Study Design: Retrospective case series.

Purpose: To investigate the oncological outcomes, including distant relapse, after en bloc spondylectomy (EBS) for spinal metastases in patients with a minimum of 2-year follow-up.

Overview of Literature: Although EBS has been reported to be locally curative and extend survival in select patients with spinal metastases, detailed reports regarding the control of distant relapse after EBS are lacking.

Methods: We conducted a retrospective review of 18 consecutive patients (median age at EBS, 62 years; range, 40–77 years) who underwent EBS for spinal metastases between 1991 and 2015. The primary cancer sites included the kidney (n=7), thyroid (n=4), liver (n=3), and other locations (n=4). Survival rates were estimated using the Kaplan–Meier method, and groups were compared using the log-rank method.

Results: The median operative time and intraoperative blood loss were 767.5 minutes and 2,375 g, respectively. Twelve patients (66.7%) experienced perioperative complications. Five patients (27.8%) experienced local recurrence of the tumor at a median of 12.5 months after EBS, four of which had a positive resection margin status. Thirteen patients (72.2%) experienced distant relapse at a median of 21 months after EBS. The estimated median survival period after distant relapse was 20 months (95% confidence interval, 0.71–39.29 months). No association was found between resection margin status and distant relapse. Overall, the 2-year, 5-year, and 10-year survival rates after EBS were 72.2%, 48.8%, and 27.1%, respectively. Importantly, the era in which EBS was performed did not impact the oncological outcomes.

Conclusions: Our results suggest that EBS by itself, even if margin-free, cannot prevent further dissemination, which occurred in >70% of patients at a median of 21 months after EBS. These results should be considered and conveyed to patients for clinical decision-making.

Keywords: Spine; Neoplasm metastasis; Margins of excision; Recurrence; Survival
Introduction

Spinal metastases can cause bony compromise and tumor invasion into the epidural space, progressing to axial pain and neurologic deficits. These symptoms negatively affect the quality of life (QOL) and life expectancy of patients with cancer [1-3]. Thus, the efficient control of primary and metastatic lesions is critical for prolonging survival. 

*En bloc* spondylectomy (EBS) is a surgical procedure that enables the complete resection of vertebral malignant lesions [4,5]. Although metastasis generally indicates systemic cancer, EBS has been shown to be locally curative and extend survival among patients with spinal metastases [6-11]. However, most previous reports focused on local recurrence, and reports providing detailed long-term data on the control of distant metastases (‘distant relapse’) after EBS for spinal metastases are lacking. Because distant relapse after EBS can negatively affect QOL and lifespan, the following questions must be considered during the decision-making process: (1) What is the incidence and risk rate for distant relapse after EBS; (2) For how long can distant relapse be controlled; (3) What kind of treatment(s) will be administered; and (4) How long is the expected survival period after distant relapse? With these questions in mind, the purpose of the present study was to investigate oncological outcomes, including local and distant relapse, using a single center’s 24-year experience with EBS for spinal metastases patients with a minimum of 2-year follow-up.

Materials and Methods

The ethics committee of the Niigata University Graduate School of Medical and Dental Sciences approved this study (approval no., 2017-0103). A retrospective review of all 18 consecutive patients who underwent EBS for spinal metastasis between 1991 and 2015 at Niigata University Medical and Dental Hospital, Niigata, Japan was performed. No patients were lost to follow-up. The surgical indicators for spinal metastases requiring EBS were as follows: (1) a solitary metastasis existing on the spine or a spinal metastasis with radically resectable skip lesions; (2) a tumor involving less than three consecutive vertebral levels; (3) no evidence of tumors at the primary cancer site; (4) no other metastases, or if present, metastases are stable and controllable; and (5) the patient was in good general condition (Eastern Cooperative Oncology Group performance status score ≤3). Oncologists made all decisions about adjuvant chemotherapy and radiation therapy prior to and after EBS.

