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Comparison of outcomes between total en bloc spondylectomy and palliative spinal surgery in metastatic spinal tumor patients: propensity score matching analysis

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Abstract

Background Total en bloc spondylectomy (TES) was considered aggressive spinal surgery aim to achieved marginal and wide surgical margin in spinal tumor treatment. However, there was limited comparison information between TES and other palliative spinal surgery treatments. This study aimed to report the comparison between TES and Palliative Spinal Surgery (PSS) in terms of clinical and oncologic outcomes.

Methods A retrospective cohort study was conducted. The medical records of Spinal Metastasis (SM) treated by a single surgeon were reviewed between January 2014 and December 2020. The propensity score matching was calculated. survivorship, local recurrence, surgical complications, operative blood loss, and time between TES and PSS were reviewed and analyzed.

Results A total of 44 patients with a mean age of 56 were included. Twenty-two TES and 22 PSS patients were recruited into the study—no significant difference in demographics data. The TES showed significantly better survival at 6 ($p=0.010$) and 12 months ($p=0.020$). The local recurrence in the TES group was 4.6% (1 of 22). However, TES showed significantly longer operative time (6 h (5.5–6.5) and 3 h (2.0-3.5), p-value < 0.001) and more intraoperative blood loss (1150 mL (1000–1800) and 575 mL (350–800), p-value = 0.0002).

Conclusions TES showed better survivorship after 6 and 12 months than PSS. The TES also achieved favorable local control of tumors after surgery. Further randomized control of more patients should be conducted to clarify the benefits of TES vis-à-vis metastasis.

Keywords Metastatic spinal tumor, Total En bloc Spondylectomy, Palliative surgery, Survival analysis, Oncologic outcomes

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Introduction

Bone metastasis is the third most common site of metastasis after the lung and liver [1]. Spinal metastasis (SM) is one of the most serious oncological problems, lowering the quality of life. Patients with spinal metastasis develop pain, instability, pathological fractures, and neurological deficit due to spinal cord or nerve root compression. The annual incidence of spinal metastasis was 6.04-26.0 per 100,000 [2]. The primary origin of SM arises from the lung (24.6%), prostate (20.7%), and breast (16.5%) [2]. The goal of the treatment was to relieve back pain, increase stability, preserve neurological function, and improve quality of life.

Total En bloc Spondylectomy (TES) was considered radical spinal-tumor resection surgery. TES might prevent local recurrence since the whole vertebra is resected without tumor exposure [2, 3, 4, 5, 6, 7, 8, 9]. The palliative spinal surgery (PSS) was defined as an operation that aims to relieve pain, increase stability, or gain neurological function, thereby improving quality of life. The operative might be palliative surgical debulking, decompressive laminectomy, separation surgery and/or posterior spinal instrumentation.

Nowadays, separation surgery followed by stereotactic radiosurgery and systemic therapies based on the NOMS framework are considered standard care in spinal metastasis, showing favorable local control of the disease and good survival outcomes [10]. However, stereotactic radiosurgery and targeted therapy are high-cost treatments and are not available in every country around the world. The adequacy of local control in spinal metastasis may affect oncologic outcomes in patients in the absence of these high-cost therapies [3, 7, 11].

For local control of disease in spinal metastasis, Feng et al. showed that the revision rate of palliative spinal surgery, including separation surgery, ranged from 2.3 to 15.8%, with the highest rate observed in decompression surgery [12]. In contrast, TES demonstrated a lower revision rate in patients with spinal metastasis who survived more than two years after surgery [3, 4, 11, 12, 13]. However, the aggressiveness of TES raises concerns about increased peri-operative and post-operative complications in spinal metastasis patients [14]. Recently, second-generation TES surgical techniques have been developed to reduce aggressiveness and minimize operative-related complications [3, 11, 15]. Due to limited information comparing the survival outcomes between TES and PSS in metastatic spinal patients [6]. The current study thus compared overall survivorship at 6 and 12 months and other oncologic and surgical outcomes between TES and PSS in spinal metastasis.

