Hybrid therapy versus Total En Bloc Spondyectomy in the treatment of Solitary Radioresistant Spinal Metastases：A propensity score-matched analysis

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Research Article

Keywords: Hybrid therapy, Total en bloc spondylectomy, Spinal metastases, High-grade epidural spinal cord compression, propensity score-matched analysis

Posted Date: May 17th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-522631/v1

Abstract

Background

Both hybrid therapy (HT) and total en bloc spondylectomy (TES)can lead to good results for solitary radioresistant metastatic spinal tumors with high-grade epidural spinal cord compression (ESCC). However, there is still a lack of comparative studies on the treatment efficacy of these two methods.

Methods

We retrospectively reviewed patients with the above-mentioned tumors between January 2012 and May 2019. A total of 157 patients underwent surgery, among whom 64 received HT, and 93 were treated with TES. Propensity score matching allowed the generation of best-matched pairs for the 2 categories (1:1 ratio). Local control rates and survival rates were estimated using the Kaplan–Meier method.

Results

All patients received a minimum of 2-year follow-up. The longest follow-up time was 88 months. The survival rates and local progression-free survival rates after HT were comparable with TES at 1 year (84.6% vs. 83.1%; 90.2% vs. 90%), 2 year (60.8% vs. 64.3%; 64.1% vs. 62.1%), and 5 year (18.8% vs. 24.1%; 24.4% vs. 28.4%). There were no significant differences in pain control, improvement of neurological status, spine stabilization restoration, and improvement in quality of life between groups. However, HT showed more advantages in shortening operative time and reducing intraoperative blood loss than TES.

Conclusion

Our results suggest that HT can obtain satisfactory results comparable to TES for solitary radioresistant metastatic spinal tumors with high-grade ESCC. In addition, compared with TES, HT has the advantages of shortening operative time and reducing perioperative complications. For solitary radioresistant metastatic spinal tumors with a high degree of ESCC, HT may be a promising treatment in the future.

Introduction

The spinal column is the most common site of bony metastases. Approximately 70% of patients with cancer will develop metastatic disease at this site [1]. The thoracic and lumbar spine are the most common affected location. The most common primary tumors causing spinal metastasis include breast, prostate, kidney, lung, and thyroid cancer [2]. Metastatic spinal tumors with high-grade ESCC usually lead to neurologic deficits and instability, and lastly, injure the health-related quality of life (HRQOL). So, reconstructing spine stability and decompressing the spinal cord is necessary for patients with spinal

metastasis to improve HRQOL [3]. When high-grade ESCC spinal metastases are histologically resistant to conventional external beam radiotherapy (cEBRT), their therapeutic effects are often unsatisfactory. Therefore, the best treatment option for this type of spinal metastases is still lacking. In the past decade, the emerging roles of stereotactic radiosurgery (SRS) and the concept of multidisciplinary collaboration, the treatment of spinal metastases is changing [4]. The multidisciplinary spine team at Memorial Sloan-Kettering Cancer Center has developed and used a neurologic, oncologic, mechanical, and systemic (NOMS) decision framework for metastatic spine disease [5], which is being used widely in the decision-making process. Although this decision framework has clarified the treatment options for high-grade ESCC spinal metastases, there are still controversies about the best treatment options for solitary radioresistant high-grade ESCC spinal metastases.

If the primary tumor is well controlled and the life expectancy is more than 6 months, it should be treated with TES combined with postoperative SRS. TES can improve tumor local control with its radical extra-lesional resection of tumors. The tumor histology-independent characteristics of postoperative SRS treatment will increase the local control rate further [6–7]. However, there are many shortcomings including prolonged surgical duration, excessive intraoperative blood loss, high perioperative complication rates, and poor overall survival [8]. Besides, TES failed to affect the oncology results of spinal metastases [7]. In terms of the NOMS decision framework, solitary radioresistant metastatic spinal tumors with high-grade ESCC should be treated with HT. HT is the combination of separation surgery followed by SRS. Firstly, separation surgery provides circumferential decompression of the spinal cord, and then, SRS is added to decrease local recurrence. Studies have shown that the local control rate of HT could reach up to 90% [24]. However, such studies were highly heterogeneous, and the current results did not truly reflect the treatment effect for solitary high-grade ESCC spinal metastases. Besides, comparative studies on the treatment efficacy of the HT and TES two are lacking. So, the efficacy of the HT for solitary radioresistant high-grade ESCC spinal metastases still needs to investigate. Therefore, the objective of this study is to review, analyze and compare clinical data of both groups from our hospital in the past seven years to provide some theoretical basis for selecting the best treatment for solitary high-grade ESCC spinal metastases that are resistant to radiotherapy.

Materials And Methods

Patients

This was a single-center, retrospective study of treatment for patients with solitary radioresistant metastatic spinal tumors with high-grade ESCC. The ethics committee of our university hospital approved this study. From the clinical records database of our hospital, we reviewed data from 157 patients between January 2012 and May 2019. All 157 patients underwent an operation and were divided into two groups based on different therapy (HT and TES). The patient inclusion criteria were as follows: (1) treatment received between January 2012 and May 2019; (2) diagnosis of solitary spinal metastases involving the thoracic or lumbar spine; (3) magnetic resonance imaging (MRI) documenting high-grade

epidural cord compression (grades 2 and 3) according to the Bilsky criteria[9]; (4) the tumor histology were resistant to radiotherapy; (5) life expectancy was more than 6 months (Revised Tokuashi Score, 9-11) and (6) the patient was in good general condition (Eastern Cooperative Oncology Group performance status score ≤3). The exclusion criteria were as follows: (1) the case data was not intact; (2) there were surgical contraindications; (3) the primary tumor was poorly controlled; (4) tumor combined with other metastatic lesions, and (5) patient with previous spinal tumor resection.

