ORIGINAL PAPER

Nagoya J. Med. Sci. **72**. 13 ~ 21, 2010

SURVIVAL AND AMBULATORY FUNCTION AFTER ENDOPROSTHETIC REPLACEMENT FOR METASTATIC BONE TUMOR OF THE PROXIMAL FEMUR

Hiroatsu Nakashima[1], Hirohisa Katagiri[2], Mitsuru Takahashi[2] and Hideshi Sugiura[3]

[1]*Department of Orthopedic Surgery, Aichi Hospital, Aichi Cancer Center*
[2]*Department of Orthopedic Surgery, Shizuoka Cancer Center Hospital*
[3]*Department of Orthopedic Surgery, Aichi Cancer Center Hospital*

ABSTRACT

The purpose of this study was to clarify the ambulatory functional and oncological outcomes of tumor excision and endoprosthetic reconstruction for a metastatic lesion of the proximal femur. Subjects comprised 40 patients (18 women, 22 men; average age 63.4 years). The mean follow-up periods were 15.2 months for patients dying of the disease, and 38.7 months for survivors. Seven patients were lost to follow-up for 1.9 to 13.1 months. Endoprosthesis was performed after intralesional aggressive curettage in 20 patients and following excision of the lesion with a clear margin, in another 20. Postoperative radiation therapy was carried out on 27 limbs (intralesional 13, marginal 6, wide 8). Chemotherapy was administered to 19 patients after discussion with the medical oncologist. The cumulative survival rates at 6 and 12 months were 60% and 35%, respectively, while the rates with ambulant status were 48% at 6 months and 34% at 12 months. An analgesic effect was achieved for all patients. Ambulatory function was restored in 34 patients with a mean ambulant period of 17.8 months; however, the other 6 patients remained non-ambulatory. The ambulant period expressed as a percentage of survival time averaged 75.9%. Though there was local recurrence in 4 of 40 patients, ambulant function was not affected. Postoperative ambulatory function was inferior in patients with a short life expectancy; those with moderate or long life expectancy are good candidates for endoprosthetic replacement after tumor excision and can regain ambulant function for as long as nearly 80% of the survival period.

Key Words: Metastatic bone tumor, Endoprosthetic replacement, Femur, Ambulatory function, Prognosis

INTRODUCTION

The aim of surgical treatment for metastatic bone tumors is not to cure the disease but rather to improve the quality of life by relieving pain and maintaining ambulatory function as long as possible in the remaining years. The proximal part of the femur is one of the most common sites for skeletal metastasis and the most frequent site for surgery.[1)] With advances in radiation therapy and chemotherapy, limb salvage became a viable option in the early 1980s, and the introduction of modular-type endoprostheses in the late 1980s permitted the reconstruction of a

Corresponding author: Hiroatsu Nakashima
Department Orthopedic Surgery, Aichi Hospital, Aichi Cancer Center,
18 Kuriyado, Kake-machi, Okazaki 444-0011, Japan
Phone: +81-564-21-6251, Fax: +81-564-21-6467, E-mail: hnakasima@acc-aichi.com

wide variety of skeletal defects after tumor resection.[2,3] Advances in cancer treatment have extended the survival period even for patients with skeletal metastasis, thus requiring reconstruction with long-term stability in some cases. Internal fixation with plates and screws or intramedullary rods using polymethylmethacrylate augmentation for metastatic bone lesions is well established, but internal fixation devices entail the risk of breakage in long-term survivors.[3,4] In contrast, endoprosthetic reconstruction is durable and implants are generally long-lasting. Until now, there have been no reports on the period of maintaining ambulatory function, the correlation between local recurrence and treatment as well as that between prognosis and postoperative function after endoprosthetic replacement for skeletal metastasis of the proximal femur. The purpose of this study is to assess the outcomes of tumor resection and endoprosthetic reconstruction for impending or pathological fractures from skeletal metastasis in the proximal femur, and to clarify the abovementioned issues.

