European Spine Journal (2020) 29:3237–3244
https://doi.org/10.1007/s00586-020-06461-0

ORIGINAL ARTICLE

# Clinical outcomes and survivals after total en bloc spondylectomy for metastatic leiomyosarcoma in the spine

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Received: 7 January 2020 / Revised: 2 May 2020 / Accepted: 10 May 2020 / Published online: 18 May 2020


## Abstract

**Purpose** Leiomyosarcoma (LMS) is generally resistant to radiation and chemotherapy. Our study aimed to examine the outcomes of total en bloc spondylectomy (TES) for spinal metastatic LMS and to analyze potential factors associated with survival.

**Methods** This study included 10 consecutive patients who underwent TES for spinal metastatic LMS at our institute between 2005 and 2016 and were followed up at a minimum of 3 years after surgery. At the time of TES, all the 10 patients had solitary bone metastases in the spine. Seven patients had a lowered performance status (PS) with an eastern cooperative oncology group (ECOG) grade of 2 or 3 due to back pain or neurological symptoms. The cancer-specific survival (CSS) time from TES to death or last follow-up was the main endpoint. Potential factors associated with survival were evaluated using the Kaplan–Meier analysis and the log-rank test.

**Results** Five patients underwent a single vertebral resection, and the other five patients underwent two or three consecutive vertebral resections. Three patients developed perioperative complications including pulmonary thromboembolism and pneumothorax. Nine patients improved or fairly maintained their PS with an ECOG grade of 1. The 1-, 3-, and 5-year CSS rates after TES were 90%, 70%, and 47%, respectively. Only postoperative disability (ECOG PS grade 3) was significantly associated with short-term survival after TES.

**Conclusions** The clinical outcomes of 10 patients who underwent TES for spinal metastatic LMS were favorable without severe complications. Postoperative disability was significantly associated with short-term survival after TES.

**Keywords** Clinical outcome · Leiomyosarcoma · Spinal metastasis · Survival · Total en bloc spondylectomy

## Introduction

Leiomyosarcoma (LMS), which originates from smooth-muscle cells, is one of the most frequent soft tissue sarcomas, with an estimated incidence ranging between 10 and 20% of all newly diagnosed soft tissue sarcomas [1]. Although LMS can develop from any site where smooth-muscle cells exist, most arise in the uterus, gastrointestinal tract, retroperitoneum, and subcutaneous tissue of the extremities [2, 3]. Distant metastatic lesions generally occur in the lungs, liver, kidney, brain, and skin [4]. Osseous metastatic lesions are rare; the spine is one of the more common sites of osseous metastatic spread [5, 6]. Osseous metastases originating from LMS are difficult to manage because they tend to be large, highly destructive, hypervascular, and resistant to chemotherapy and radiation therapy [7], resulting in pathologic fractures and spinal cord compression that severely compromise the performance status (PS) and quality of life of the patients. It is uncommon, however, for a spinal metastatic lesion to be the presenting manifestation of LMS. Similarly, it is rare for osseous metastatic disease to be the initial presentation of recurrence in patients with a history of LMS [5]. In fact, there is very little information in the current literature about metastatic LMS in the spine, and

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there is no clear consensus on how to best proceed with treatment. It was generally known that patients undergoing metastasectomy from soft tissue sarcomas had significantly prolonged survival compared to patients with unresectable metastases [8].

Spondylectomy for the treatment of spinal neoplasms was first described by Stener [9]. In the 1990s, investigators from our institute developed and popularized a surgical procedure known as total en bloc spondylectomy (TES), which was aimed at complete resection of diseased vertebrae [10]. Improvements in surgical techniques and preoperative embolization achieved excellent clinical results with low morbidity [11, 12], and TES has been applied in selected patients with solitary spinal metastasis [13–15]. There are several reports of surgery for the treatment of metastatic LMS in the spine [4, 7, 16, 17]. However, no studies have evaluated the clinical outcomes of curative surgical resection of metastatic LMS in the spine. Thus, our study aimed to examine the survival of patients who underwent TES for metastatic LMS in the spine and to analyze potential prognostic factors.