Preoperative Evaluation

All patients in our series were evaluated meticulously by our team after admission. We identify possible primary lesions through the history of cancer, physical examination, CT scan of chest, abdomen, and pelvis or positron emission tomography/computed tomography (CT), and bone scan. The preoperative evaluation of spinal tumors was guided by the NOMS framework [5]. All patients underwent an X-ray, computed tomography with the 3-dimensional reconstruction of the spine, and magnetic resonance imaging to evaluate the location and size of tumors and extent of pedicle involvement and spinal cord compression. Percutaneous biopsy under local anesthesia determines the nature of metastases. Life expectancy was estimated preoperatively by revised Tokuashi Score [10]. Eastern Cooperative Oncology Group Performance Status (ECOG-PS) [11] was used to evaluate the patient's general condition preoperatively. Pain, Neurologic function, and tumor-related instability were assessed preoperatively by Visual Analogue Scale (VAS), American Spinal Injury Association (ASIA) impairment scale [12], and Spinal Instability Neoplastic Score system (SINS) [13] respectively. The quality of life in patients was assessed using the Results Questionnaire of the Spine Oncology Study Group Outcomes Questionnaire (SOSG-OQ) [14].

Surgical Procedure

Hybrid Therapy Group: The patient was anesthetized with endotracheal general anesthesia and then placed in the prone position. The posterior procedure was performed. After sterilization and preparation, a dorsal midline incision was made and the lumbar dorsal fascia was divided. The paraspinal muscles were dissected subperiosteally from the spinous process, lamina, and transverse process. Then, the paraspinal soft tissues were retracted laterally by a retractor. With the assistance of an intraoperative radiograph, bilateral pedicle screws were placed in a minimum of 2 levels superior and inferior to the involved level. Circumferential decompression was achieved by laminectomy, facetectomy, and transpedicular approach to the ventral epidural space. Adequate tumor excision provided 2 to 3 mm of separation between the tumor and spinal cord, generally indicated by complete re-expansion of the thecal sac. Rod and crosslinks were then placed. Finally, a negative pressure drain was placed and the wound was closed by layers. (**Figure 1**)

Total en Bloc Spondylectomy Group: The way of anesthetization, position, approach, and fixation of patients were the same as patients in the hybrid therapy group. For cases involving the thoracic spine, about 3cm ribs were removed to access the thoracic cavity, where segmental nerve roots were identified

and ligated. For lumbar cases, we developed a plane lateral to the vertebral body and medial to the psoas muscle, identifying and protecting traversing nerve roots. Bilateral pedicles were cut off, and posterior decompressive laminectomy associated with transverse processes and the spinous process was conducted. Blunt dissection was performed to develop a plane between the vertebral body and the great vessel. Afterward, discectomies were performed above and below the level of the corpectomy. The affected vertebra was then detached from the spinal column. Titanium mesh filled with autogenous and allograft bone was inserted. Following the implantation of suitable titanium mesh, a gentle compression using the posterior instrumentation was performed to ensure the ends of the mesh firmly engaged with vertebral endplates and correct the loss of vertebral height, local kyphosis, or coronal deformity (if any). Crosslinks were then placed to strengthen the fixation. At last, a negative drain was put in and the wound was closed in the same way. (**Figure 2**)

Postoperative Treatment: Postoperative management included antibiotics used for 2–3 days. All resected specimens were analyzed histologically to determine the surgical margin status. Personalized systemic chemotherapy and other adjuvant treatments were recommended according to primary tumor type. SRS was delivered at least 2 weeks after surgery for wound healing without the risk of wound complications. Single-fraction, high-dose radiotherapy (24Gy) was delivered for each patient.

Follow-up

We established local control as the primary endpoint, which is defined as the time from surgery to local relapse. The secondary endpoints were to evaluate the overall survival, perioperative complications, and functional outcomes. The survival time was measured from the date of surgery to the date of death from any cause or to the last follow-up. All patients were followed up with radiological examinations (X-ray, CT, and/or MRI), which evaluated changes in the treated segments and lesions in other sites 1, 3, 6, and 12 months after surgery and every 6 months thereafter. Data on functional outcomes were collected and compared at 6 months after the operation.

Statistical Analysis

Data analysis was performed in SPSS, version 26.0 (IBM Corp., Armonk, New York, USA). Group data are presented as mean standard deviation. Differences between pre-operation and post-operation were compared with the paired *t*-test or Wilcoxon signed-rank test. Differences between groups were evaluated using a two-sample *t*-test or Mann-Whitney U test (before PSM) and paired *t*-test or Wilcoxon signed-rank test (after PSM). Categorical data were analyzed with the chi-square test, Fisher's exact test, or McNemar test. A propensity score-matched analysis was done using a multivariable logistic regression model based on age, sex, involved spinal level, histology, Revised Tokuashi Score, ECOG-PS, ESCC Scale, VAS, SINS, ASIA Scale, and SOSG-OQ. Pairs of patients receiving HT or TES were derived using 1:1 greedy nearest neighbor matching within a PS score of 0.02. This strategy resulted in 55 matched pairs in each group. Kaplan-Meier method was used to assess local progression or overall survival over time for each treatment group. P values <0.05 were considered statistically significant.