PATIENTS AND METHODS

From 1993 to December 2006, 40 patients with a total of 41 metastatic lesions in the proximal part of the femur were treated surgically at our institutes. They included 18 women and 22 men with an average age of 63.4 years (range: 31 to 81 years). The mean postoperative follow-up period was 17 months (range: 1 to 92.5 months) for all patients, while for terminal patients and survivors it was 15.2 months (range: 1 to 92.5 months) and 38.7 months (range: 4.7 to 52.9 months), respectively. Seven were lost to follow-up from 1.9 to 13.1 months. The most common primary lesion was breast carcinoma, which was seen in 11 patients, including one with bilateral femoral lesions. Other primary lesions were lung carcinoma in 8, gastrointestinal tract carcinoma in 7, renal cell carcinoma in 4, thyroid carcinoma in 3, and in 1 patient each with hepatocellular carcinoma, cervical carcinoma, parotid carcinoma, bladder carcinoma, prostate carcinoma, malignant lymphoma, and multiple myeloma.

The indications for surgery were as follows: 1) a pathologic or impending fracture according to Harrington's criteria[5] requiring prophylactic treatment, i.e., a lytic zone of more than 2.5 cm in diameter, destruction of the cortex involving more than 50% of the bone, or a lesion for which radiation therapy had failed; 2) a sufficiently good general condition to survive an operation; and 3) a life expectancy of more than 2 months.[6]

Endoprosthetic replacement was performed after intralesional aggressive curettage in 20 patients and after excision of the lesion with a clear margin in another 20. If the lesion was localized in the femoral head and neck region, an endoprosthesis with an ordinary stem or a calcar-replacement femoral endoprosthesis (Zimmer, Warsaw, IN) was used. If the lesion extended from the femoral neck to the subtrochanteric region, a modular-type long-stem proximal femoral endoprosthesis (Japan Medical Materials, Osaka, Japan) was used. Polymethylmethacrylate (PMMA) was used in all cases to achieve immediate stability. Postoperative radiation therapy (20–40 Gy) was carried out on 27 limbs (intralesional 13, marginal 6, wide 8). Chemotherapy was administered to 19 patients following a discussion with the medical oncologist.

We retrospectively analyzed i) the correlation between local recurrence and treatment, ii) analgesic effect, iii) postoperative ambulatory function, iv) overall and ambulant function maintaining survival, and v) the correlation among survival, function and prognostic score.[7] The cumulative survival rate was determined using the method of Kaplan and Meier and was calculated from the date of the operation. The log-rank test was used to evaluate the significance of differences between groups, with p values less than 0.05 considered significant. Surgical procedures were evaluated according to the Enneking evaluation system[8] into radical, wide, marginal, and intralesional. Local recurrence was defined as radiographic expansion of an osteolytic lesion or tumor regrowth around the operated area. The analgesic effect was evaluated 2 to 4 weeks after surgery according to Suzuki's criteria,[9] in which postoperative analgesic effects are grouped into 4 categories: excellent (no pain whatsoever, no need for pain relievers), good (pain has mostly disappeared, but pain relievers are sometimes needed), fair (some pain alleviation, but periodic pain relievers are needed), and poor (no pain reduction). Postoperative functions of the lower extremity were also evaluated using Suzuki's criteria,[9] in which postoperative ambulatory functions are grouped into 4 categories: excellent (able to walk outdoors with or without an aid), good (able to walk only indoors with or without an aid), fair (unable to walk, but can use a wheelchair), and poor (bedridden).

RESULTS

Clinical data of the 40 patients with tumor resections and/or endoprosthetic replacements were shown in Table 1. Prognostic scores (Katagiri score) of point 0 was 4 patients, point 1 was 6, point 2 was 10, point 3 was 8, point 4 was 9, point 5 was 2 and point 6 was one.

Local recurrence

Wide, marginal and intralesional procedures were performed on 12, 9 and 20 limbs, respectively. Additional radiation therapy was performed on 8 out of 12 limbs with wide procedure, 6 out of 9 with marginal procedure, and 13 out of 20 with intralesional procedures. Local recurrence was found on plain radiographs in 4 patients, 2 of whom underwent an intralesional procedure and radiation therapy, 1 with a marginal procedure and radiation therapy, and 1 with marginal excision alone. However, no salvage operation was required in any recurrent cases, and none of their ambulant functions were affected by this local recurrence for their remaining lifespan. Local recurrence was not extensive and did not lead to failures including those of periprosthetic fracture and loosening.