Materials and methods

Our institutional review board approved this retrospective cohort study (HE611450). We included patients with thoracic, lumbar, or thoracolumbar spinal metastasis diseases treated with TES or PSS by a single surgeon in a tertiary hospital between January 2014 and December 2020. All patients must have a pathological report and routine investigation such as MRI whole spine, CT chest and abdomen, bone scan, and blood test. Patients with hematological malignancy or inadequate medical records (for example loss of prognostic scoring parameters data, no information of post-operative adjuvant treatment, missing data of intra-operative, and post-operative record). were excluded. Patient demographic data (sex, age, origin of malignancy, lesion level, Tomita score, revised Tokuhashi score, The Skeletal Oncology Research Group (SORG) nomogram, Eastern Cooperative Oncology Group (ECOG), Frankel scale, American Spinal Injury Association (ASIA), and preoperative hematocrit) were collected. Adjuvant treatments such as chemotherapy, radiotherapy, and targeted therapy were also documented. Primary outcomes included survivorship at 6 and 12 months and overall (from the date of surgery to death). The local recurrence in TES detected by post-operative MRI follow up, complications of the two treatments, and the hospital cost were considered as the secondary outcomes. Patients live-status on December 31, 2021, was checked from the Bureau of Registration Administration records after surgery. Secondary outcomes included operative time (h), intraoperative blood loss (mL), units of blood transfusion within 14 d after surgery, hospital stay (days), and hospital cost (Thai baht). The hospital costs were extracted from the hospital's information technology system.

The indication for TES and PSS in this study was (a) spinal metastasis of 1–3 contiguous vertebral bodies, (b) Tomita surgical classification type 1 to 6 (and occasionally 7), and (c) predicted survival of more than 6–12 months by SORG nomogram, Tomita, and modified Tokuhashi score, and Eastern Cooperative Oncology Group (ECOG) score of 4 or less. All patients had no obvious visceral metastasis on chest and abdominal CT scan images. Second generation TES was implemented in the institution from early 2018. Consequently, all patients indicated for TES before early 2018 underwent PSS surgery.

The definitive surgical treatment for patients was extensively discussed and carefully selected by the orthopaedist, radiologist, medical oncologist, radiotherapist, the patients themselves, and their relatives.

Surgical technique

TES was performed using the second-generation TES techniques described by Ishii et al. [15] TES consists

of 2 steps in a prone position. The first step is en bloc laminectomy using a T-saw to cut bilateral pedicles. Rib resection is performed if the lesion is located at the thoracic level. Then posterior spinal instrumentation is performed—inserting pedicular screws into two vertebrae above and below the affected vertebral level. The second step is en bloc corporectomy by blunt dissection around the vertebral body. Decompression and protection of the spinal cord were performed. Disc cutting at the upper and lower discs was performed, then removed as one piece of body and replacement space by vertebral prostheses such as a titanium mesh cage and bone graft [3, 16, 17]. Palliative surgical debulking or decompressive laminectomy, or posterior spinal instrumentation were operated in standard modern techniques which aim to relieve pain, increase stability, and remove mass as possible for gaining neurologic function. There was no pre-operative embolization in either of the two patient groups due to lack of resources.

PSS was performed by decompression and debulking the compressed tumor from the posterior of the spinal cord and nerve roots, followed by stabilization with pedicle screws and rods, without freeing the spinal cord and nerve roots from the vertebral body.

Post-operative management and follow-up

Every patient received rehabilitation, including chest physical therapy, mobilization, and strengthening to improve quality of life and physical function and to decrease complications. Patients obtained other adjuvant therapies depending on the attending oncologist. Follow-up was by outpatient evaluation at 2 weeks, 4 weeks, 3 months, 6 months, and annually thereafter with radiographic evaluation or MRI if recurrence of the disease is suspected.

The decision for radiotherapy and chemotherapy treatment was carefully evaluated and finalized by the medical oncologist and radiotherapist.

Statistical analysis

Data analysis was performed in STATA, version 10.1. Demographic data were analyzed with Pearson chi-square and Fisher's exact test for categorical data and independent t-test or Mann-Whitney U test for continuous data. We used logistic regression to estimate the propensity matching score to compare both treatment groups, controlled using the Tomita, revised Tokuhashi, *SORG*, and preoperative Frankel scores. A log-rank test was used to compare both groups. The Kaplan-Meier method was used to analyze survivorship. A p-value of <0.05 was considered statistically significant. The incidence rate was used to estimate the recurrence rate.