1. Surgical technique

In the present series, three approaches for EBS were utilized: a single posterior approach, a combined anterior and posterior approach, or a simultaneous anterior and posterior approach. EBS through the single posterior approach was performed as described by Tomita et al. [4,6]. However, to reduce the risk of vascular complications, EBS was more frequently performed through a combined anterior and posterior approach [5], dissecting around the tumor vertebrae via the anterior incision and following with a posterior *en bloc* corpectomy. Still, injury to major vessels, such as the aorta and vena cava, during *en bloc* corpectomy through the posterior incision was possible, and surgeons experienced difficulty in handling injured vessels, beyond the neural elements, through the posterior approach. Therefore, beginning in September 2004, EBS was performed via the simultaneous anterior and posterior approach, in one or two stages, and the surgical technique of this approach is described below.

Patients were placed in the prone position, and the posterior procedure was performed. After performing both a laminectomy at the tumor-free site and pediculotomies, dissection on the lateral aspect of the vertebrae for the non-dominant side of the tumor was performed. Posterior reconstruction involved a pedicle screw system with dual rods positioned at least two vertebral levels above and below the lesion. The simultaneous anterior and posterior procedure was either performed on the same day as the posterior procedure or 2–3 weeks after the first surgery. To begin, the patient was placed in a lateral decubitus position, with the tumor-dominant side facing upward. After a standard transpleural and/or retroperitoneal approach performed through an oblique thoracolumbar skin incision re-opened the posterior wound, a 360° dissection around the tumor vertebrae was made, and discectomy or osteotomy was performed using a T-saw. Finally, the tumor vertebra was removed in an *en bloc* fashion through the anterior incision by pushing the tumor vertebra from the posterior side. Anterior reconstruction was performed using autologous bone, with or without a titanium cage. The posterior procedures were completed by the application of compression forces between the pedicle screw...
heads above and below the bone graft.

2. Histological assessment and surgical classification

All resected specimens were analyzed histologically to determine the surgical margin status [12,13]. The surgical margin was classified as ‘positive’ if a visible tumor tissue was present, the tumor was cut through during the operation, or the excision margins were positive at the microscopic level. The surgical margin was classified as ‘negative’ for both wide and marginal resections.

3. Evaluations

All patients were followed-up with radiological examinations (X-ray, computed tomography, and/or magnetic resonance imaging), which evaluated changes in the treated segments and lesions in other sites. Local recurrence was defined as recurrence in the area where EBS was performed or in an adjacent area contiguous to the EBS area. Distant relapse was defined as a new occurrence of metastasis in an area other than the EBS or surrounding areas. The distant relapse-free period was defined as the duration between EBS and the first occurrence of distant metastasis after EBS.

4. Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows ver. 21.0 (IBM Corp., Armonk, NY, USA). Survival rates were estimated using the Kaplan–Meier method, and group differences were evaluated using the log-rank method. For categorical variables, group differences were evaluated using the chi-square or Fisher’s exact tests. In all analyses, a \( p \)-value <0.05 was considered statistically significant.

Results

1. Patients

The demographics of the patients are shown in Table 1. The median age at EBS was 62 years (range, 40–77 years), and the primary cancer sites included the kidney (n=7), thyroid

| Case | Age (yr) | Sex | Primary cancer site | Level | Tomita classification | Metastasis to vital organ | Metastasis to extraspinal bone | Frankel grade | Tokuhashi score |
|------|----------|-----|---------------------|-------|-----------------------|--------------------------|-------------------------------|---------------|-----------------|
| 1    | 55       | F   | Breast              | T6    | 2                     | No                       | No                            | E             | 13              |
| 2    | 40       | F   | Thyroid             | T12   | 5                     | No                       | No                            | D             | 14              |
| 3    | 53       | M   | Kidney              | T10, 11 | 6                  | No                       | No                            | C             | 9               |
| 4    | 45       | F   | Salivary gland      | T7    | 5                     | Lung                     | No                            | D             | 10              |
| 5    | 54       | M   | Kidney              | T6    | 5                     | No                       | No                            | D             | 12              |
| 6    | 73       | M   | Kidney              | T10   | 6                     | No                       | No                            | D             | 12              |
| 7    | 73       | M   | Kidney              | L3    | 6                     | Lung                     | No                            | D             | 10              |
| 8    | 77       | M   | Liver               | T4, 8, 9, 10 | 7                  | No                       | No                            | E             | 9               |
| 9    | 70       | M   | Kidney              | L1    | 6                     | No                       | No                            | C             | 10              |
| 10   | 68       | M   | Kidney              | T9    | 4                     | No                       | No                            | E             | 11              |
| 11   | 62       | M   | Liver               | T12   | 4                     | No                       | No                            | E             | 11              |
| 12   | 62       | F   | Thyroid             | L3    | 6                     | No                       | No                            | D             | 14              |
| 13   | 60       | M   | Thyroid             | L5    | 4                     | No                       | ilium                         | C             | 11              |
| 14   | 65       | F   | Pulmonary epithelioid hemangioendothelioma | T2, 12, L1 | 7                  | No                       | ilium, femur                   | D             | 7               |
| 15   | 65       | F   | Thymoma             | T12   | 5                     | No                       | No                            | D             | 10              |
| 16   | 47       | M   | Liver               | T12   | 1                     | No                       | No                            | D             | 9               |
| 17   | 59       | F   | Kidney              | T11, 12 | 5                  | No                       | No                            | E             | 13              |
| 18   | 62       | F   | Thyroid             | L2    | 5                     | No                       | No                            | D             | 14              |