Results

Patient characteristics

Between January 2012 and May 2019, a total of 215 patients were diagnosed as solitary radioresistant metastatic spinal tumors with high-grade ESCC, and 157 patients were screened for the study. 157 patients were divided into two groups based on different therapy (HT and TES). There were 64 patients in the HT group and 93 patients in the TES group. The series included 36 women and 121 men. The mean age at the time of admission was 57.88±6.60 years (range 40-72 years). Primary tumors were made up of 58 cases of Renal cell carcinoma (RCC), 41 cases of thyroid cancer, 12 cases of liver cancer, 13 cases of rectal cancer, 23 cases of colorectal cancer, and 10 cases of melanoma. Involved vertebrae included 112 thoracic vertebrae and 45 lumbar vertebrae. The preoperative data of the two groups are shown in **Table 1**. There was no statistical difference in baseline data between groups except for age. After adjustment of PSM, a final cohort of 110 patients (55 HT and 55 TES patients) had data eligible for further analysis (**Figure 3**). The 2 groups were well matched and had no significant differences in baseline characteristics (**Table 2,** P>0.05).

Table 1. Baseline characteristics of patients and tumors in two groups before PSM

Baseline characteristics	HT (n=64)	TES (n=93)	*P*
Age (mean, SD)	56.640.74	58.730.72	0.035*
Sex [n (%)]			0.518
Male	51 (80)	70 (75)	
Female	13 (20)	23 (25)	
Involved spinal level [n (%)]			0.902
Thoracic	46 (72)	66 (71)	
Lumbar	18 (28)	27 (29)	
Histology [n (%)]			0.888
RCC	24 (37)	34 (36)	
Thyroid	19 (30)	22 (24)	
Liver	4 (6)	8 (9)	
Rectal	4 (6)	9 (10)	
Colorectal	10 (16)	13 (14)	
Melanoma	3 (5)	7 (7)	
Revised Tokuashi Score (mean, SD)	10.390.11	10.430.90	0.719
ECOG-PS [n (%)]			0.679
1	10 (16)	14 (15)	
2	33 (51)	45 (48)	
3	21 (33)	34 (37)	
ESCC Scale [n (%)]			0.631
2	45 (70)	62 (67)	
3	19 (30)	31 (33)	
VAS (mean, SD)	7.160.11	7.420.87	0.068
SINS (mean, SD)	12.860.20	13.200.18	0.188
ASIA Scale [n (%)]			0.499
B	13 (20)	24 (26)	
C	24 (38)	33 (35)	

D	27 (42)	36 (39)	
SOSG-OQ (mean, SD)	63.720.89	64.880.70	0.327

* indicates siganificant differences between groups (P <0.05)

RCC, Renal cell carcinoma; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; ESCC, Epidural spinal cord compression; VAS, Visual Analogue Scale; SINS, Spinal Instability Neoplastic Score system; ASIA, American Spinal Injury Association; SOSG-OQ, Spine Oncology Study Group Outcomes Questionnaire; PSM, Propensity score matching.

Table 2. Baseline characteristics of patients and tumors in two groups after PSM

Baseline characteristics	HT (n=55)	TES (n=55)	*P*
Age (mean, SD)	57.32±5.97	57.046.00	0.816
Sex [n (%)]			0.629
Male	42 (76)	45 (82)	
Female	13 (24)	10 (18)	
Involved spinal level [n (%)]			1.000
Thoracic	38 (69)	39 (71)	
Lumbar	17 (31)	16 (29)	
Histology [n (%)]			0.769
RCC	21 (38)	21 (38)	
Thyroid	14 (25)	15 (27)	
Liver	4 (7)	6 (11)	
Rectal	3 (6)	4 (7)	
Colorectal	10 (18)	6 (11)	
Melanoma	3 (6)	3 (6)	
Revised Tokuashi Score (mean, SD)	10.360.89	10.270.78	0.650
ECOG-PS [n (%)]			0.993
1	10 (18)	7 (13)	
2	25 (46)	31 (56)	
3	20 (36)	17 (31)	
ESCC Scale [n (%)]			0.847
2	37 (67)	38 (69)	
3	18 (33)	17 (31)	
VAS (mean, SD)	7.240.88	7.290.81	0.773
SINS (mean, SD)	12.931.64	13.051.80	0.558
ASIA Scale [n (%)]			0.829
B	12 (22)	14 (25)	
C	21 (38)	18 (33)	

D	22 (40)	23 (42)	
SOSG-OQ (mean, SD)	64.337.20	64.456.93	0.870

RCC, Renal cell carcinoma; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; ESCC, Epidural spinal cord compression; VAS, Visual Analogue Scale; SINS, Spinal Instability Neoplastic Score system; ASIA, American Spinal Injury Association; SOSG-OQ, Spine Oncology Study Group Outcomes Questionnaire; PSM, Propensity score matching.

Local control

All patients received a minimum of 2-year follow-up. The longest follow-up time was 88 months. No difference was found in local control between the two therapies (**Figure 4 A**, *P*=0.956). In the overall patient cohort, 62 patients (56%) developed local relapse, 26 of whom received HT and 35 TES during the follow-up period. The 1-year, 2-year, and 5-year local progression-free survival rates after HT was 90.2%, 64.1%, and 24.4% respectively. The 1-year, 2-year, and 5-year local progression-free survival rates after TES were 90%, 62.1%, and 28.4% respectively. The estimated median local progress-free survival period after HT was 36 months (95% confidence interval, 13.77-58.23 months). The estimated median local progress-free survival period after TES was 37 months (95% confidence interval, 18.60-55.40 months). These results indicated that both HT and TES could result in comparable durable local control.