Pain relief and ambulation

The analgesic effect was evaluated as excellent in 34 limbs and good in 7. Pain relief was good to excellent even in non-ambulatory patients. Twenty-nine patients achieved excellent results functionally, 5 were good, 3 were fair and 3 were poor. A total of 34 patients (85%) were able to regain or maintain ambulatory function, while 6 (15%) were not. The reasons for remaining non-ambulatory were as follows: 2 because of skeletal metastasis to other bone (ipsilateral acetabulum with contralateral femur in 1, and cervical spine in another), 2 due to their deteriorating general condition from cancer progression, 1 from dementia, and 1 from brain metastasis.

Overall and ambulant function maintaining survival

The overall survival rate of all patients was 60% at 6 months, 35% at 12 months and 21% at 24 months. The cumulative survival rate with ambulant status was 48% at 6 months, 34% at 12 months and 17% at 24 months (Fig. 1). The mean ambulant period was 17.8 months in the 34 patients with excellent or good functional results. The ambulant period expressed as a percentage of survival time averaged 75.9% (57 to 100%).

Correlation among survival, function, and prognostic score

The prognostic scoring system developed by Katagiri[7] is shown in Table 2. The score was calculated by adding scores for each prognostic factor, with possible scores ranging from 0 to 8.

Table 1 Clinical data in 40 patients with tumor resection and endoprosthetic replacement

Case	Gender	Age (year)	Primary tumor	Follow-up period (month)	Prog-nosis	Margin	Recur-rence	RT	CT	Analgesic effect	Ambulatory function	Ambula-tory period (month)	Katagiri score
1	F	66	GIT	7	DOD	I			Yes	Excellent	Excellent	7	3
2	F	56	Cervical	4.2	DOD	I		20 Gy	Yes	Excellent	Excellent	3	3
3	F	43	Breast	30.1	DOD	M		40 Gy	Yes	Excellent	Excellent	28	3
4	M	64	HCC	22	DOD	I		30 Gy		Excellent	Excellent	22	4
5	F	75	GIT	6.4	DOD	M	Yes	40 Gy	Yes	Good	Excellent	4	3
6	M	60	Lung	8	DOD	W			Yes	Good	Excellent	7	4
7	M	55	Lung	3.4	DOD	W		40 Gy		Excellent	Excellent	3	3
8	F	52	Lung	7.1	DOD	M	Yes		Yes	Good	Excellent	5	4
9	M	72	Prostate	6.8	DOD	W				Excellent	Excellent	6	0
10	F	45	Breast	92.5	DOD	W		20 Gy	Yes	Excellent	Excellent	90	1
11	F	68	Breast	9.8	DOD	W		40 Gy	Yes	Excellent	Excellent	9	2
12	M	60	Bladder	3.1	DOD	W				Excellent	Excellent	3	4
13	M	72	Lymphoma	2	Lost	I			Yes	Excellent	Good	2	1
14	M	81	Thyroid	1.9	Lost	M		40 Gy		Good	Excellent	2	0
15	F	58	Lung	2.1	Lost	M		29 Gy	Yes	Excellent	Excellent	1	4
16	F	82	GIT	13.1	Lost	I	Yes	40 Gy		Excellent	Excellent	13	2
17	F	79	Breast	4.7	AWD	W		40 Gy		Excellent	Good	4	0
18	F	46	Breast	72	AWD	I		40 Gy	Yes	Good	Excellent	72	2
				70		I		40 Gy		Good	Excellent		
19	M	68	RCC	40	DOD	M				Excellent	Excellent	38	2
20	M	78	Myeloma	19	DOD	I		40 Gy	Yes	Excellent	Good	19	1
21	F	58	Breast	64	DOD	M		36 Gy		Excellent	Excellent	64	1
22	F	35	Breast	13.6	DOD	I				Excellent	Excellent	14	0
23	M	31	Lung	4.2	DOD	I		30 Gy		Good	Poor	0	4
24	F	72	Breast	18	DOD	I	Yes	36 Gy		Excellent	Excellent	18	2
25	F	70	Breast	10.6	DOD	I			Yes	Excellent	Good	6	2
26	M	71	RCC	10.3	DOD	I				Excellent	Excellent	10	2
27	M	62	Lung	2.7	DOD	M		37.5 Gy	Yes	Excellent	Good	2	4
28	M	46	GIT	6.5	DOD	W			Yes	Excellent	Excellent	7	5
29	M	71	Lung	6.6	DOD	I		30 Gy	Yes	Excellent	Excellent	5	5
30	F	71	Breast	3.3	DOD	I				Excellent	Fair	0	2
31	M	40	GIT	1.3	DOD	I				Excellent	Poor	0	3
32	M	73	Parotid	1.8	Lost	I		39 Gy		Excellent	Fair	0	3
33	M	79	RCC	1	DOD	M				Excellent	Poor	0	4
34	M	75	RCC	52.9	AWD	W		20 Gy	Yes	Excellent	Excellent	53	3
35	F	55	Breast	2.5	Lost	I		30 Gy	Yes	Excellent	Good	3	4
36	M	71	GIT	3.6	Lost	I		20 Gy		Excellent	Excellent	4	2
37	M	73	GIT	23.5	DOD	W		40 Gy	Yes	Excellent	Excellent	17	2
38	M	66	Tyroid	42.4	AWD	W		20 Gy		Excellent	Excellent	42	1
39	M	65	Lung	1.5	DOD	I		30 Gy	Yes	Excellent	Fair	0	6
40	F	70	Tyroid	21.6	AWD	W		20 Gy		Excellent	Excellent	22	1