## Methods

### Patients

After acquiring authorization by the Ethics Committee of our University Hospital, a database of patients with spinal metastases who underwent TES at our institution between 2005 and 2016 was retrospectively reviewed at the end of 2019. We obtained the minimum 3-year follow-up data of patients who underwent TES for metastatic LMS in the spine. We examined and analyzed the charts and imaging tests including radiography, computed tomography (CT), and magnetic resonance imaging (MRI) of the patients. Surgical indications for TES of metastatic LMS were based on the following criteria: solitary metastasis in the spine, surgical feasibility (the tumor involved ≤ 3 consecutive spinal levels), operability (eastern cooperative oncology group PS [ECOG PS] grade ≤ 3), and stable disease with no other metastases or a limited number of ≤ 3 metastases in other organs. Informed consent was obtained from the patients and/or their guardians. All ten patients underwent CT-guided biopsy preoperatively. The surgical technique employed in the patients has been described in detail elsewhere [11].

### Outcome measures

Patients were followed up through an outpatient clinic visit or a telephone survey at least every 6 months until 3 years after TES. After the 3-year postoperative follow-up, the 6- or 12-month follow-up was continued until the patient's death. During an outpatient clinic visit, chest and abdominal CT were performed routinely to examine the previously recognized metastases and to detect new metastases. Survival was defined as the time from TES to death or last follow-up. Vertebral body collapse of the tumor-affected vertebrae before surgery and the integrity of the reconstructed spine after surgery were evaluated using multiplanar reconstruction CT. Spinal instability was evaluated using the spinal instability neoplastic score (SINS) [18]. The degree of epidural spinal cord compression (ESCC) was evaluated using a 6-point scoring system on MRI [19]. Cancer-specific survival (CCS) was the main endpoint of the study. The Kaplan–Meier analysis was used to calculate CSS in all patients, and the log-rank test was used to compare CSS among patient groups in univariate analyses. To identify predictors of survival, we analyzed the following clinical parameters and outcome data: age (> 50 years), sex (male), preoperative and postoperative disability (ECOG PS grade 3), metastases in other organs at the time of surgery, enlarged tumors involving multilevel vertebrae, spinal instability (SINS ≥ 10), synchronous metastases detected ≤ 1 year after surgery for the primary lesion, history of systemic therapy or radiation therapy, abnormal level of serum albumin (< 4.0 g/dl), and tumor recurrence in the operated spine. All significance levels were set at 0.05. SPSS software version 19.0 for Windows (IBM Corp., Armonk, NY, USA) was used for all statistical analyses.

## Results

The case series consisted of 10 consecutive patients (5 men and 5 women) with a mean age of 52.8 years (range: 24–69, Table 1). Primary LMS originated from the retroperitoneum in three patients: the uterus, stomach, and upper extremity in two patients; and the maxillary sinus in one patient. All but one patient underwent excisional surgeries for primary LMS prior to the detection of spinal metastases. One patient (number 6 in Table 1) underwent TES for isolated spinal metastasis from an unknown primary cancer. Physical examinations after TES revealed a gastric LMS, which was surgically resected 3 months after TES. Four patients had other organ metastases at the time of TES, including previously operated lesions. Eight patients had metachronous spinal metastases detected > 1 year after surgery for the primary lesion. In the nine patients who underwent excisional surgery for the primary tumor before TES, the mean interval between primary resection and TES was 50.2 months (10–204 months). Pre- and/or postoperative chemotherapy was administered in six patients. Irradiation of spinal metastases was performed in three patients. Two patients received a preoperative radiation dose of 47.0 Gy each for a spinal lesion, and one patient received a postoperative radiation dose of 39.0 Gy for tumor recurrence 2 years after TES.