Overall survival

No difference was found in overall survival between the two therapies (**Figure 4 B**, *P*=0.701). The 1-year, 2-year, and 5-year survival rates after HT were 84.6%, 60.8%, and 18.8% respectively. The 1-year, 2-year, and 5-year survival rates after TES were 83.1%, 64.3%, and 24.1% respectively. The estimated median survival period after HT was 36 (95% confidence interval, 17.28-54.72 months). The estimated median survival period after TES was 39 (95% confidence interval, 27.05-50.95 months). These results indicated that both HT and TES could result in comparable satisfactory overall survival.

Operative time, Blood loss, Hospitalization duration, and Interval time to SRS

The mean total operative time and blood loss of patients in the HT group were significantly less than in the TES group (*P*<0.05). There was no statistical significance in hospitalization duration (*P*=0.054) and interval time to SRS between groups (*P*=0.613). **(Table 3)**

Table 3. Comparison of operative time, blood loss, hospitalization duration and interval time to SRS between groups

	HT group (n=55)	TES group (n=55)	*P*
Operative time(h)	3.400.37	6.010.64	0.000
Blood loss(ml)	728.18199.02	1721.82281.98	0.000
Hospitalization duration(d)	11.982.65	13.354.56	0.054
Interval time to SRS(d)	22.981.82	23.002.77	0.613

Functional outcomes

There was no statistical significance in functional outcomes between HT and TES (**Table 4**).

VAS decreased significantly in both groups after surgery ($P<0.05$). There was no significant difference in pain relief between HT and TES after surgery ($P=0.739$). These results suggested that the two treatments played the same important role in pain relief.

All patients had improved or preserved the ASIA scale after surgery. Six months after HT, Of the 12 patients presenting with a preoperative ASIA grade of B, 2 (17%) improved to ASIA E, 4 improved (33%) to ASIA D, 3 (25%) improved to ASIA C, and 3(25%) remained stable at ASIA B. Of the 21 patients presenting with a preoperative ASIA grade of C, 12 (57%) improved to ASIA E, 6 improved (29%) to ASIA D, 3 (14%) remained stable. Of the 22 patients with a preoperative ASIA grade of D, 20 improved (91%) to ASIA E, 2 (9%) remained stable. In the TES group, Of the 14 patients presenting with a preoperative ASIA grade of B, 3 (21%) improved to ASIA E, 4 improved (29%) to ASIA D, 5 (36%) improved to ASIA C, and 2(14%) remained stable at ASIA B. Of the 18 patients presenting with a preoperative ASIA grade of C, 11 (61%) improved to ASIA E, 5 improved (28%) to ASIA D, 2 (11%) remained stable. Of the 23 patients with a preoperative ASIA grade of D, 22 improved (96%) to ASIA E, 1 (4%) remained stable. There was no statistical significance concerning the ASIA scale between the two groups ($P=0.699$). These results suggested that the two therapies could achieve comparable effects in improving or preserving the neurologic function of patients.

The mean SOSG-OQ overall score was significantly lower after surgery ($P<0.05$), and both treatments were similarly effective in improving the quality of life of patients after surgery. There was no statistical difference in SOSG-OQ outcomes between the two groups ($P=0.435$). Both treatment strategies could lead to the same stable improvement in the quality of life of patients postoperatively.

The spinal stability of patients in the two groups recovered significantly after surgery ($P<0.05$), and there was no significant difference in restoring spinal stability after surgery between the two treatments ($P=0.503$)

Complications

The rate of perioperative complications was 18% (10/55) in the HT group, which was lower but with no significant difference than that in the TES group (31%, 17/55; $P=0.121$). In the HT group, Two patients

had deep vein thrombosis, 4 patients had intermuscular venous branch thrombosis, 2 had superficial wound infection, 1 had a transient aggravated neurological deficit, and 1 had cerebrospinal fluid leakage. In the TES group, there were 4 cases with superficial wound infection, 2 cases with pneumonia, 3 cases with deep vein thrombosis, 3 patients had intermuscular venous branch thrombosis, 1 case with stress ulcer, 3 cases with cerebrospinal fluid leakage, and 1 case with transient aggravated neurological deficit. All were successfully treated conservatively.

Table 4. Comparison of functional outcomes in the HT versus the TES group

Functional Outcomes	**HT group**	**TES group**	*P*
Preoperative VAS (mean, SD)	7.240.88	7.290.81	0.773
Postoperative VAS (mean, SD)	1.110.69*	1.150.68*	0.739
Preoperative SOSG-OQ (mean, SD)	64.337.20	64.456.93	0.870
Postoperative SOSG-OQ (mean, SD)	41.50.54*	43.2510.91*	0.435
Preoperative SINS (mean, SD)	12.931.64	13.051.80	0.558
Postoperative SINS (mean, SD)	4.800.85*	4.710.76*	0.503
Preoperative ASIA [n (%)]			0.829
A	0 (0)	0 (0)	
B	12 (22)	14 (25)	
C	21 (38)	18 (33)	
D	22 (40)	23 (42)	
E	0 (0)	0 (0)	
Postoperative ASIA [n (%)]			0.699
A	0 (0)	0 (0)	
B	3 (5)	2 (4)	
C	6 (11)	7 (3)	
D	12 (22)	10 (18)	
E	34 (62)	36 (65)	

