Prognostic effect of factors involved in revised Tokuhashi score system for patients with spinal metastases: a systematic review and Meta-analysis

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Abstract

Background: Cancer patients’ survival time has obviously improved, with the development of systemic treatment techniques. However, the probability of metastases to the vertebrae has also been increased which makes some adverse effects on patients’ quality of life. The prediction of survival plays a key role in choosing therapeutic modality, and Tokuhashi Score was established as one of the most commonly used predictive systems for spinal metastases. Thus, this study was conducted to identify the prognostic effect of factors involved in revised Tokuhashi Score (RTS).

Methods: Two investigators independently retrieved relevant literature on platforms of PubMed, Embase and Cochrane Library. We identified eligible studies through title/abstract and full-text perusing. Data was extracted including general information of studies, participants’ characteristics, therapeutic modality, overall survival and prognostic effect of factors. Hazard ratio (HR) for each factor was synthesized if available through fixed- or random-effect models as appropriate.

Results: A total of 63 eligible studies with 10,411 participants were identified. Overall, cases with thyroid cancer had the highest survival rate, while the ones with non-small cell lung cancer and hepatocellular carcinoma lived for the shorted survival time. Performance status, bone metastasis, number of involved vertebrae, visceral metastasis, primary tumor and neurological status were regarded as significant predictors in 71.4, 40.0, 18.2, 63.4, 73.1 and 44.7% of the involved studies respectively. Thirty-eight articles were included in meta-analysis, and prognostic effects of five factors (apart from primary tumor) were analyzed. Factors were all proved to be significant except comparisons between KPS (Karnofsky Performance Status) 10–40 VS. 50–70 and single VS. multiple spinal metastases.

Conclusion: All factors of RTS were significant on prognosis predicting and should be considered when choosing therapeutic modality for spinal metastases. What’s more, we believe that more accurate prognosis may be obtained after removal of the cut-offs for KPS 10–40 VS. 50–70 and single VS. multiple involved vertebrae.

Keywords: Spinal metastasis, Prognostic factor, Overall survival, Revised Tokuhashi score
Background

With the improvements of systemic treatment techniques, cancer patients’ survival has obviously extended. However, the probability of metastases to the vertebrae has greatly increased, up to about 70%, which would make adverse effects on patients’ life quality [1, 2]. Patients suffered from spinal metastases usually have symptoms of intractable pain, neurological deficit and spinal instability, as the results of metastatic spinal cord compression (MSCC). In general, most of these patients are likely to benefit from aggressive surgery interventions while some are not if their life expectancies are extremely limited. Hence, for selecting of the optimal therapeutic modality, prognostic factors of the overall survival should be identified and taken into consideration.

Many studies have attempted to identify prognostic factors that predict survival of patients with spinal metastasis, and some handy scores have been established such as Tokuhashi [3, 4], Sioutos [5] and Tomita [6], Bauer [7], North [8] and Van der Linden [9]. Tokuhashi score is one of the most popularly used score systems for spinal metastases and most commonly reported in literature, which was originally established in 1990 and finally revised in 2005 [3, 4]. This score includes the following prognostic factors: performance status, bone metastases, number of involved vertebrae, visceral metastases, primary tumor type and neurological status. The type of primary tumor was scored between 0 and 5, while the other factors were scored between 0 and 2, which was added up to a maximum score of 15 (Table 1). According to this scoring system, if the total score is ranged 0–8, the predicted survival time will be less than 6 months and the conservative treatment or palliative surgery will be the optimal therapeutic modalities. For patients with a score of 12–15, the predicted survival time will be more than 12 months and more aggressive excisional surgery should be selected. And for patients with a score of 9–11, the predicted survival will be 6–12 months and more conservative therapies (i.e. targeted therapy), the consistence and accuracy of RTS further decreased. As reported by Quraishi et al. [10], the prognostic criteria using RTS could only be moderately useful in predicting actual survival (66%). Pointillart et al. [11] also concluded from a prospective study that the original or revised Tokuhashi scores were reliable in predicting survival in European population.

be less than 60%, and the prognostic effect of the factors showed conflicting results. For example, Tokuhashi [3, 4] included neurological deficit in the score, whereas Tomita [6], Bauer [7], North [8] and Van der Linden [9] did not. Thus, the current study aimed to assess the effect of different parameters in RTS for predicting survival of patients with spinal metastases, and modify on the contents of RTS according to the significance of each parameter.