**Table 1** Summary of demographics, disease condition, and treatment history

| Patient no./ sex/ age, year | Affected vertebra | Primary organ | Other metastases site at the time of TES | History of chemotherapy | History of irradiation | Serum albumin level (g/dl) | Vertebral body collapse/SINS | ESCC scale | Pre-op ECOG PS | Pre-op Frankel grade (duration[b]) | Duration between primary surgery and TES |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 / F / 52 | T7 | Retroperitoneum | None | None | 51 Gy (pre-op) | 4.0 | +/ 10 | 2 | 2 | E | 40 months |
| 2 / F / 59 | T12-L2 | Uterus | None | None | None | 3.9 | +/ 11 | 3 | 3 | C (2 weeks) | 43 months |
| 3 / M / 49 | T12 | Stomach | Liver, peritoneum | Post-op | None | 3.8 | −/ 8 | 1a | 1 | E | 39 months |
| 4 / M / 56 | L2-L3 | Maxillary sinus | None | None | None | 4.4 | − / 8 | 1b | 2 | E | 204 months |
| 5 / F / 62 | T12 | Extremity | Lung, peritoneum, lymph node | Pre-, and post-op | 51 Gy (pre-op) | 3.9 | +/ 9 | 3 | 2 | E | 43 months |
| 6 / M / 69 | T10-T11 | Stomach | None | Post-op | None | 4.5 | +/ 8 | 2 | 1 | E | Not applicable[a] |
| 7 / F / 24 | T7-T8 | Retroperitoneum | Lung, peritoneum | Post-op | None | 3.9 | +/ 6 | 1a | 1 | E | 10 months |
| 8 / M / 57 | T10 | Extremity | None | Pre-, post-op | None | 4.1 | +/ 9 | 3 | 3 | C (4 weeks) | 28 months |
| 9 / M / 56 | T3-T5 | Retroperitoneum | None | None | None | 3.5 | +/ 12 | 3 | 3 | B (2 weeks) | 19 months |
| 10 / F / 44 | L1 | Uterus | Lung | Post-op | 39 Gy (post-op) | 4.0 | +/ 14 | 2 | 3 | D (3 weeks) | 26 months |

*ECOG PS* eastern cooperative oncology group performance status, *ESCC scale* epidural spinal cord compression scale [19], *F* female, *M* male, *Pre-op* preoperative period, *Post-op* postoperative period, *SINS* spinal instability neoplastic score [18], *TES* total en bloc spondylectomy

[a]The patient (number 6) underwent TES isolated spinal metastasis from unknown primary cancer. Physical examinations after TES revealed a gastric leiomyosarcoma, which was surgically resected 3 months after TES.

[b]It indicated the duration from occurrence of muscle weakness of the lower extremities to surgery.

Preoperative chemotherapy and radiation were administered by the attending physicians for primary LMS, before the patients were referred to our institute. At the time of TES, all 10 patients had solitary bone metastases in the spine. The other sites of metastases, which already existed at the time of TES, were the lungs and peritoneum in three patients and the lymph node and liver in one patient. Prior to surgery, the PS decreased due to back pain or neurological symptoms of the lower extremities in all patients. Seven patients (70%) had a significantly lowered PS with an ECOG grade of 2 or 3 (Table 1). Spinal canal involvement by the tumor and vertebral body collapse were observed in all ten patients (the 6-point ESCC scale: 1a-3) and eight patients, respectively.