Results

At first, 22 TES and 35 PSS patients were recruited for the study. Logistic regression was analyzed for the propensity matching score with controlled variables such as the Tomita, revised Tokuhashi, *SORG* and Preoperative Frankel scores. After performing the propensity matching score, 22 patients were in the PSS group, similar to the TES group vis-à-vis confounding factors. The standardized percent of bias across covariates in the selected variables is shown in Fig. 1—a total of 44 patients with a mean age of 56. There was no significant difference in demographics data (e.g., sex, age, the origin of malignancy, preoperative hematocrit, Tomita score, revised Tokuhashi score, SORG nomogram, ECOG, Preoperative Frankel score, or ASIA score) between the two groups (Table 1). There was no significant difference in adjuvant radiotherapy treatments (Table 2). All patients received chemotherapy based on their specific pathological results

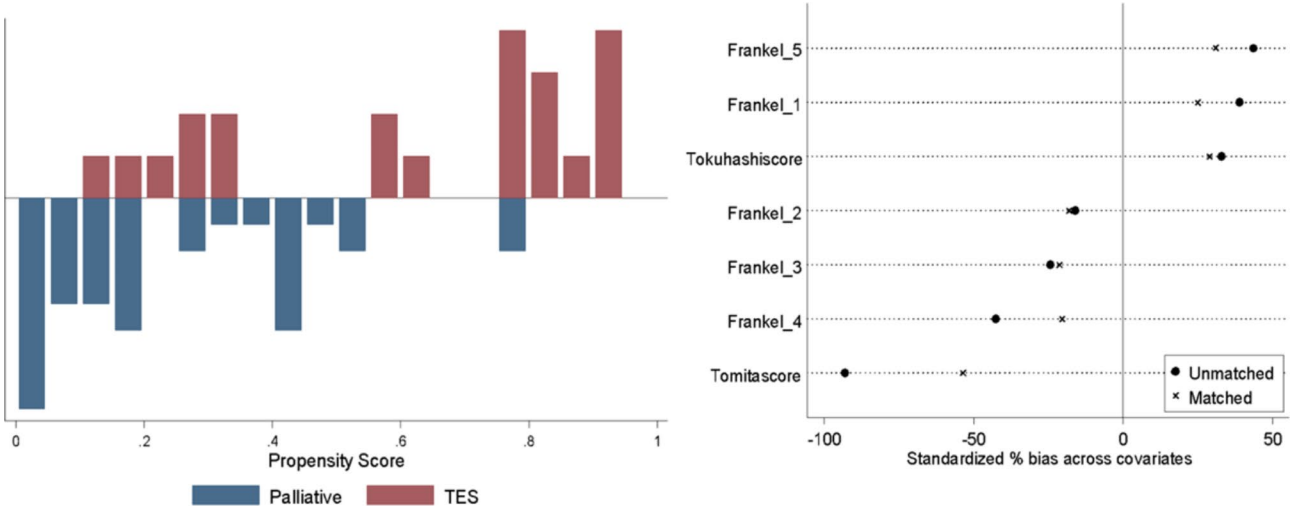

Fig. 1 Variables used in propensity score matching and standardized percent of bias across covariates before and after matching

Table 1 Showed the demographic data of all patients

	Total (*n* = 44)	**Palliative (*n* = 22)**	**TES (*n* = 22)**	***p*-value**
Sex				0.763
Male	21 (47.73)	11 (50.00)	10 (45.45)	
Female	23 (52.27)	11 (50.00)	12 (54.55)	
Age; mean(sd)	55.75 (11.51)	58.73 (11.96)	52.77 (10.48)	0.086
Origin				0.462
Breat	9 (20.45)	5 (22.73)	4 (18.18)	
Lung	11 (25.00)	4 (18.18)	7 (31.82)	
Liver	2 (4.55)	-	2 (9.09)	
CCA	8 (18.18)	5 (22.73)	3 (13.64)	
Colon	4 (9.09)	3 (13.64)	1 (4.55)	
RCC	2 (4.55)	1 (4.55)	1 (4.55)	
Sarcoma	1 (2.27)	-	1 (4.55)	
Thyroid	1 (2.27)	-	1 (4.55)	
Bladder	1 (2.27)	1 (4.55)	-	
Endometrium	3 (6.82)	1 (4.55)	2 (9.09)	
Prostate	2 (4.55)	2 (9.09)	-	
Hct (pre-op) mean(sd)	36.83 (4.90)	35.94 (4.85)	37.73 (4.89)	0.228
Tomita score; mean(sd)	5.25 (2.23)	5.82 (2.54)	4.68 (1.76)	0.092
Tokuhashi score; mean(sd)	8.20 (2.69)	7.82 (2.52)	8.59 (2.86)	0.347
SORG total point mean(sd)	144.56 (20.68)	145.9(20.57)	143.18(21.19)	0.091
ECOG				0.075
0	1 (2.27)	1 (4.55)	-	
1	6 (13.64)	3 (13.64)	3 (13.64)	
2	7 (15.91)	5 (22.73)	2 (9.09)	
3	14 (31.82)	3 (13.64)	11 (50.00)	
4	16 (36.36)	10 (45.45)	6 (27.27)	
Pre op Frankel scale				0.727
A	8 (18.18)	3 (13.64)	5 (22.73)	
B	3 (6.82)	2 (9.09)	1 (4.55)	
C	10 (22.73)	6 (27.27)	4 (18.18)	
D	10 (22.73)	6 (27.27)	4 (18.18)	
E	8 (36.36)	5 (22.73)	8 (36.36)	
ASIA				0.116
A	8 (18.18)	3 (13.64)	5 (22.73)	
B	1 (2.27)	-	1 (4.55)	
C	8 (18.18)	7 (31.82)	1 (4.55)	
D	13 (29.55)	7 (31.82)	6 (27.27)	
E	14 (31.82)	5 (22.73)	9 (40.91)	