Methods

Data sources and searches

This review was conducted according to the guidelines outlined in Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement. Two individual researchers (Yang XG and Lun DX) conducted platform searches on the PubMed, Embase and Cochrane Library. Literature retrieving was carried out through a

| Table 1 Revised Tokuhashi Score System for the Prognosis of Spinal Metastasis |
| --- |
| Factors Score |
| General condition (Karnofsky Performance Status, KPS) |
| Poor (KPS 10–40) 0 |
| Moderate (KPS 50–70) 1 |
| Good (KPS 80–100) 2 |
| Extrapinal bone metastases |
| ≥3 0 |
| 1–2 1 |
| 0 2 |
| No. of metastases in the vertebral body |
| ≥3 0 |
| 2 1 |
| 1 2 |
| Metastases to the major internal organs |
| Unremovable 0 |
| Removable 1 |
| No metastases 2 |
| Primary site of the cancer |
| Lung, osteosarcoma, stomach, bladder, esophagus, pancreas 0 |
| Liver, gallbladder, unidentified 1 |
| Others 2 |
| Kidney, uterus 3 |
| Rectum 4 |
| Thyroid, breast, prostate, carcinoid tumor 5 |
| Neurological Status |
| Complete (Frankel A, B) 0 |
| Incomplete (Frankel C, D) 1 |
| None (Frankel E) 2 |
combined searching of subject terms (“MeSH” on PubMed and “Emtree” on Embase) and free terms on PubMed and Embase, and through keywords searching on Cochrane Library. Searching strategies used on PubMed and Embase was presented in Additional file 1: Appendix 1. And the searching on Cochrane Library was conducted with the following keywords: “spinal metastasis; overall survival; prognostic factor”. Additionally, some else reference studies of relative articles and reviews were screened and hand-searched for possible inclusion.

Inclusion and exclusion criteria for studies
Complete texts published between January 1997 and October 2017 (over the last two decades) with designs of cohort or case-control study approaching the survival and prognostic effect of factors included in RTS for patients with spinal metastases were included. The publication language was restricted in English but there were no limitations on the participants’ nationalities.

Studies would be excluded for the following reasons: (1) literature review, systematic review and/or meta analysis and letter to editors; (2) studies with less than 10 participants; (3) studies using repeated cohorts; (4) studies with high risk of bias according to the quality assessment; (5) duplicated studies.

Study selection
After all duplicates were recognized and merged together by the software of EndNote X7 version 17.0 (Clarivate Analytics, Philadelphia, USA), the remained titles and abstracts were screened. Then, full texts of potentially relevant papers were obtained and assessed by full-text perusing for eligibility. The whole process of selection was strictly followed with the inclusion and exclusion criteria by two review authors (Yang XG and Lun DX) independently. Discrepancies in study selection between the two reviewers were handled by face-to-face discussion or judged by the third reviewer (Liu YH).

Data extraction and quality assessment
Data was extracted by the two review authors pair independently and entered into a pre-built Microsoft Excel spreadsheet. Collected data included the following information: (1) characteristics of studies (title, author, publication year, country, study period, study design and quality of study), (2) participants’ characteristics (age, percentage of male, number of patients, number of patients with MSCC, primary tumor and spinal metastasis location); (3) therapeutic modality; (4) follow-up and overall survival; (5) prognostic effect of the factors and effect sizes for hazard ratio (HR) combined with their 95% confidence interval (95%CI) representing the prognostic value of factors included in RTS. We figured out causes of diversities on obtained information and resolved disagreements after discussion.

The Newcastle-Ottawa Scale (NOS) [12] was used for the assessment on risk of bias of the studies. This scale employs a 9 stars system that assesses three domains: patient selection, comparability of study groups and ascertainment of study outcome. Studies with a score of 8–9 stars have low risk of bias whereas scores of 6–7 mean medium bias risk and a score of 5 or less than 5 indicates a high chance of bias. Studies with a score of ≤5 stars would be excluded from this study.