F: female; M: male
GIT: Gastrointestinal tract carcinoma; RCC: Renal cell carcinoma; HCC: Hepatocellular carcinoma
Lost: Lost to follow-up
I: Intra-lesional; M: Marginal; W: Wide
RT: Postoperative radiation therapy; CT: Chemotherapy

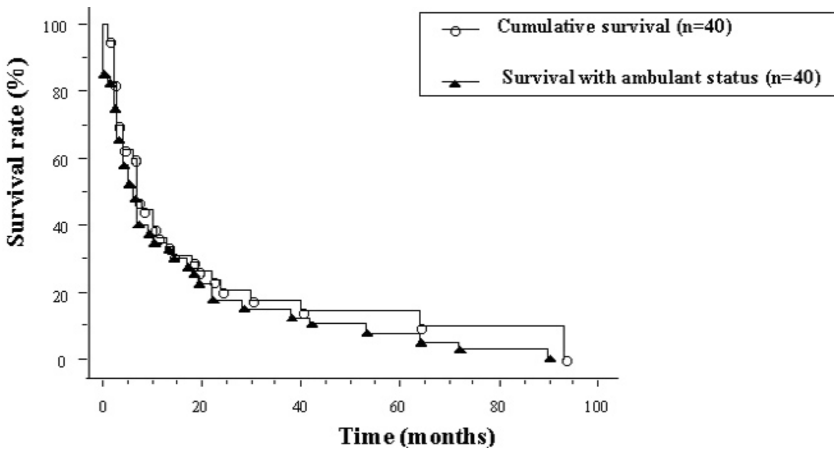

Fig. 1 Kaplan-Meier cumulative survival rate and survival with ambulant status.

Table 2 Prognostic scoring system according to Katagiri[7)]

Prognostic factor	Score
Primary lesion	
Hepatocellular carcinoma, gastric carcinoma, lung carcinoma	3
Breast carcinoma, prostate carcinoma, multiple myeloma, malignant lymphoma, thyroid carcinoma	0
Other carcinoma and sarcoma	2
Visceral or cerebral metastases	2
Performance status 3, 4	1
Previous chemotherapy	1
Multiple skeletal metastasis	1

The patients were divided into two groups with prognostic scores of 0 to 2 and ≥ 3, respectively. The survival rates in the respective groups were 77.4% and 40% at 6 months, and 56% and 13.7% at 12 months (Fig. 2, Table 3); these data showed a significant difference (log-rank test, $p = 0.004$). The survival rates with ambulant status in the respective groups were 65% and 22.5% at 6 months, and 51.7% and 13.3% at 12 months (Fig. 3, Table 3); again a significant difference was observed (log-rank test, $p = 0.01$). The mean survival periods with ambulant status in the respective groups were 22.6 months and 7.6 months, with a significant difference noted (*t*-test, $p = 0.025$).

Among patients with prognostic scores of 0 to 2, 19 (95%) were evaluated as excellent or good, and 1 (5%) as fair. In contrast, among patients with prognostic scores of ≥ 3, 15 (75%) were evaluated as excellent or good, and 5 (25%) as fair or poor. All patients showing either fair or poor functional results, had a postoperative survival period of less than 3 months.

The ambulant period, as mentioned above, averaged 75.9% of the survival period, but the reasons for those remaining non-ambulant patients were due either to their deteriorating general condition to skeletal metastasis to another site, rather than to problems with endoprosthesis.