TES: Total en bloc spondylectomy

CCA: Cholangiocarcinoma

RCC: Renal cell carcinoma

Hct: Hematocrit

SORG: The Skeletal Oncology Research Group

ECOG: the Eastern Cooperative Oncology Group

ASIA: American Spinal Injury Association

Statistical test

Categorical data; Pearson chi-square or Fisher's exact test. Continuous data; Independent t-test

Table 2 External beam radiotherapy treatment **Statistical test**: pearson chi-square or Fisher's exact test

	Total (*n* = 44)	**Palliative (*n* = 22)**	**TES (*n* = 22)**	***p*-value**
External Beam Radiotherapy	16 (36.36)	10 (45.45)	6 (27.27)	0.210

at their respective hospitals. For radiotherapy, only 10 fractions (60 Gy) of conventional beam radiotherapy were administered to both patient groups. The decision was made solely by the radiotherapists, patients, and their relatives. In the TES group, post-operative radiotherapy was not recommended. Post-operative radiotherapy was performed only in patients with positive or unavailable margin evaluations (6 patients).

TES showed significantly better survival in 6 months with a survival rate of 98.3% (95%CI95.86-99.28) and a mean survival time of 34.6 (95%CI 26.90-42.28) compared to PSS with a survival rate of 91.1% (95%CI 84.93–94.72) p-value was 0.010 (Table 3; Fig. 2). In 12 months, TES was also significantly better than PSS, with a survival rate of 97.6 (94.93–98.85) and a mean survival time of 30.9 (95%CI 22.57–39.28) compared to PSS with a survival rate of 90.44 (84.14–94.24), a mean survival time of 13.53 (95%CI 6.8-20.26), and a p-value of 0.020 (Table 3; Fig. 3). However, the two groups had no significant difference in overall survivorship (p-value 0.100) (Table 3). *The local recurrence at the cephalad spinal level in the TES group was 4.6% (1 patient), detected by MRI post-operatively at the 1-year follow-up, and subsequently treated with external beam radiotherapy.* —no significant difference in complications between the two groups. In the TES group, regarding surgical margins, 16 patients (72.7%) achieved a clear surgical margin, 4 had positive margins, and data on surgical margin availability for 2 patients were unavailable. For the PSS group, the local recurrence rate of tumors causing neurological symptoms was found to be 18.18%, with 4 patients affected, and 2 patients required a second decompression surgery. Only 3 cases (13.6%) of the TES had a dural tear that healed sequentially without serious events. None of the TES group had a surgical site infection. Deterioration of neurological function was found in 2 cases of the palliative group and 1 case of the TES (9.1% and 4.6%, p-value > 0.999) (Table 4).