Quantitative data analysis
All recorded HRs and CI95% from eligible literature was pooled by an exploratory time-to-event meta-analysis with a random- or fixed-effect model as appropriate and heterogeneity was tested with I² [13]. In case with significant heterogeneity (I² > 50%), random-effect model would be employed, while fixed-effect model would be selected when presenting with excellent homogeneity (I² < 50%). A test for the pooled effect sizes by Z test was performed and statistical significance was defined at a two-sided P value of less than 0.05. A sensitivity analysis would be performed when significant heterogeneity existing and studies causing instability would be removed. Publication bias was assessed with Begg’s and Egger’s regression asymmetry test (P < 0.050 and P < 0.100 were considered to be with significant publication bias respectively) [14]. In case with significant publication bias, a nonparametric trim and fill method will be performed to rectify the bias [15]. The whole process of meta-analysis was performed by Stata version 13.0 (StataCorp LLC, College Station, Texas, USA).

Results
Search result and study selection
The flow chart of eligible literature selection was shown in Fig. 1. The initial searching on electronic platforms yielded a total of 2194 studies and another 3 articles were obtained by hand-searching. After exclusion of 293 duplicates, 1904 articles remained. Then by preliminary glancing over titles and abstracts and further perusing at full-texts, a number of 1503 and 338 articles were excluded respectively. The 338 full texts were excluded with the following reason: 304 studies didn’t involve prognostic effect of the factors involved in Tokuhashi Score; 28 studies were literature or systematic reviews; 3 studies of Lei [16–18] used repeated patients cohort, thus only the one [18] identified primary tumor histology as non-small cell lung cancer(NSCLC) was included; and another 4 studies of Rades [19–22] were also excluded for using repeated patients cohorts with other studies. Finally, 63 studies [6, 8, 9, 18, 24–72, 74–82] with 10,411 participants and 38 studies [8, 9, 18, 26, 28–38, 40, 41, 43, 44, 46, 47, 49, 51–53, 56, 58, 60, 63, 64, 66, 69, 71, 76, 78–81] with 7462 participants were included in the qualitative and quantitative synthesis respectively.
General information of studies