F, female; M, male.
(n=4), liver (n=3), and other locations (n=4). In accordance with the surgical classifications of spinal tumors proposed by Tomita et al. [6] and on the basis of the anatomical location of the spinal tumors, one patient had type 1 (vertebral body), one patient had type 2 (pedicle extension), three patients had type 4 (spinal canal extension), six patients had type 5 (paravertebral extension), five patients had type 6 (adjacent vertebral extension), and two patients had type 7 (multiple skip lesions in the spinal column). Additionally, two patients had lung metastases, and another two had metastases in extraspinal bones. The preoperative Frankel grade was C for three patients, D for 10 patients, and E for five patients [14]. The median preoperative Tokuhashi score was 11 points (range, 7–14 points) [15].

2. Surgical procedures and clinical outcomes

Two patients (cases 8 and 14) had skip lesions in the spinous process and laminae of the upper thoracic spine (Table 2). As a result, these patients also underwent en bloc resection for upper thoracic lesions via a posterior approach at the same time as the EBS. The median operative time and intraoperative blood loss for all patients were 767.5 minutes (range, 447–1,110 minutes) and 2,375 g (range, 330–18,070 g), respectively. Ten patients (55.6%) received adjuvant therapies. Two patients received radiation therapy as adjuvant therapy: one for lung metastases (case 4) and one for iliac metastases and contaminated resected margins in the EBS area (case 13).

In 12 patients (66.7%), 18 perioperative complications occurred. Four patients (22.2%) underwent revision surgery for perioperative complications (surgical site infection in three patients and neurological deficits due to misplaced pedicle screws in one patient). Among the three patients with postoperative neurological deficits, neurological function was partially recovered after revi-

| Case | Date of EBS (yr) | Approach | Resected area | Time (min) | Intraoperative blood loss (g) | Adjuvant therapy | Perioperative complications | Frankel grade |
|------|-----------------|----------|---------------|------------|------------------------------|-----------------|----------------------------|---------------|
| 1    | 1991            | C-AP     | T6            | 715        | 4,300                        | None            | None                      | Pneumonia     | E             |
| 2    | 1995            | C-AP     | T12           | 680        | 2,625                        | C+RAI           | None                      | None          | E             |
| 3    | 2001            | C-AP     | T9, 10, 11    | 1,073      | 3,478                        | None            | None                      | Paralytic ileus | D             |
| 4    | 2001            | P        | T (6), 7, (8) | 1,067      | 410                          | R               | None                      | Pneumonia     | D             |
| 5    | 2004            | C-AP     | T6, (7)       | 713        | 1,744                        | None            | None                      | None          | E             |
| 6    | 2004            | S-AP     | T10, (11)     | 1,015      | 18,070                       | None            | None                      | ND, UTI       | D             |
| 7    | 2005            | S-AP     | L3            | 922        | 3,891                        | C               | None                      | None          | E             |
| 8    | 2007            | S-AP     | T8, 9, 10     | 1,110      | 2,125                        | C               | None                      | ND, SSI       | E             |
| 9    | 2008            | S-AP     | (T12), L1     | 834        | 8,245                        | C               | Durotomy                  | None          | E             |
| 10   | 2009            | S-AP     | T9            | 627        | 1,670                        | C               | None                      | None          | E             |
| 11   | 2010            | S-AP     | T12           | 755        | 1,235                        | None            | None                      | None          | E             |
| 12   | 2011            | S-AP     | L (2), 3, (4) | 632        | 7,512                        | R               | Durotomy                  | None          | E             |
| 13   | 2012            | S-AP     | L5            | 881        | 3,215                        | R               | Vena cava tear            | ND, DVT       | E             |
| 14   | 2013            | S-AP     | T12, L1       | 780        | 1,715                        | None            | Durotomy                  | None          | D             |
| 15   | 2013            | S-AP     | T12           | 609        | 1,790                        | None            | Durotomy                  | None          | E             |
| 16   | 2014            | P        | T12           | 447        | 1,180                        | None            | None                      | None          | E             |
| 17   | 2014            | S-AP     | T11, 12       | 783        | 330                          | C               | None                      | SSI           | E             |
| 18   | 2015            | S-AP     | L (1), 2      | 712        | 3,245                        | None            | Aorta and vena cava tear   | SSI           | D             |