The TES showed significantly longer operative time (6 h (5.5–6.5) and 3 h (2.0-3.5), p-value < 0.001) and more intraoperative blood loss (1150 mL (1000–1800) and 575 mL (350–800), p-value = 0.0002). Blood transfusion units within 14 d in the TES were significantly more than in the PSS group (5 units (3-12.5) and 2 units (2–5),

Table 3 Survival analysis at 6, 12 months, and overall

	Palliative	TES
Survival at 6 months	22	22
Time at risk: person-months	156.9	289.83
Incidence rate per 100 (95%CI)	8.92 (5.28–15.07)	1.73 (0.72–4.14)
Mean survival time (95%CI), months	14.85 (7.84–21.85)	34.59 (26.90–42.28)
Survival probability		
At 2 mo. (95%CI)	63.64% (40.29–79.88)	86.12% (62.86–95.31)
At 4 mo. (95%CI)	45.45% (24.44–64.33)	76.56% (52.49–89.52)
At 6 mo. (95%CI)	36.36% (17.43–55.67)	76.56% (52.49–89.52)
Survival at 12 months		
Time at risk: person-months	156.9	289.83
Incidence rate per 100 (95%CI)	9.56 (5.76–15.86)	2.42 (1.15–5.07)
Mean survival time (95%CI), months	13.53 (6.80–20.26)	30.92 (22.57–39.28)
Survival probability		
At 3 mo. (95%CI)	54.55% (32.07–72.39)	77.27% (53.74–89.85)
At 6 mo. (95%CI)	36.36% (17.43–55.67)	72.73% (49.10–86.71)
At 9 mo. (95%CI)	31.82% (14.18–51.11)	67.13% (42.90–82.89)
At 12 mo. (95%CI)	31.82% (14.18–51.11)	67.13% (42.90–82.89)
Overall Survival		
Time at risk: person-months	156.9	289.83
Incidence rate per 100 (95%CI)	11.47 (7.23–18.21)	5.52 (3.38–9.01)
Median survival time (95%CI), months	3.13 (0.64–5.62)	9.97 (6.14–13.80)
Survival probability		
At 5 mo. (95%CI)	40.91% (20.85–60.07)	72.73% (49.10–86.71)
At 10 mo. (95%CI)	27.27% (11.12–46.37)	50.00% (28.18–68.43)
At 15 mo. (95%CI)	16.36% (4.39–35.06)	40.91% (20.85–60.07)
At 20 mo. (95%CI)	16.36% (4.39–35.06)	36.36% (17.43–55.67)
At 25 mo. (95%CI)	16.36% (4.39–35.06)	29.09% (11.23–49.79)
At 30 mo. (95%CI)	16.36% (4.39–35.06)	14.55% (1.33–42.29)
At 35 mo. (95%CI)	16.36% (4.39–35.06)	14.55% (1.33–42.29)
At 40 mo. (95%CI)	-	14.55% (1.33–42.29)