Summary of individual study was listed in Table 2. Majority of the studies were of favourable quality assessed by NOS, with an average score of 7.8 ± 1.0 stars. None of the studies were excluded by quality assessment, which means no studies showed high risk of bias (NOS ≤ 5 stars). As for the delimitation, 57 and 4 studies were retrospective and prospective cohorts respectively, but only 1 each was case-control study and semi-retrospective cohort with a prospective manner on part of the information collection. Primary tumor histology was various among included studies, with 29 non-specified tumor type (7577 patients), 8 prostate cancer (842 patients), 6 non-small cell lung cancer (NSCLC, 667 patients), 6 breast cancer (648 patients), 4 renal cell cancer (355 patients), 4 hepatocellular carcinoma (371 patients), 4 thyroid cancer (110 patients) and 1 each for lung cancer (114 patients) and nasopharynx cancer (87 patients) (Fig. 2a).
| Author               | Character of studies | Country          | Study design | Follow-up | NOS (Stars) | Primary tumor | Case with MSCE | Male (%) | Age | Overall survival (median/mean) |
|----------------------|----------------------|------------------|--------------|-----------|-------------|---------------|----------------|----------|-----|-------------------------------|
| van der Linden [9]   | 2005 1996–1998       | Netherlands      | retrospective cohort | ≤32 m or until death | 8           | NI            | 342            | 12       | 53  | mean: 66 median: 7 m          |
| Patchell [23]        | 2005 1992–2002       | USA              | marched-pair study | Median: surgery group: 3.4 m; radiation group: 3.1 m | 9           | NI            | 101            | 101      | 70  | median: 60 NS                  |
| Chen [24]            | 2007 2000–2005       | China            | retrospective cohort | NS        | 8           | NSCLC         | 31             | 31       | 61  | mean: 61.4 median: 8.8 m      |
| Leithner [25]        | 2008 1998–2006       | Austria          | prospective+retrospective cohort | ≥12 m | 7           | NI            | 69             | NS       | 54  | median: 60 median: 14 m       |
| Park [26]            | 2011 2001–2008       | Korea            | retrospective cohort | Mean: 25.8 m | 8           | NI            | 103            | 103      | 62  | mean: 54.6 median: 10 m       |
| Arrigo [27]          | 2011 1999–2009       | USA              | retrospective cohort | NS        | 9           | NI            | 200            | 172      | 61  | mean: 58.9 median: 8 m        |
| Rades [28]           | 2012 1992–2010       | Germany          | retrospective cohort | NS        | 8           | NSCLC         | 356            | 356      | 74  | median: 64 NS                  |
| Crnalic [29]         | 2012 2003–2010       | Sweden           | retrospective cohort | NS        | 7           | PCa           | 68             | 68       | 100 | median: 71 NS                  |
| Chong [30]           | 2012 2002–2010       | Korea            | retrospective cohort | NS        | 8           | NI            | 105            | 105      | 69  | mean: 58.3 median: 6 m        |
| Rades [31]           | 2013 1992–2011       | Germany          | retrospective cohort | NS        | 8           | NI            | 2029           | 2029     | NS  | NS NS NS NS                    |
| Ju [32]              | 2013 2002–2011       | USA              | retrospective cohort | NS        | 8           | PCa           | 27             | 27       | 100 | median: 65 median: 10.2 m     |
| Bakker [33]          | 2014 2006–2013       | Netherlands      | retrospective cohort | NS        | 6           | RCC           | 21             | NS       | NS  | NS NS NS NS                    |
| Bollen [34]          | 2014 2001–2010       | Netherlands      | retrospective cohort | Median: 6.6y | 9           | NI            | 1043           | NS       | 52  | mean: 64.8 median: 4.8 m      |
| Vanek [35]           | 2015 2006–2012       | Czech            | retrospective cohort | NS        | 8           | NI            | 166            | 166      | NS  | mean: 62 median: 16 m         |
| Tang [36]            | 2015 2002–2013       | China            | retrospective cohort | Median: 13.5 m | 9           | NSCLC         | 116            | 116      | 65  | median: 55 NS                  |
| Lei [18]             | 2015 2005–2015       | China            | retrospective cohort | Mean: 9.7 m | 9           | NSCLC         | 64             | 64       | 66  | median: 57 median: 6.3 m      |
| Chen [37]            | 2015 2000–2010       | China            | retrospective cohort | NS        | 8           | NSCLC         | 50             | 50       | 68  | mean: 61.6 median: 7.5 m      |
| Meng [38]            | 2016 2002–2012       | China            | retrospective cohort | NS        | 7           | PCa           | 29             | NS       | 100 | median: 71 median: 44 m       |
| Park [39]            | 2016 2010–2014       | Korea            | prospective cohort | NS        | 8           | NSCLC         | 50             | 50       | 54  | mean: 58.0 median: 5.2 m      |
| Huddart [40]         | 1997 1984–1992       | UK               | retrospective cohort | NS        | 8           | PCa           | 69             | 69       | 100 | NS NS NS NS                    |
| North [8]            | 2005 NS              | USA              | retrospective cohort | NS        | 9           | NI            | 61             | NS       | 56  | mean: 52.4 median: 10 m       |
| Williams [41]        | 2009 1993–2005       | USA              | retrospective cohort | NS        | 9           | PCa           | 44             | NS       | 100 | median: 68 median: 5.4 m      |
| Rades [42]           | 2012 1992–2010       | Germany          | retrospective cohort | NS        | 7           | PCa           | 218            | 218      | 100 | NS NS NS NS                    |
Table 2 Summary of included studies (Continued)