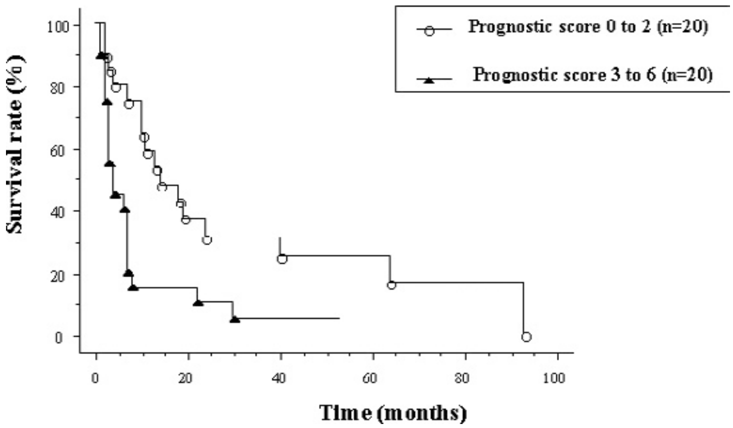

Fig. 2 Kaplan-Meier survival curves for patients with prognostic scores of 0 to 2 and more than 3. The rates of survival for the two groups are significantly different (log-rank test, $p = 0.004$).

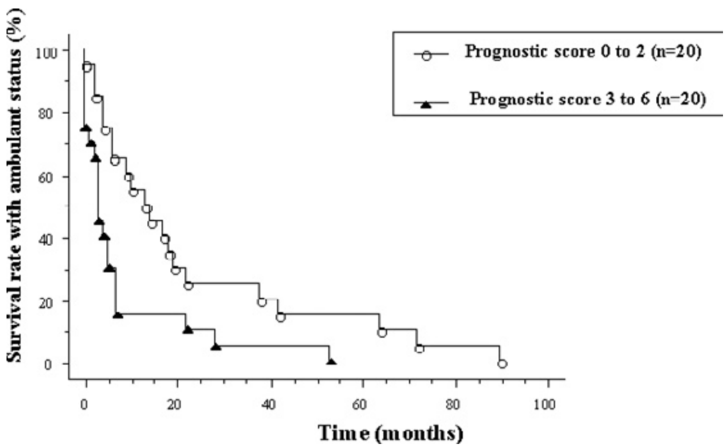

Fig. 3 Kaplan-Meier survival curves with ambulant status for patients with prognostic scores of 0 to 2 and more than 3. The rates of survival for the two groups are significantly different (log-rank test, $p = 0.01$).

Table 3 Prognostic score and survival rate, survival rate with ambulant status at three, 6, and 12 months

		Survival rate (months)		
Prognostic score[7]	Survival rate	3	6	12
0 to 2	OS	0.85	0.774	0.56
	SAS	0.8	0.65	0.517
≥ 3	OS	0.55	0.4	0.137
	SAS	0.45	0.225	0.133

OS, overall survival rate; SAS, survival rate with ambulant status

Complications

Complications included liver dysfunction in patient, deep infection in another, and central migration in a third. Deep infection in the second patient eventually healed after a debridement and intermittent daily wound irrigation. The patient with a central migration of the bipolar head was only monitored, but was able to walk with a cane.

DISCUSSION

For metastatic bone tumors of the proximal part of the femur, the aims of surgical treatment are pain relief and a restoration of the ambulatory function with immediate full-weight bearing and durability during the remainder of life. For metastatic lesions involving the femoral neck and head, conventional bipolar endoprosthetic replacement with a regular-length stem is the treatment of choice.[1] If an intralesional procedure is performed, adjuvant radiation therapy should be used to lessen the chance of metastatic lesion progression within the operative field.[1,4] However, when the metastatic lesion involves the intertrochanteric and subtrochanteric regions, the treatment of choice is either excisional surgery followed by reconstruction with a modular-type endoprosthesis or internal fixation with or without augmentation by polymethylmethacrylate (PMMA).[1,10] However, for long-term survivors, endoprosthetic reconstruction is preferred because of its lower risk of implant breakage.[4]

Although several reports have described endoprosthetic reconstruction for bone metastasis in the proximal femur,[3,10,11] most have focused on its utility and its complications, such as implant failure and infection. There have been very few detailed reports on clinical and functional outcomes after endoprosthetic replacement for bone metastasis in the proximal femur, and, to our knowledge, no reports on the ambulatory period following that replacement procedure.