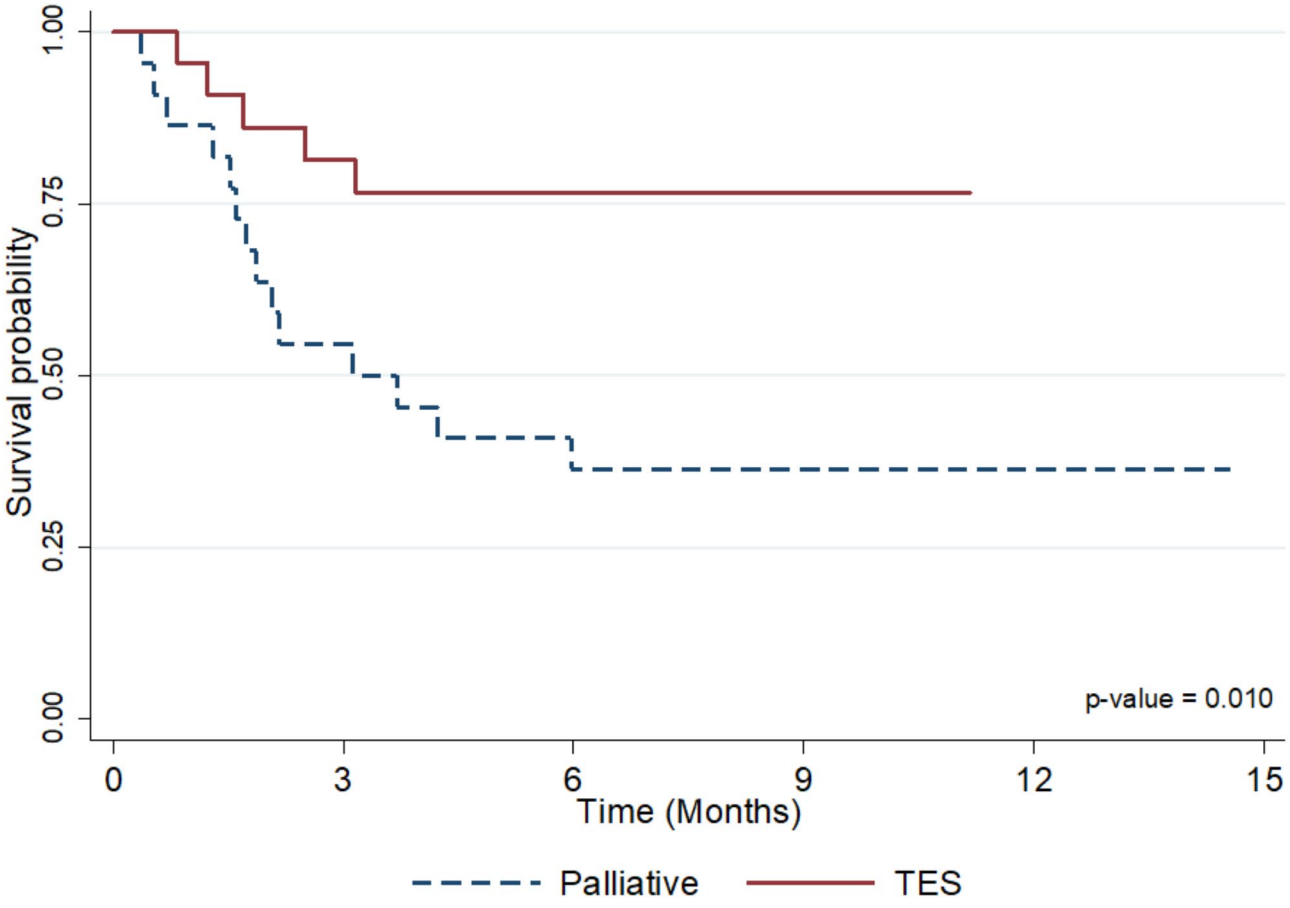

Fig. 2 Kaplan-Meier plot of survival at 6 months

p-value 0.033). The hospital cost of TES was more than PSS 50,000 Thai baht. No significant difference in hospital stay was noted (p-value 0.769) (Table 5).

Discussion

This study is the first to compare outcomes between TES and PSS in spinal metastasis. Since an indication for TES is usually single metastasis or primary spinal malignancy [6]. To control the confounding factor between the two groups, we calculated the propensity matching score via the selection of three variables as Tomita score, the revised Tokuhashi score, and the Preoperative Frankel score. There were significant differences in age, Tomita score, and preoperative ASIA classification before matching. However, after matching, the demographic data, including SORG nomogram total point, was not a significant difference at all. The results demonstrate that TES compared with PSS, had significantly more survivorship at 6 and 12 months, albeit with no difference in overall survivorship. This might be because the prognosis in cases that survive more than one year is relevant for the natural course of disease. TES was good at controlling local recurrence evidenced by an incidence rate of 4.6%. TES, over against PSS, is particularly good for local control, because PSS does not aim to remove all the tumor mass. Consequently, TES requires more operative time and results in greater blood loss without any significant difference in complications or hospital stay. With respect to social issues, TES might be inferior, as it costs more than PSS at 50,000 Thai baht due to the difference between implants and surgical instrumentation.

Previous results of TES show a good prognosis and appreciated outcomes. Murakami et al. report results of TES in lung cancer metastasis in that 4 of 6 patients still live after a mean of 46.3 months after TES. None of the patients had local recurrence [18]. S Kato et al. reported that 25–33% of patients with solitary SM who underwent TES could survive more than 10 years [4, 19]. There was no tumor recurrence in any of the 23 patients who underwent TES. Abe et al. reported that 3 cases from 14 were found to have local recurrence at a mean of 3.2 years after TES. No serious complications occurred [20]. Paholpak et al. reported clinical results of TES in SM, and 13 patients were included [3]. No perioperative complications occurred. No local recurrences were detected, but 15.38% have distant metastasis to adjacent and

