reconstructive surgery, for instance partial pelvis replacement in a 62-year-old patient with diffuse osseous metastases of mammary cancer who was still able to move without pain or walking aids 23 months after the operation.

Patients with skeletal metastases of mammary cancer constituted the largest group which came for treatment (50% of the patients studied here), followed by patients with bronchial carcinoma (11%), hypernephroma (8%) and non-Hodgkin's lymphomas (8%). In comparison with

the previous 5-year period, there was a slight increase in the percentage of patients with mammary cancer metastases (50% vs 45.5% previously), probably due to improved adjuvant therapies.

Nevertheless, according to our study it appears that the widely reported trend towards increasingly prolonged survival of patients with certain tumours after the occurrence of pathologic fractures is levelling off. During the 1950s the majority of patients died within 6 months after the occurrence of pathologic fractures. Two decades later in 1976, Harrington et al. reported an average life expectancy of 15.6 months [15, 34]. Our data document an average postoperative survival of 15.8 months and thus do not show any possibility of improving the prognosis further. These results are corroborated by reports in the current literature [4, 5, 10, 22].

Analysis of the type of primary tumour revealed that patients with osseous metastases of bronchial carcinomas had the worst prognosis, with an average postoperative survival of 9 months. Renal cell cancer patients lived only slightly longer, with an average survival of 9.7 months. Mammary cancer patients had the best prognosis with 16.8 months. These results are also confirmed in the current literature. Mutschler [24] reports slightly worse prognoses, with average postoperative survivals of 15.8 months for metastasizing mammary cancer, 7.3 months for bronchial carcinoma and 6.1 months for hypernephroma.

Comparison of the survival period following primary diagnosis of the tumour with the period between the primary diagnosis and manifestation of osseous metastases shows clearly that the long overall survival of patients with mammary cancer is largely due to the relatively late development of osseous metastases and is not so much the result of prolonged postoperative survival. The short survival of patients with bronchial carcinoma corresponds to an early development of osseous metastases.

The question as to whether too many patients with limited life expectancy are subjected to the stress of an operation is often discussed in literature. One answer to this lies in the experience with osseous metastases in the 1960s where conservative therapy resulted in immobility, excessive intake of analgesics and nursing problems (decubitus) at an early stage. With regard to our patient group, the decision to perform surgery was made taking the primary diagnosis with an estimated survival of at least 4 weeks into account. Of course, errors concerning the prognosis cannot always be avoided [33], but on the day of discharge 86.1% of our patients with osteolysis or pathologic fractures of the lower extremities were mobilized and capable of full (64.6%) or partial (21.5%) weight-bearing. All of the patients available for follow-up were also fully mobile after 6–12 months at home. More than half of these patients considered the result of their operation to be good or very good.

Dijkstra et al. [4] considers that, particularly in view of the uncertain prognosis, the risk involved in surgery for almost every patient with a pathologic fracture is justified, even if the psychological benefit is the main or only reason for the operation. For other authors [24, 35] the preconditions for surgery are ability to undergo anaesthesia and a probable survival of 2–4 weeks, or they expect additionally an adequate general state of health which will allow subsequent mobilization with a probable survival of 6 weeks. Bedridden patients are not considered for surgery [5, 9, 10, 13, 25, 32].

Using clinical data, Bauer and Wedin [1] developed prognostic variables with regard to the postoperative survival of patients with skeletal metastases. Solitary metastases and mammary and hypernephroma as the primary tumours were graded as positive variables. This is confirmed by the results in our study, which revealed average survival after primary diagnosis of 95 months for mammary cancer and 47 months for renal cell cancer, in contrast to only 18 months for bronchial carcinoma. Correspondingly, according to Bauer, bronchial carcinoma, pathologic fractures, multiple and cerebral metastases are graded as negative variables. In our study the average postoperative survival after the occurrence of pathologic fractures was 10.3 months and much lower than the survival after preventive stabilization (16.2 months).

Along with the prognosis quoad vitam, assessment of the risk of fracture is especially important for the surgical procedure. As well as preventing spontaneous fractures, operations at this stage are of significantly shorter duration and often technically simpler. The operative risk is reduced substantially by the avoidance of emergency surgery [8, 13, 23].

In our own group of patients, an operation was indicated in those with osteolysis of the long bones which had reached a diameter of more than 2.5 cm and/or affected more than 50% of the cortical circumference [8, 9, 18, 24, 31]. A further indication for surgery was metastasis-related, intractable pain. In the opinion of Chao et al. [3], lesions which are larger than 3 cm or affect more than 50% of the circumference represent a 50% risk of fracture. The risk is considerably greater when 75% of the circumference is affected. For other authors local pain is the decisive criterion, based on the assumption that painful metastases are generally at risk of fracture [12].

Regarding the choice of surgical procedure, a large number of authors have for some time been recommending extralesional resection and endoprostheses or intramedullary osteosynthesis (if necessary as compound osteosynthesis) to span defects [9, 10, 16, 17, 30, 33]. Peltier [26, 27, 28] proved in experiments that intramedullary pressure during impaction of the nail increases significantly. The shorter the intervals between the blows by the mallet and the larger the diameter of the nail, the more the pressure increased. The assumption that this increase in pressure would lead to a general systemic dissemination of the tumour was not confirmed in other studies, and a much improved life expectancy was documented [15, 29, 33]. Bouma et al. [2] proved in experiments with animals that the incidence of pulmonary metastases rises significantly following pathologic fractures. Preventive stabilization, in contrast, reduced the number of fractures and therefore did not lead to an increase in the number of pulmonary metastases.

Only in a very few cases, such as in 1 of our patients with rectum cancer metastases, did we observe local dissemination along the nail shaft or into the subcutaneous region [15, 35]. Due to the prognosis of the tumour itself, this was not clinically significant. We therefore did not carry out local postoperative radiation as recommended by some authors [10, 32]. Closed reduction internal fixation without exposure of the focus can be performed carefully and generally enables fast and largely pain-free mobilization with a low rate of complications [19, 21, 31, 34].

The data concerning postoperative intake of analgesics need to be differentiated. At first, it would seem that reports by other authors on reductions in postoperative intake of pain-killing medication ranging from 66% to 98% surpass our results by far. But in contrast to other studies, our results document the total intake of analgesics in a pre- and postoperative comparison, regardless of whether the patient was pain-free in the stabilized extremity but needed pain relief for other reasons, e.g. other metastases. When the intake of analgesics was related to pain in the operated extremity alone, our results corresponded to those generally found in literature.

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