The clinical results are summarized in Table 2. Five patients underwent a single vertebral resection, three patients underwent two consecutive vertebral resections, and two patients underwent three consecutive vertebral resections. All patients underwent preoperative embolization of segmental arteries supplying the tumor-affected vertebra. The mean intraoperative blood loss was 935 ml (range 100–2900 ml), and the mean operating time was 490 min (range 356–750 min). Four patients required blood transfusions in the perioperative period. Three patients developed perioperative complications including pulmonary thromboembolism in two patients and pneumothorax in one patient. However, these diseases did not become severe. The two pulmonary thromboembolisms were asymptomatic and detected on routine CT images acquired 1 week after surgery. There were no operation-related deaths. All but one patient improved or maintained their PS with an ECOG grade of 1 and Frankel E after TES. One patient (number 9 in Table 2) retained Frankel type B paralysis with a low PS (ECOG grade 3) after surgery. There were tumor recurrences in the operated spine in two patients during the follow-up periods. One patient (number 1 in Table 2) had additional excisional surgeries, and another patient (number 10 in Table 2) underwent radiation therapy. The mean follow-up time was 47.0 months (range, 12–97 months). Eight patients had already died from disease progression, and two patients were still alive at the final follow-up. Three patients died < 3 years after surgery (range of survival time after surgery, 12–16 months; Table 2), whereas seven patients survived ≥ 3 years after surgery. The 1-, 3-, and 5-year CSS rates after TES for metastatic spinal LMS were 90%, 70%, and 47%, respectively (Fig. 1). The estimated median CSS time after TES was 52.6 months. The 3-, 5-, and 10-year CSS rates after excisional surgery for primary LMS were 80%, 80%, and 31%, respectively. Among the variables examined in a univariate analysis (Table 3), postoperative disability (ECOG PS grade 3) was significantly associated with short-term survival after TES ($P < 0.05$). In the nine patients who recovered or maintained their postoperative PS with an ECOG grade of 1, the 3- and 5-year CSS rates after

**Table 2** Summary of surgical data and postoperative outcomes

| Patient no./ sex/ age, year | Resected vertebra | Surgical approach | Operating time (minute) | Operative blood loss (ml) | Tumor recurrence in the operated spine | Perioperative complication | ECOGPS Post-op (pre-op) | Frankel grade Post-op (pre-op) | Status | Survival after TES (month) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1/F/52 | T7 | Posterior | 505 | 2900 | 11 months post-op | None | 1 (2) | E (E) | DOD | 72 |
| 2/F/59 | T12-L2 | AP | 750 | 2010 | None | None | 1 (3) | E (C) | DOD | 97 |
| 3/M/49 | T12 | Posterior | 383 | 1000 | None | None | 1 (1) | E (E) | DOD | 55 |
| 4/M/56 | L2-L3 | Posterior | 450 | 750 | None | None | 1 (2) | E (E) | DOD | 13 |
| 5/F/62 | T12 | AP | 567 | 650 | None | None | 1 (2) | E (E) | DOD | 45 |
| 6/M/69 | T10-T11 | Posterior | 465 | 260 | None | PTE | 1 (1) | E (E) | DOD | 16 |
| 7/F/24 | T7-T8 | Posterior | 391 | 440 | None | Pneumothorax | 1 (1) | E (E) | DOD | 62 |
| 8/M/57 | T10 | Posterior | 356 | 690 | None | None | 1 (3) | E (C) | NED | 62 |
| 9/M/56 | T3-T5 | Posterior | 562 | 550 | None | PTE | 3 (3) | B (B) | DOD | 12 |
| 10/F/44 | L1 | Posterior | 474 | 100 | 24 months post-op | None | 1 (3) | E (D) | AWD | 36 |

*AP* anterior–posterior combined, *AWD* alive with disease, *DOD* dead of disease, *ECOG PS* eastern cooperative oncology group performance status *F* female, *M* male, *NED* no evidence of disease, *Post-op* postoperative state, *Pre-op* preoperative state, *PTE* pulmonary thromboembolism, *TES* total en bloc spondylectomy

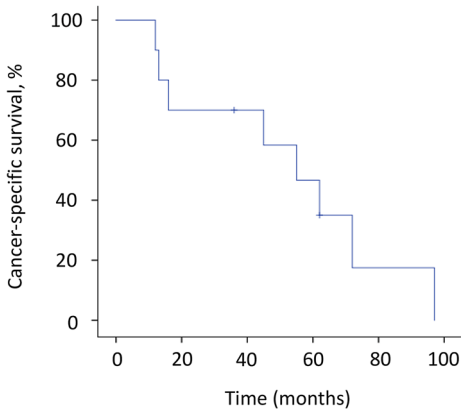


**Fig. 1** Cancer-specific survival (CSS) of 10 patients who underwent TES for spinal metastatic leiomyosarcoma. The 3- and 5-year CSS rates after TES were 70% and 47%, respectively. The estimated median CSS time after TES was 52.6 months. The tick marks indicate last date of follow-up

TES were 78% and 52%, respectively. All four patients with vital organ metastases at the time of TES survived > 3 years after spine surgery.