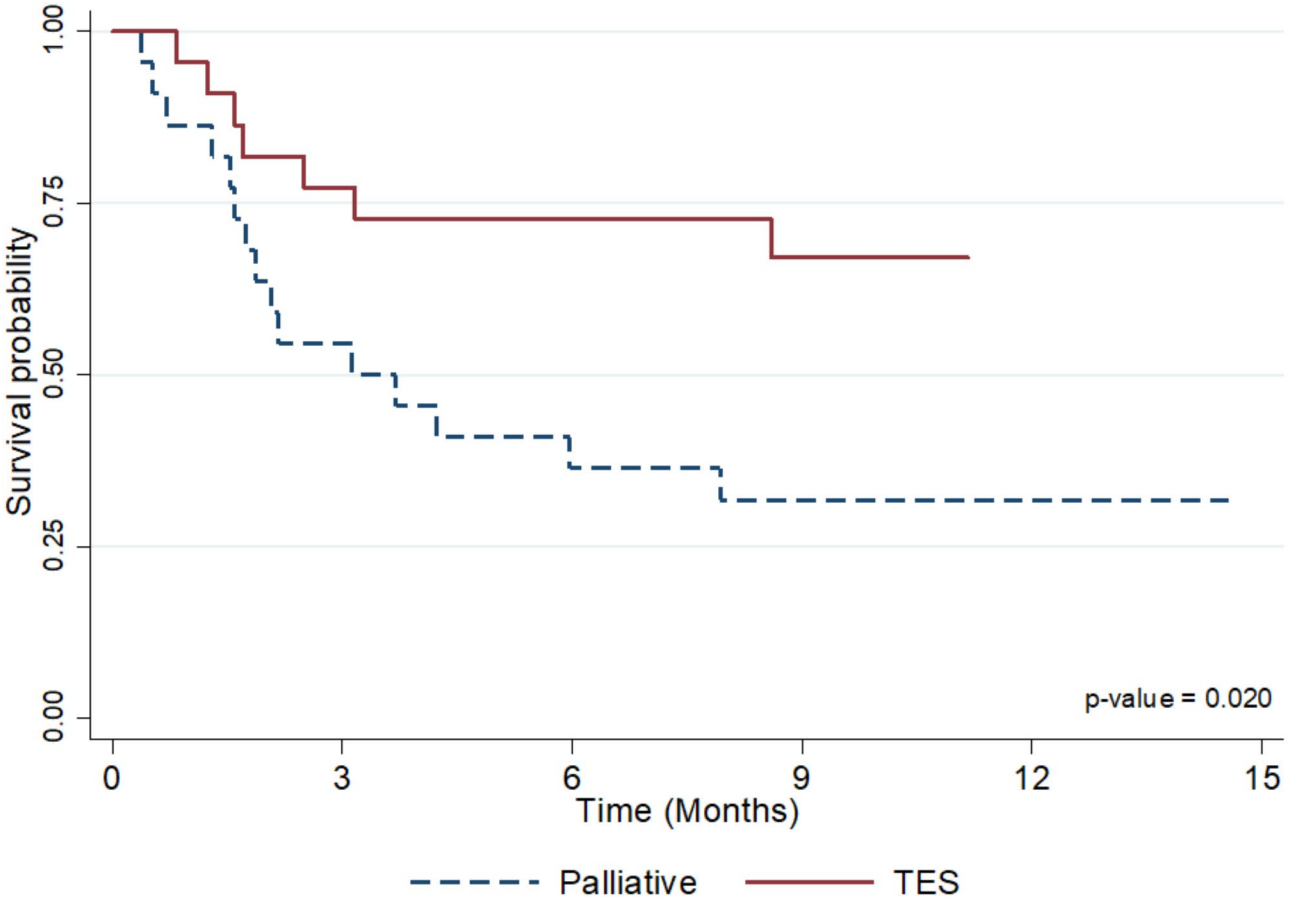

Fig. 3 Kaplan-Meier plot of survival at 12 months

Table 4 Complications statistic test; Fisher's exact test

	Total (*n* = 44)	Palliative (*n* = 22)	TES (*n* = 22)	*p*-value
Dural tear	3 (6.82)	-	3 (13.64)	0.233
Surgical site infection	3 (6.82)	3 (13.64)	-	0.233
Deterioration of neurological function	3 (6.82)	2 (9.09)	1 (4.55)	> 0.999

remote vertebrae. Six patients showed improved ECOG status. This contrasts with other study, which reported complications from TES with 134 patients. He found that 27 patients had severe complications, with 3 deaths, 10 reoperations, 6 deep infections, and 4 major vessel tears [14, 21]. Recently, the surgical technique of TES has been developed in order to reduce aggressiveness and complications [11, 15].