EBS, en bloc spondylectomy; C-AP, combined anterior and posterior approach; C, chemotherapy or hormonal therapy; RAI, radioactive iodine therapy; P, posterior approach; R, radiation therapy; S-AP, simultaneous anterior and posterior approach; ND, neurological deficits; UTI, urinary tract infection; SSI, surgical site infection; DVT, deep venous thrombosis.

Parentheses indicate resections coupled with part of adjacent vertebrae. Frankel grade indicates the highest grade after EBS.
sion surgery in one patient (case 6) and fully recovered without revision in two patients (cases 8 and 13).

Five patients (27.8%) required revision surgeries because of the mechanical failure of spinal instrumentation, including rod breakage due to pseudarthrosis (n=4), and fractures in the uppermost (n=1) or lowermost (n=1) instrumented vertebra. All patients had improved or preserved Frankel grade after EBS. Sixteen patients (88.9%) could walk independently after EBS, and two patients required walking aids (cane, n=1; walker, n=1).

3. Oncological outcomes and overall survival

In total, 10 patients had negative margins, and eight patients had positive margins (Table 3). Intralesional procedures were performed in eight patients: During the dissection of the tumor vertebral bodies (n=1); during pediculotomy, using a fine thread wire saw (T-saw, n=1); during anterior column osteotomy, using a T-saw (n=2); during dissection of an epidural tumor (n=2); and during the removal of the tumor vertebrae, which caused other vertebral fractures (n=2). Tumor remnants were completely resected piece-by-piece in patients with a macroscopic tumor tissue remaining.

Five patients (27.8%) experienced a local recurrence. Of these, four patients had positive margins of the resected lesion, and one patient had a negative margin with a thin (<1 mm) tumor-free layer. The incidence of local tumor recurrence was higher for patients with positive margins (4/8 patients, 50%) compared to those with negative margins (1/10 patients, 10%). However, this difference did not reach statistical significance (p=0.12). The median duration between EBS and local recurrence was 12.5 months (range, 6–53 months), with three patients having undergone revision surgery. In two patients (cases 5 and 11) with local recurrence, the recurrent tumor around the cage caused neurological deficits and required a revision surgery (debulking) with adjuvant therapies. In one pa-