## Case presentation

The patient was a 59-year-old woman with a solitary spinal metastasis at L1 from uterine LMS (number 2 in Tables 1 and 2). The metastatic tumor was expanding to the adjacent vertebrae through the spinal canal and paravertebral space (Fig. 2a). Prior to surgery, she had a Frankel type C paraparesis and significant back pain, which severely deteriorated her activities of daily life and PS. She underwent TES via a combined anterior–posterior approach. In the first step, with the patient in the right lateral decubitus position, dissection between the affected vertebral bodies and major vessels and detachment of the crus from the vertebrae via a retroperitoneal (extrapleural) approach were performed. Next, in the prone position, TES of three consecutive vertebrae (T12-L2) with minimal transpedicular osteotomies was performed (Fig. 2b). One month after the surgery, the patient was able to walk independently with a Frankel type E classification. Radiograph and CT results 5 years after TES showed that the integrity of the reconstructed spine was well maintained (Fig. 2c). Ninety-seven months after surgery, the patient died from tumor progression to the liver and lungs.

**Table 3** Univariate analysis to search risk factors for prognosis

| Factor | Cut point | *n* | % of ≥ 3-yr survivors | *P* value |
|---|---|---|---|---|
| Age (year) | ≥ 50 | 7 | 57.1 (4/7) | 0.994 |
| | < 50 | 3 | 100 (3/3) | |
| Gender | Male | 5 | 40.0 (2/5) | 0.149 |
| | Female | 5 | 100 (5/5) | |
| Preoperative ECOG PS | 3 | 4 | 75.0 (3/4) | 0.153 |
| | 1–2 | 6 | 66.7 (4/6) | |
| Postoperative ECOG PS | 3 | 1 | 0 (0/1) | 0.003 |
| | 1–2 | 9 | 77.8 (7/9) | |
| Other organ metastases | Yes | 4 | 100 (4/4) | 0.671 |
| | No | 6 | 50.0 (3/6) | |
| Enlarged tumor involving multi-level vertebrae | Yes | 5 | 40.0 (2/5) | 0.467 |
| | No | 5 | 100 (5/5) | |
| Spinal instability neoplastic score | ≥ 10 | 4 | 75.0 (3/4) | 0.258 |
| | < 10 | 6 | 66.6 (4/6) | |
| Synchronous metastases | Yes | 2 | 50.0 (1/2) | 0.478 |
| | No | 8 | 75.0 (6/8) | |
| History of systemic therapy | Yes | 6 | 83.3 (5/6) | 0.853 |
| | No | 4 | 50.0 (2/4) | |
| History of irradiation | Yes | 3 | 100 (3/3) | 0.811 |
| | No | 7 | 57.1 (4/7) | |
| Serum albumin level | ≥ 4.0 g/dl | 5 | 60.0 (3/5) | 0.825 |
| | < 4.0 g/dl | 5 | 80.0 (4/5) | |
| Tumor recurrence in the operated spine | Yes | 2 | 100 (2/2) | 0.482 |
| | No | 8 | 62.5 (5/8) | |