***** indicates siganificant differences compared with preoperation (P <0.05)

Discussion

Treatment of patients with spinal metastases is palliative to achieve the following principal goals: pain control, spine stabilization, maintenance or improvement of neurological status, local disease control, and improvement in quality of life [15]. In recent years, with the successful application of SRS and the proposed NOMS decision framework, treatment options for spinal metastases have been mostly clear, but the best treatment option for solitary radioresistant high-grade ESCC spinal metastases remains controversial. The two modalities of surgery currently available for the treatment of the above-mentioned spine metastases are HT and TES. The data presented in this study retrospectively evaluated the treatment efficacy of the two treatments. The results showed that both HT and TES could result in comparable durable local control and satisfactory overall survival. Also, there were no significant differences in pain control, spine stabilization, improvement of neurological status, and quality of life. Nevertheless, when compared with TES, HT showed more advantages in shortening operative time and reducing intraoperative blood loss and perioperative complications.

In 1994, TES was used to treat solitary spine metastases by Tomita [16] and showed satisfactory results in local control and overall survival. The treatment of spinal metastases through TES not only achieved satisfactory results in local tumor control [6-7] [16] but also lead to satisfactory oncology and neurological results [17]. Besides, Kato et al. [18] reported satisfactory long-term therapeutic outcomes for solitary spinal metastases. Radiotherapy after surgery has been advocated for regardless of the surgical extent as concerns have been raised with the possible remainders of microscopic tumor cells on the dura [19]. The results of this study showed that a satisfactory local control rate was achieved in the TES group, which may be related to radical excision of the tumor and timely SRS treatment after surgery. TES can minimize local tumor cells to the maximum extent, and thus effectively inhibit the local diffusion of tumor cells. The postoperative supplementary SRS can further kill tumor cells that may remain in the focus. These combined roles can finally result in timely and effective local tumor control, which is consistent with the reported results. In addition, TES was also effective in early pain relief. The results of this study showed that patients with high-grade ESCC spinal metastatic tumors treated with TES could get prominent pain relief at 6 months after surgery, and such satisfactory results may be closely related to the following factors: 1) TES can minimize tumor cells as much as possible to reduce pain origin of tumor; 2) TES can eliminate the pain caused by instability by achieving immediate and reliable fixation of the unstable spine and 3) TES can completely relieve neurogenic pain by excision of the whole involved vertebrae. Although the radical removal of the tumors could achieve good therapeutic results, correspondingly lead to more postoperative complications [20]. This study showed that TES not only led to more perioperative complications but also induced many problems such as longer operative time, more blood loss. The long-term existence of these problems and the satisfactory results of multidisciplinary collaborative treatment for spinal metastases make TES less and less applied in clinical treatment.

The integration of SRS into treatment planning has shifted the goal from maximal tumor resection surgery to HT for spinal metastases [21]. HT, composed of separation surgery and postoperative SRS, is a kind of treatment strategy recommended by the NOMS decision framework developed by the multidisciplinary team at the Sloan-Kettering Memorial Cancer Center. The term separation surgery was

coined by Lilyana Angelov and Edward Benzel to designate a procedure in which tumor resection is limited to decompression of the spinal cord to create a gap to the tumor and provide a safe target for spine SRS. The goal of surgical decompression is to achieve a 360° decompression that allows full re-expansion of the dura and affected nerve roots [22]. With the application of SRS, metastatic tumors that once demonstrated poor responses to cEBRT are now being recognized as radiosensitive to SRS [3]. Spine SRS delivers high doses of radiation accurately to tumors and spares adjacent healthy tissues, such as the spinal cord and nerve roots, and lastly improves pain and neurological symptoms caused by spinal cord compression in patients with spinal metastases [23]. HT has achieved good results in the treatment of spinal metastatic tumor with the advantages of durable local control, effective palliation of pain, and improvement of neurological symptoms while minimizing operative morbidity [23-25]. The results of this study showed that the operative time and blood loss in the HT group were significantly less than that in the TES group, but the same local control, pain improvement, and overall survival could be achieved. At the same time, HT treatment could lead to satisfactory recovery of neurological deficit, improvement in quality of life, and reconstruction of spinal stability. It could be seen that HT for solitary radioresistant high-level ESCC spinal metastases not only had the advantages of less operative time and blood loss but also obtained the same therapeutic effect as the TES group after surgery. These results are consistent with those of current research reports. Although the results of this study showed that the perioperative complications and hospitalization duration in the HT group were less than those in the TES group, there was no statistical difference, which may be related to the smaller sample size.

Previous studies have reported that intralesional resections and EBS with contaminated margins will have a negative effect on local recurrence [7] [26]. It can be inferred that the local control after SS may theoretically be worse. However, the results of our study showed that both therapies led to durable local tumor control (5 patients with positive margins postoperatively in the TES group, 55 patients in the HT group). The reasons were as follows: firstly, patients in both groups obtained SRS postoperatively at the most appropriate interval time. Most authors recommended delaying postoperative SRS about 3–4 weeks [20] [27]. In our study, all patients in both groups received SRS during this interval, of which the HT group was 22.98±1.82 days and the TES group was 23.00±2.77 days. There was no significant difference (P=0.613); Secondly, high-dose single-fraction SRS could provide more effective local tumor control. High-dose single-fraction SRS achieved better local control and reduced the cumulative local failure rate to 2%, which was independent of tumor histology, and especially suitable for radioresistant spinal metastases [20] [28].