| Case | Surgical margin | Duration after EBS (mo) | Treatment | Local recurrence | Region | Duration after EBS (mo) | Treatment | Prognosis | Follow-up (mo) |
|------|-----------------|------------------------|-----------|-----------------|--------|------------------------|-----------|-----------|---------------|
| 1    | -               | No                     | Bone      | 15              | C      | DOD                    | 24        |
| 2    | -               | No                     | Neck      | 228             | R      | AWD                    | 266       |
| 3    | +               | No                     | Bone      | 28              | S+R    | DOD                    | 48        |
| 4    | -               | No                     | Bone, choroid plexus, eye | 1     | BSC    | DOD                    | 9         |
| 5    | +               | Yes                    | Bone      | 46              | C+R    | DOD                    | 72        |
| 6    | +               | No                     | None      | 13              | R      | None                   | 39        |
| 7    | +               | Yes                    | None      | 13              | R      | None                   | 39        |
| 8    | -               | No                     | None      | 13              | R      | None                   | 39        |
| 9    | -               | No                     | Lung, bone, lymph nodes | 7    | BSC    | DOD                    | 10        |
| 10   | -               | No                     | Bone, lung, kidney, pancreas | 36   | C+R    | DOD                    | 97        |
| 11   | -               | Yes                    | Lung, lymph nodes | 6    | S+C    | DOD                    | 14        |
| 12   | +               | No                     | Bone      | 18              | R      | AWD                    | 72        |
| 13   | +               | Yes                    | BSC       | 53              | S+R+C  | DOD                    | 55        |
| 14   | +               | No                     | Bone      | 6               | BSC    | DOD                    | 20        |
| 15   | +               | Yes                    | None      | 21              | RAI    | AWD                    | 24        |
| 16   | -               | No                     | Bone      | 18              | S      | AWD                    | 36        |
| 17   | -               | No                     | None      | 18              | S      | AWD                    | 36        |
| 18   | -               | No                     | Lung      | 21              | RAI    | AWD                    | 24        |

EBS, en bloc spondylectomy; C, chemotherapy; DOD, dead of disease; R, radiation therapy; AWD, alive with disease; S, surgery; DOC, dead from other causes; NED, no evidence of disease; BSC, best supportive care; RAI, radioactive iodine therapy.
tient with an accidental durotomy during EBS (case 15),
the tumor recurred as an intradural-extramedullary tu-
mor; this was removed completely during revision surgery
and further treated by radiation therapy. Another patient
(case 7) experienced tumor recurrence on the psoas major
muscle and was treated with radiation therapy. Another
tumor recurred paravertebral, at the retroperitoneal area,
in one patient (case 13). This patient did not undergo fur-
ther treatment given his poor general condition.

In the five patients without a new occurrence of distant
relapse, the tumor origin was the kidney in three patients,
liver in one patient, and thymoma in one patient. The
distant relapse-free 1-year, 2-year, 3-year, and 5-year sur-

Fig. 1. Distant relapse-free survival curves. (A) Distant relapse-free
survival in 18 patients who underwent en bloc spondylectomy for
spinal metastases. (B) Comparison of the distant relapse-free survival
curves for patients with (green line) and without (blue line) contami-
nated resected margins. No significant difference was found between
groups (p=0.62).

vival rates after EBS were 72.2%, 50%, 38.9%, and 29.2%,
respectively (Fig. 1). Overall, distant relapse was detected
in 13 patients (72.2%). The estimated median duration be-
tween EBS and distant relapse was 21 months (95% con-
fidence interval [CI], 0.21–41.79 months) (Fig. 1A). The
incidence of distant relapse was 80% in patients with neg-
ative margins and 62.5% in patients with positive margins,
with no significant differences between groups (p=0.61).
The differences in the surgical margin of the resected le-
sion did not affect the distant relapse-free survival period
(p=0.62) (Fig. 1B). Systemic adjuvant therapies, including
chemotherapy and radioactive iodine therapy, also did
not have a significant effect on the incidence of distant re-

Fig. 2. Survival curve after distant relapse in 13 patients who experi-
cenced distant relapses after en bloc spondylectomy for spinal metas-
tases.

lapse, which occurred in 57.1% and 81.8% of patients who
received and did not receive systemic adjuvant therapies,
respectively (p=0.33). Moreover, three of the four patients
(75%) with extraspinal metastatic lesions at the EBS site
and 10 of the 14 patients (71.4%) without extraspinal met-
astatic lesions at the EBS site experienced a new distant
relapse occurrence after EBS. Still the incidence of distant
relapses did not significantly differ between patients with
and without extraspinal lesions at the EBS site (p>0.99). In
the 13 patients with distant relapses, the 6-month, 1-year,
2-year, 3-year, and 5-year survival rates after distant
relapse were 92.3%, 67.1%, 49.0%, 39.2%, and 26.1%, re-
respectively (Fig. 2). The estimated median survival period
after a distant relapse was 20 months (95% CI, 0.71–39.29
months) (Fig. 2). The overall 2-year, 5-year, and 10-year
survival rates after EBS were 72.2%, 48.8%, and 27.1%, re-
respectively, and the estimated median survival period was 55.2 months (95% CI, 16.57–93.43 months) (Fig. 3).