% of ≥ 3-yr survivors, percentage of ≥ 3-year survivors after TES

*ECOG PS* eastern cooperative oncology group performance status

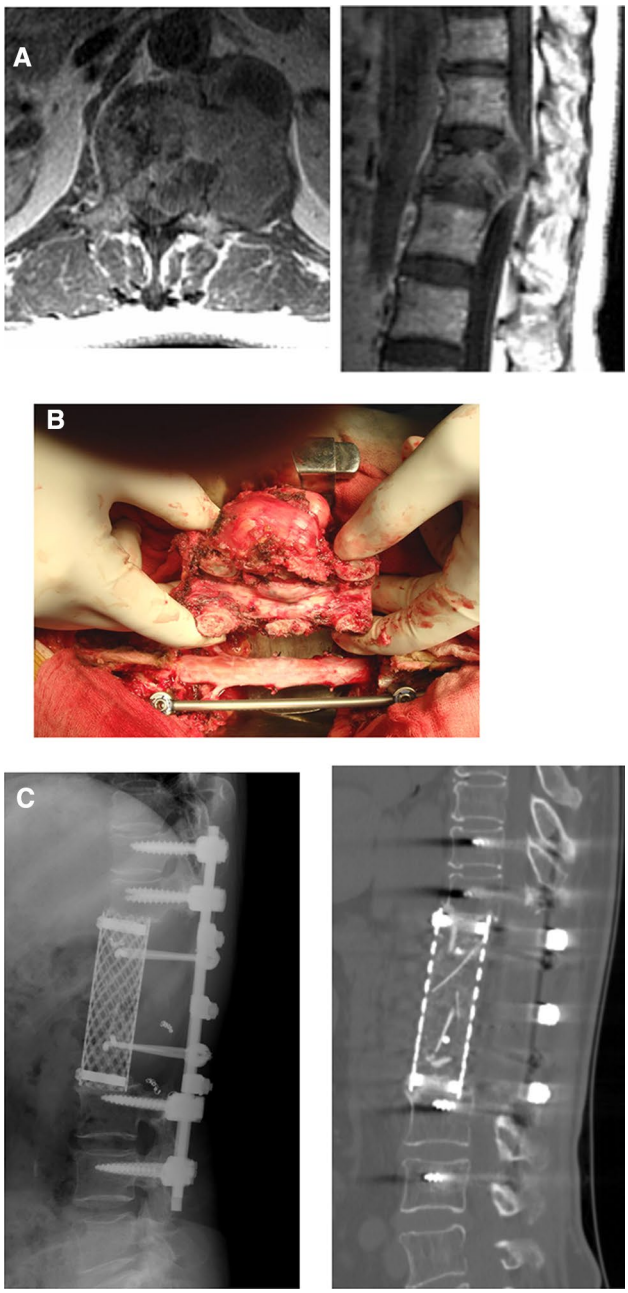


**Fig. 2** Metastatic leiomyosarcoma at L1 in a 59-year-old woman. **a** Axial (left) and sagittal (right) images of enhanced T1-weighed magnetic resonance imaging of the L1 vertebra. **b** Intraoperative photograph of the resected specimen (total en bloc corpectomy). **c** Radiograph in lateral view (left) and computed tomography in sagittal view (right) showing the integrity of the reconstructed spine and the absence of tumor recurrence 5 years following TES.

## Discussion

We examined the clinical outcome and survival of 10 consecutive patients who underwent TES for solitary and removable spinal metastatic leiomyosarcomas. The 1-, 3-, and 5-year CSS rates after surgery were 90%, 70%, and 47%, respectively. The estimated median CSS time after TES was 52.6 months. There was no major complication associated with revision surgery and PS deterioration, or operation-related deaths. Postoperative ECOG PS grade 3 was significantly associated with short-term survival after surgery. Our results suggest that spinal metastasectomy can be indicated for TES in patients with resectable metastatic spinal LMS if they are stable, irrespective of other organ metastases. Postoperative disability has the potential to be a risk factor for a poor prognosis after TES for metastatic spinal lesions.

LMS is a soft tissue sarcoma of mesenchymal derivation with a typically poor prognosis [20]. A national prognostic survey from Norway estimated the overall 5-year survival for uterine LMS to be 15–25% [21]. All patients with extrauterine metastasis in that same study had died at 5 years. A study of nonvisceral LMS demonstrated an overall 10-year survival of 49%, although this rate included cutaneous LMS, which are thought to be more benign [22]. The prognosis of patients with metastatic LMS is limited, and objective responses to first-line systemic therapy are rare [23, 24]. A retrospective study of 122 metastatic LMS patients reported that the median survival from the time of diagnosis of metastasis was 20.5 months and the possibility of metastasectomy with curative intent was one of the indicators for better survival [24].