There are still several limitations in our study. Firstly, this is a retrospective study which makes it difficult to avoid the cofounder bias. Also, the sample size was too small to detect statistical significance in some analyses including perioperative complications and hospitalization duration. Therefore, a prospective study with increased sample size and extended follow-up time will be needed to increase the internal and external validity of the study. Nevertheless, PSM analysis, which is considered to minimize some weaknesses of retrospective studies, allowed us to compare patients with similar background characteristics.

Conclusion

In this single-center retrospective study, we found that HT can bring the same local control, overall survival, and functional outcomes as TES for patients who were diagnosed as solitary radioresistant metastatic spinal tumors with high-grade ESCC. In addition, HT has the advantage of shortening operative time, reducing intraoperative blood loss and perioperative complications. Our results suggest that for solitary radioresistant metastatic spinal tumors with a high degree of ESCC, HT may be a promising treatment in the future. These results should be considered in clinical decision-making, and our findings might provide useful information for future studies.

Abbreviations

ASIA: American Spinal Injury Association; cEBRT: Conventional external beam radiotherapy; CT: Computed tomography; ECOG-PS: Eastern Cooperative Oncology Group Performance Status; ESCC: Epidural spinal cord compression; HRQOL: Health-related quality of life; HT: Hybrid therapy; MRI: Magnetic resonance imaging; NOMS framework: Neurologic, oncologic, mechanical, and systemic framework; RCC: Renal cell carcinoma; SINS: Spinal Instability Neoplastic Score system; SOSG-OQ: Spine Oncology Study Group Outcomes Questionnaire; SRS: Stereotactic radiosurgery; TES: Total en bloc spondylectomy; VAS: Visual Analogue Scale; PSM, Propensity score matching.

Declarations

Acknowledgments

Not applicable

Authors' contributions: JP, Z. made substantial contributions to the analysis and interpretation of data and was involved in drafting the manuscript and revising it critically for important intellectual content. **LY. W.** made substantial contributions to the acquisition and analysis of data and was involved in revising the manuscript for important content. **NK. N.** and **JD. S.** made huge contributions to conception and design. **ZQ. Y.** and **HQ. D.** were responsible for project administration. **JD. S.** gave final approval of the version to be published and agreed to be responsible for all aspects of the work. All authors read and approved the final manuscript.

Funding

This work was supported by Ningxia Natural Science Foundation Project (NZ16128, 2019AAC03193).

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate: The collection of patient's clinical data was approved by the Ethics Committee of the General Hospital of Ningxia Medical University and performed in accordance with the Declaration of Helsinki.

Consent for publication: Written informed consent was obtained from the patient for publication of this research and accompanying images. A copy of this written consent is available for review by the Editor-in-Chief of this journal.

Competing interest

The authors declare that they have no competing interests.