Finally, because EBS was performed from 1991 to 2015, the year in which EBS was performed was evaluated in relation to oncological outcomes. There were no significant differences according to the year EBS was performed (median [interquartile range]) between the positive (2005 [2004–2012]) and negative (2008.5 [2002.5–2013]) resection margin groups (p = 0.96), between groups of patients with (2010 [2005–2012]) and without (2008 [2001–2013]) local recurrence (p = 0.73), and between groups of patients with (2008.5 [2001–2011.5]) and without (2007 [2005–2013]) distant relapse (p = 0.69).

Discussion

EBS remains one of the most challenging and technically demanding procedures for spine surgeons. In the present study, the median operative time was 12.8 hours, and the median blood loss was 2.4 L, which are comparable to the values reported in previous studies [6,7]. In addition, the rate of perioperative complications was 66.7% in the present study, and the rate of perioperative mortality was 0%. The higher rate of perioperative complications observed here, compared to previous reports [7,16,17], might be due to the differences in the definition of complications. Indeed, despite the high incidence of perioperative complications, the results for survival are comparable to those of previous investigations [6,7,18,19]. Ultimately, lifespan extension was achieved, suggesting that the indicators used and perioperative care implemented during EBS for spinal metastases were appropriate.

Previous studies have reported that intraleisional resections and EBS with contaminated margins will have a negative effect on local recurrence [7,10,18,20]. Certainly, the rate of local recurrence for EBS in the present study (27.8%) was slightly higher than that of previous reports (5%–20%) [6,7,10,18,20]. This difference may be due to the high frequency (44.4%) of EBS procedures with positive margins in the present study. Indeed, local recurrence tended to be observed more often in patients with positive margins than in patients with negative margins (50% versus 10%) in the present study.

In the present series, 72.2% of patients experienced newly formed distant metastases occurring after EBS. Cloyd et al. [7] conducted a systematic review and reported that the rate of any tumor recurrence (both local and distant relapses) after en bloc resection of metastatic spinal tumors was 37.7%. The higher rate of distant relapses demonstrated in this study may be influenced by the longer follow-up period (median, 40.5 months versus 16 months). Indeed, the estimated duration between EBS and a distant relapse event had a median of 21 months, which is longer than the median follow-up period of the systematic review. Interestingly, the incidence of distant relapse was not associated with resection margin status or the presence of extraspinal metastatic lesions at the EBS site in the current study. In addition, obvious differences in distant relapse events were not observed among the tumors of different origins; however, the small sample size did not allow statistical analysis in this matter. Thus, EBS was not determined to completely prevent the occurrence of distant relapses in patients with spinal metastases. In the present study, 84.6% of patients with distant relapses received some treatment (radiotherapy, chemotherapy, or a combination of both) for distant metastases. Despite these treatments, more than half of the patients with distant relapses died within 2 years after relapse.

The limitations of the current study include its retrospective design, small sample size, and the inclusion of heterogeneous primary cancer sites. Because patients with spinal metastases requiring EBS are uncommon, future studies should involve prospective, multicenter collaborations. Moreover, although the era in which EBS was performed did not impact the surgical and oncological outcomes in this study, the 25-year span of the study was sufficiently long for cancer treatment to advance during
the study period. Therefore, it should be noted that the outcomes in this study represent the minimum expected outcomes, given the present state of cancer treatment. In the future, the outcomes for EBS could be improved.

**Conclusions**

In conclusion, margin-free EBS is effective for the local control of spinal metastases. However, EBS by itself, even if margin-free, cannot completely prevent further dissemination. The present results regarding distant relapses after EBS will assist spinal surgeons in the clinical decision-making process and should be conveyed to patients and their families to help in treatment choices.

**Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

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**Author Contributions**

Masayuki Ohashi wrote and prepared the manuscript. Masayuki Ohashi, Kei Watanabe, Toru Hirano, Kazuhiro Hasegawa, Keiichi Katsumi, Hirokazu Shoji, and Tatsuki Mizouchi contributed to the conception and design of this study, data acquisition, and analysis and interpretation of the data. Takao Homma and Naoto Endo contributed to the study design, analysis and interpretation of data, and supervision. All authors have read, reviewed, and approved the article.

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