Rompe *et al.*[11] have compared endoprosthetic replacement to plate osteosynthesis for patients with a metastatic lesion of the proximal femur, and have reported a local recurrence in 4 (44.4%) of 9 patients treated intralesionally and in 3 (18.8%) of 16 treated extralesionally with a prosthesis. However, the local recurrence rate in plate osteosynthesis was 48%. In our study, local recurrence was observed in only 4 (10%) of 40 patients, and neither affected their stability nor ambulatory function.

Wedin *et al.*[10] have also compared endoprosthetic reconstruction to osteosynthesis for pathologic fractures of a metastatic bone tumor of the proximal femur. They reported that the local failure rate was 16.2% in osteosynthesis, and 8.3% in endoprosthesis, and that, of 9 cases of prosthetic failure, 4 were due to periprosthetic fracture, 3 to technical error and 1 to loosening, with no failure due to local recurrence being observed. Rather than use reconstruction nails and other devices, they recommended endoprosthetic reconstruction for the treatment of metastatic lesions in the proximal third of the femur because of fewer local failures and a lower risk of the need for a second operation.

Rompe *et al.*[11] have demonstrated that the function of the hip joint based on measurements of active motion was better in patients who had undergone osteosynthesis than in those who had undergone endoprosthesis. However, they evaluated only the joint function at three months postoperatively, and their findings included neither ambulatory function nor the period of maintaining ambulatory function. Lane *et al.*[3] have reported a study of 163 patients treated with endoprosthetic replacement for pathologic or impending fractures of the hip. They found that 56 (72%) of 78 patients who were able to walk before their fracture regained ambulatory function, and that 40 (46%) of 85 patients who were non-ambulatory prior to fracture recovered ambulatory function.

In this study, we have shown that all patients obtained long-lasting pain relief, and that 34 (85%) of 40 had restored or regained ambulatory function over a mean ambulant period of 17.8 months. The ambulant period expressed as a percentage of survival time averaged 75.9%. Our results indicated that endoprosthetic replacement permitted patients with bone metastasis of the proximal femur to regain long-lasting ambulatory function.

An excisional procedure followed by reconstruction with endoprosthesis is more costly than a simple internal fixation or an internal fixation with PMMA augmentation, and a tumor resection followed by endoprosthetic reconstruction requires a larger and deeper incision than that needed for internal fixation with or without PMMA augmentation, with a higher risk of wound infection. Therefore, when deciding on the best treatment procedure, the patient's life expectancy must be taken into account.

Katagiri *et al.*[7] have identified five significant prognostic factors for survival: the site of the primary lesion; the performance status (Eastern Cooperative Oncology Group[12] status 3 or 4); the presence of visceral or cerebral metastases; any previous chemotherapy; and multiple skeletal metastases in patients with bone metastasis. We compared the survival of patients with prognostic scores of 0 to 2 with those of patients with scores of ≥ 3, and found a significantly longer survival period in the patients with lower scores. We also found that the survival rate with ambulatory status among patients with prognostic scores of 0 to 2 was better than that in patients with scores of ≥ 3. In addition, postoperative ambulatory function was found to be better in patients with prognostic scores of 0 to 2, suggesting that such patients may be expected to enjoy longer-term survival with better function by excision of their metastatic lesion followed by a prosthetic replacement. Even 13 of 17 patients with a score of only 3 or 4 regained ambulatory function. Therefore, if other skeletal and visceral metastases are not life-threatening, endoprosthetic replacement may be indicated. On the other hand, only 2 out of 3 patients with a prognostic score of 5 to 6 could achieve ambulatory status postoperatively.

Although this study is retrospective and the number of patients small, we concluded that patients with a long-life expectancy (Katagiri score 0–2) are good candidates for this resection using an endoprosthetic reconstruction procedure. We further concluded that patients with a score of 3 to 4 (moderate-life expectancy) treated using an intra-lesional or excisional procedure followed by an endoprosthetic replacement, also make promising candidates if other skeletal or visceral metastasis are not life-threatening. In those with a score of 5 or more, one should decide the indications for this procedure cautiously considering their age, general condition, and other site metastasis.

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