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Figures

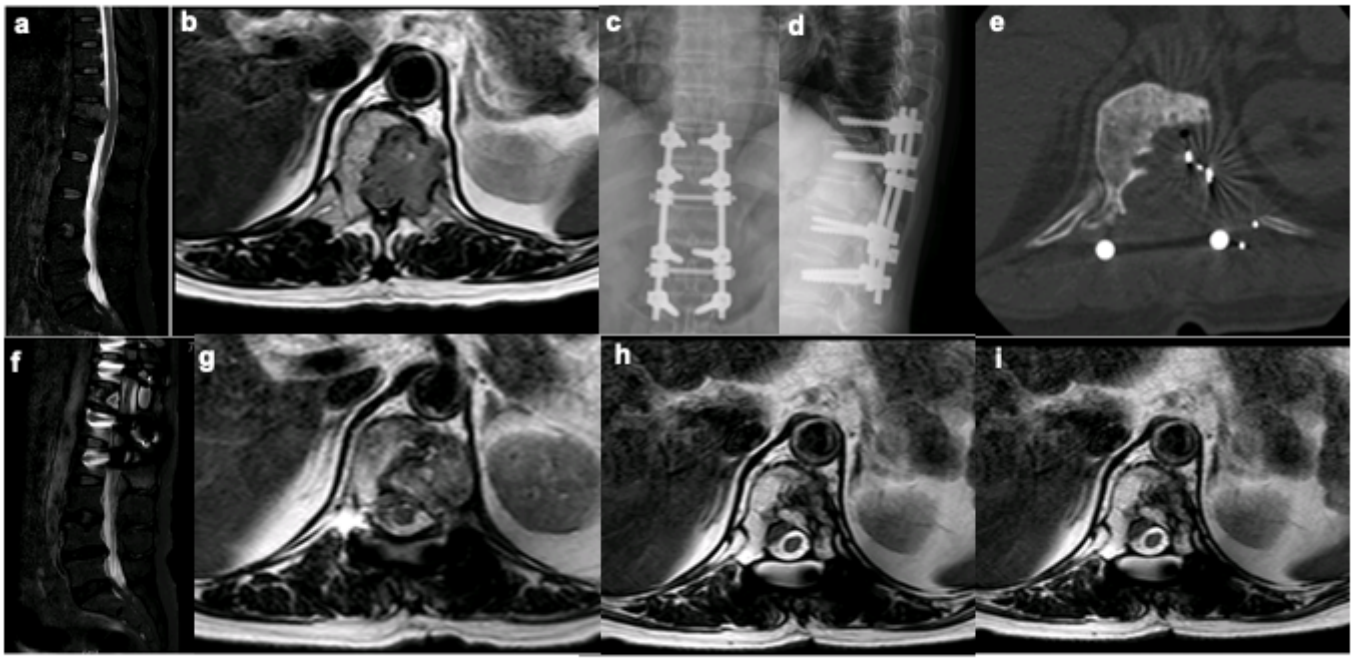

Figure 1

A 52-year-old woman with solitary metastatic spinal tumor (T12) after HT. a, b Preoperative sagittal and axial T2-weighted MRI showed high-grade ESCC spinal metastasis in T12. c, d Postoperative anteroposterior and lateral radiograph. e Postoperative axial CT scan showed resection of part of the posterior arch. f, g Postoperative sagittal and axial MRI showed a 360° decompression of the spinal cord. h, i Postoperative MRI scan demonstrating residual tumor with no significant progress at the 12 and 24-month follow-up.

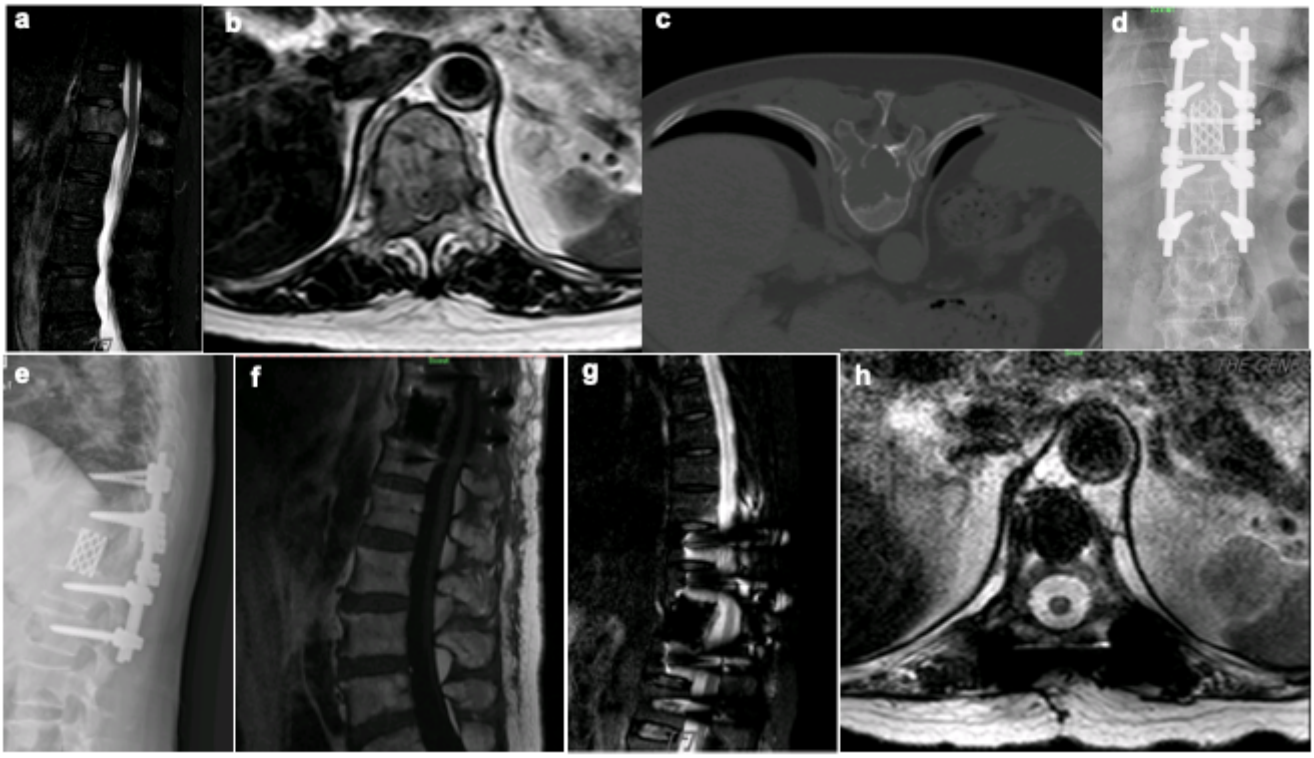

Figure 2

A 60-year-old woman with solitary metastatic spinal tumor (T11) after TES. a, b Preoperative sagittal and axial T2-weighted MRI showed high-grade ESCC spinal metastasis in T11. c Preoperative axial CT scan showed osteolytic bony destruction in T11. d, e Postoperative anteroposterior and lateral radiograph. f Postoperative sagittal MRI. g, h MRI scan demonstrating residual tumor with no significant progress at the 12-month follow-up.