LMS are generally resistant to radiation and chemotherapy [25, 26]. Most bone metastases from LMS present destructive osteolytic lesions. These features often result in intractable pain, neurological deficits, and paraplegia, thereby substantially reducing the quality of life and increasing the mortality rate, even with nonsurgical treatments. Therefore, some authors reported surgical outcomes for spinal metastatic LMS including aggressive excisional surgery. Elhammady et al. [4] reported that spinal metastatic LMS tends to symptomatically involve only one spinal level at the time of diagnosis. They recommended aggressive excisional surgery because their patients had a relatively favorable prognosis even with systemic metastatic lesions after aggressive spinal surgery [4]. Liu et al. [7] reported in their case series of spinal metastatic LMS and a literature review that the 1-year and 5-year survival after spine surgery in 16 patients was 64% and 21%, respectively, with an overall median survival of 22.5 patients. Among the 16 patients, seven patients underwent various types of tumor excision surgery and five patients underwent laminectomy only or additional fusion (no information on the other four patients). The results in this study were relatively favorable, without severe perioperative complications, and better than those of previous studies [4, 7, 16]. Only two patients (20%) developed tumor recurrence in the operated spine with a minimum 3-year follow-up. Excisional surgery for solitary metastases in the spine is considered to have clinical

benefits, including palliation or prevention of symptom and delay or withdrawal of systemic treatment, thereby preventing deteriorated PS and drug-associated toxicities [15, 27]. Considering these factors and the characteristics of spinal metastatic LMS, TES is indicated for solitary and removable spinal lesions in patients with metastatic LMS. The procedure has the potential not only for maintaining a good PS but also for prolonging survival [12, 14, 15]. However, in the analysis of this study, postoperative disability (ECOG PS grade 3) was significantly associated with short-term survival after TES. Careful patient selection and adequate surgical timing before the presence of severe neurological deterioration are important for the successful application of this surgery. All tumors in our patients showed moderate or extensive vascularity on preoperative selective angiography and were subjected to embolization within 3 days before surgery. For safe and effective tumor resection, we recommend preoperative embolization of segmental arteries supplying the tumor-affected vertebra in all cases of spinal metastatic LMS scheduled for TES.

Although the patient number was small, the presence of vital organ metastases was not associated with short-term survival in the present study ($P = 0.671$). A retrospective study of 122 metastatic LMS patients reported that the presence of lung or liver metastases was not associated with short-term survival [24]. All four patients with vital organ metastases at the time of TES received postoperative chemotherapy and survived > 3 years after spine surgery. A lowered PS of patients with metastatic spinal disease affects mortality directly as well as indirectly by hindering the delivery of systemic therapies. Long-term local control of spinal metastases afforded by TES can contribute to an adequate systemic treatment for patients with other organ metastases.

This study has limitations, including the small cohort size and the retrospective nature of the analysis without controls, which potentially could have introduced imperfect validity of the analyses and bias. It is possible that a selection bias exists owing to the relatively stable disease condition of the patients, which allowed for their consideration of TES. We could not obtain detailed information about the primary lesion (tumor size, pathologic stage, and TNM classification) and systemic therapy (indication and duration) because primary lesions were treated and therapies were performed mostly at other hospitals (patients were referred to our institute for the purpose of spinal metastasectomy). However, despite these limitations, this study indicates that TES should be considered for patients with solitary and removable spinal metastatic LMS, even with controllable metastases in other organs. Moreover, for such patients, TES can help maintain a good PS in the long-term and potentially prolong survival.

## Conclusions

TES should be considered for spinal metastatic LMS. Despite the invasiveness of the surgery, a low rate of complications was observed. The 3-year CSS rates and estimated median CSS time after surgery were 70% and 52.6 months, respectively. Postoperative disability was significantly associated with short-term survival after TES.

**Acknowledgments** The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper. We would like to thank Editage (https://www.editage.jp/) for English language editing.

### Compliance with ethical standards

**Conflicts of interest** The authors declare that they have no conflict of interest.

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