To minimize complications in TES, the author recommends employing second-generation TES techniques, as advocated by Ishii et al., which have shown a significant reduction in perioperative complications and surgical aggressiveness [15]. During TES procedures, meticulous attention is paid to surgical dissection, with gentle traction applied to the nerve root stump during anterior

Table 5 Surgical data and outcomes of patients in TES/Palliative spinal surgery

	Total (*n* = 44)	Palliative (*n* = 22)	TES (*n* = 22)	*p*-value
Operation time (hr); median (IQR)	4.5 (3–6)	3 (2–3.5)	6 (5.5–6.5)	< 0.001
Intraoperative blood loss (ml); median (IQR)	950 (500–1,400)	575 (350–800)	1,150 (1,000–1,800)	0.0002
Unit of blood transfusion (unit); median (IQR)	4 (2–6)	2 (2–5)	5 (3–12.5)	0.033
Hospital stay (days); median (IQR)	20 (16–30.5)	20 (16–27)	22.5 (16–31)	0.769
Hospital cost (Baht); mean (SD)	257,061.4 (79,117.92)	232,321.8 (76,132.4)	283,103.1 (75,503.36)	0.044
Hct (Postop); mean (SD)	31.79 (4.69)	32.70 (4.72)	30.88 (4.60)	0.204

Statistical test

Data with normal distribution; Independent t-test

Data with non-normal distribution; Mann-Whitney U test

dissection to liberate the spinal cord from the posterior vertebral body. Spinal shortening is performed cautiously in all cases, limited to no more than one-third of the resected vertebral column(s), ensuring no wrinkle forms at the spinal cord. Additionally, when tumors adhere to the spinal cord, microsurgical Metzenbaum and microsurgical dissectors are employed to carefully dissect and separate the tumor from the dural sac, thereby preventing dural injury. A headlight, complemented by the brightest light intensity available in the operating room, is utilized to enhance visualization during dissection. Throughout the surgical procedure, continuous irrigation with 0.9% NaCl solution is maintained, and cefazolin 1 g is administered intravenously every 3 h until the completion of the operation to prevent surgical site infections.

This study has some limitations, including the small population recruited. Second, there are many uncontrolled factors due to the nature of a retrospective cohort study. We try to avoid those biases by calculating the propensity matching score. Third, follow-up time is inadequate to demonstrate a significant difference in overall survivorship. Fourth, by the indications of TES, most SM cases with a good prognosis in their baseline tend to prefer more invasive surgery, which aims for better outcomes. On the other hand, a relatively poor-prognostic SM case might prefer to choose PSS or an advanced care plan. *Fifth, separation surgery was not conducted in this study due to the unavailability of stereotactic radiosurgery at our institute. Sixth, adjuvant radiation was limited to conventional external beam radiation and was administered solely to radiosensitive spinal metastasis patients, as determined by an oncology radiologist. This approach might impact local disease control and the survival of PSS patients* [10, 22]. For further study, we suggest conducting a randomized control trial, more patients, and more follow-up to reveal the difference between the two treatments in overall survivorship.

A benefit of the current study was to reveal that TES achieve local control of tumors after surgery. Although the case was a metastatic disease, they are fit for surgery if we can control the primary origin and the patient's prognosis. TES can be one of the treatment options for solitary spinal metastasis and expecting more extended survivorship patients.

Conclusion

Compared with PSS, TES showed better survivorship after 6 and 12 months. TES also showed local control of tumors after surgery with a very low local recurrence rate, especially in the limited adjuvant resources situation. No significant difference in complications or hospital stays was found between the two groups. To confirm the benefits of TES vis-à-vis metastasis, further randomized control should be conducted with more patients.

Abbreviations

TES	Total en bloc spondylectomy (TES)
PPS	Palliative Spinal Surgery
SM	Spinal metastasis
SORG	The Skeletal Oncology Research Group
ECOG	Eastern Cooperative Oncology Group
ASIA	American Spinal Injury Association

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Author contributions

Conception and design: D.Y. and P.P.Data acquisition: D.Y. and P.P.Analysis of Data: D.Y., P.P., and W.K.Drafting the manuscript: D.Y. and P.P.Supervision: T.W., W.S., W.S., W.K., T.M., Y.K., H.M.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Our institutional review board approved this retrospective cohort study (HE611450).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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