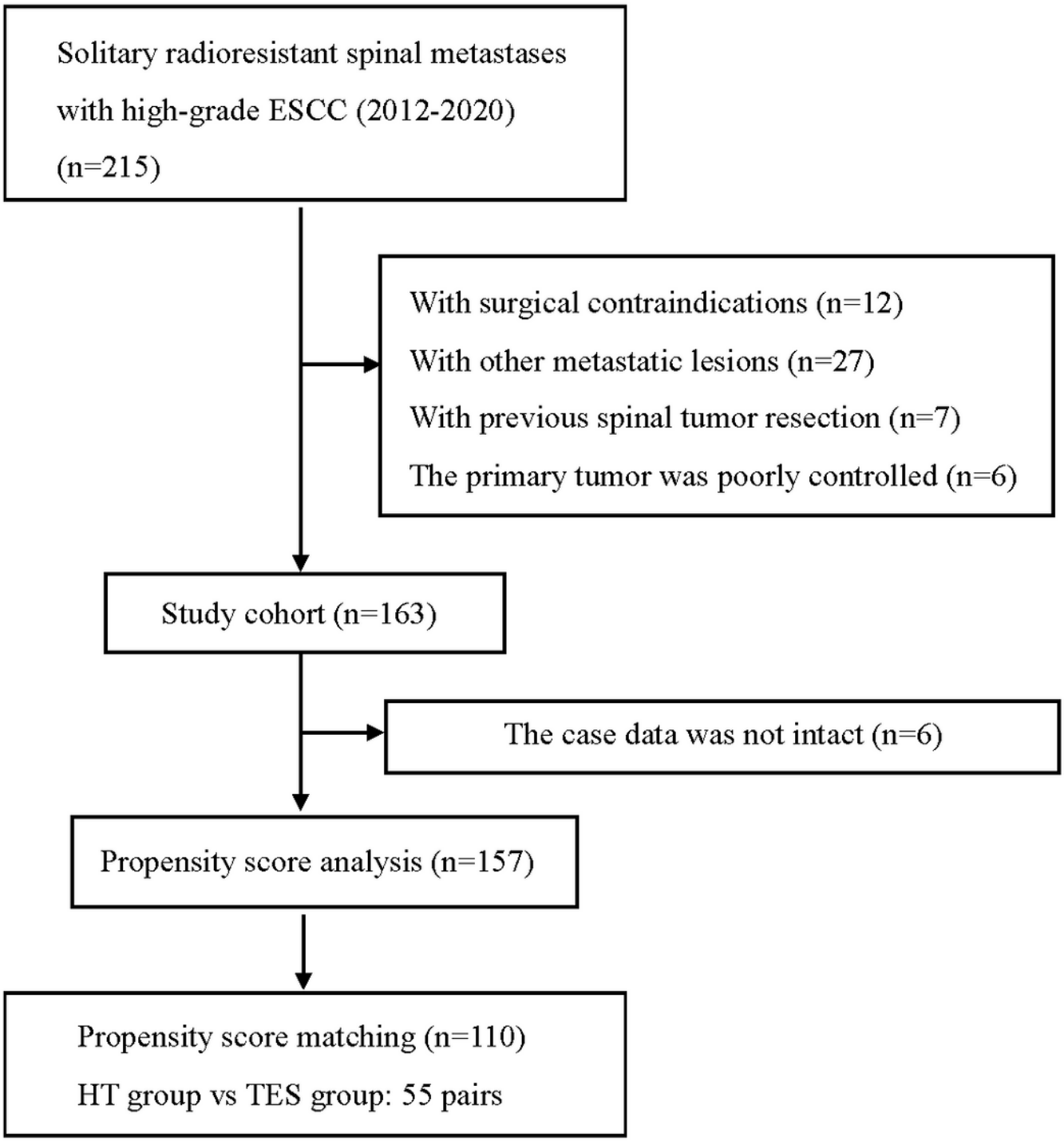

Figure 3

Flowchart of Patient selection.

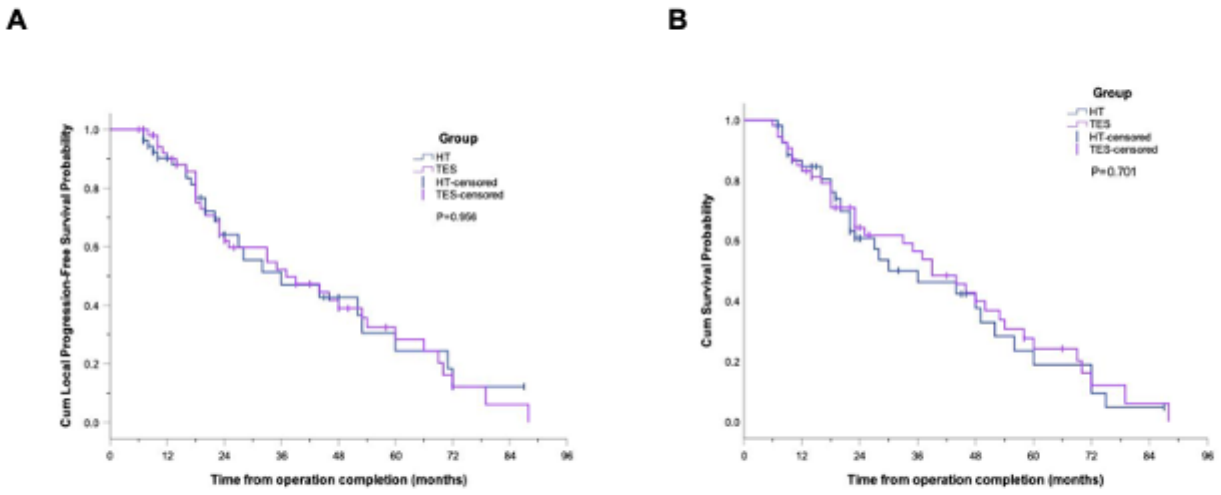

Figure 4

Local Control and Overall Survival. a Local control after HT and TES. b Overall survival after HT and TES.