| Author     | Character of studies | Country | Study design | Follow-up | NOS (Stars) | Primary tumor | Case with MSCC | Male (%) | Age | Overall survival (median/mean) |
|------------|----------------------|---------|--------------|-----------|-------------|---------------|---------------|---------|-----|------------------------------|
| Crnalic [43] | 2012 2003–2008 retrospective cohort | Sweden | Median: naïve: 26 m; refractory: 12 m | 7 | 54 54 100 NS NS |
| Lee [44] | 2014 2005–2010 retrospective cohort | Korea | NS | 7 | NI 200 NS 59 mean: 59.9 mean: 10.8 m |
| Sellin [45] | 2015 1993–2010 retrospective cohort | USA | NS | 9 | TCa 43 NS 60 NS median:15.4 m |
| Drzymalski [46] | 2010 1990–2009 retrospective cohort | USA | NS | 8 | PCa 333 77 100 median: 68 median:24 m |
| Tancioni [47] | 2012 2004–2007 retrospective cohort | Italy | NS | 9 | NI 151 151 51 median: 62 median:14 m |
| Tatsui [48] | 2014 1993–2007 retrospective cohort | USA | Median: 77.9 m | 9 | RCC 267 267 77 mean:59.2 mean:11.3 m |
| Petteys [49] | 2016 2000–2011 retrospective cohort | USA | NS | 8 | RCC 30 NS 77 mean:57.6 mean:11.4 m |
| Rades [50] | 2016 NS retrospective cohort | Germany | Median:6.5 m | 7 | TCa 14 14 29 median:70 NS |
| Kato [51] | 2016 1984–2011 retrospective cohort | Japan | NS | 7 | TCa 32 NS 22 mean:60.6 median:6.4y |
| Scuibba [52] | 2007 1993–2001 retrospective cohort | USA | Median: 13 m | 9 | BCa 87 NS 0 median: 53 median: 21 m |
| Walcott [53] | 2011 2001–2009 retrospective cohort | USA | NS | 7 | BCa 15 15 0 median: 58 median: 34.2 m |
| Tancioni [54] | 2011 2004–2009 retrospective cohort | Italy | Median:26 m | 8 | BCa 23 23 0 median:55 median:36 m |
| Zadnik [55] | 2014 2002–2011 retrospective cohort | USA | Median:18.3 m | 8 | BCa 43 NS 0 median: 56 median:26.8 m |
| Ulmar [56] | 2007 1984–2005 retrospective cohort | Germany | NS | 6 | RCC 37 20 84 median:64 mean:13.7 m |
| Jiang [57] | 2014 1999–2013 retrospective cohort | China | Mean:42.7 m | 7 | TCa 21 NS 24 median:62 NS |
| Oliveira [58] | 2015 2010–2013 retrospective cohort | Brazil | mean: 13.8 m | 7 | NI 68 45 66 mean:62.2 NS |
| Kataoka [59] | 2012 1990–2008 retrospective cohort | Japan | mean: 21 m | 9 | NI 143 NS 64 median:61 mean: 22 m |
| Aoude [60] | 2016 2003–2012 retrospective cohort | Canada | NS | 7 | NI 126 NS 44 mean:59.2 mean:27 m |
| Bartels [61] | 2007 1998–2005 retrospective cohort | Netherlands | NS | 7 | NI 219 185 58 mean:62.7 median:3 m |
| Lei [62] | 2016 2005–2015 retrospective cohort | China | mean: 11.5 m | 9 | NI 206 206 51 median:56 median:7.3 m |
| Chang [63] | 2001 1981–1997 retrospective cohort | China | NS | 7 | HCC 102 NS 93 mean:59.2 median:3 m |
| Chen [64] | 2010 2001–2007 retrospective cohort | China | NS | 7 | HCC 41 NS 78 mean:53.2 mean:10.4 m |
| Choi [65] | 2015 1992–2012 retrospective cohort | Korea | median:4.2 m | 9 | HCC 192 25 82 mean:56 median:4.5 m |
| Guo [66] | 2003 1996–1998 retrospective cohort | USA | NS | 6 | NI 60 60 NS NS median:4.1 m |
Participants’ characteristics
Of the 63 studies eligible for inclusion, 36 reported number of patients with MSCC before treatment, which added up to 5820 in 7212 patients (80.7%). Apart from 14 studies for prostate and breast cancer, 45 studies reported percentage of gender, with 4169 (59.5%) males and 2836 (40.5%) females included. An overall mean age of 4564 patients involved in the 31 studies was 61.9 years. Regarding the location of metastases, data was available in 36 studies containing 4046 patients, and maximum number of patients developed thoracic metastasis, followed by lumbar, cervical, thoracolumbar, diffused, cervicothoracic, lumbosacral and sacrum metastasis (Fig. 2b).

Therapeutic modality
Modality of therapy was available in 61 articles containing 10,004 patients (Fig. 2c). Patients predominantly received surgery or radiotherapy as major treatments. Surgery types mainly included 3324 decompression surgery with/without instrumented procedures, 108 total en bloc spondylectomy, 323 spinal fusion. Radiotherapy was performed in 5981 patients as major treatment. Other treatments, such as adjuvant therapies, radiotherapy,
chemotherapy, targeted therapy, immunotherapy, bisphosphonates, were provided alone or with various combination prior to or after major procedures.

**Follow-up and overall survival**

Data of follow-up was available in 27 studies, and 7 of them were followed for more than one year or until death. 7 were followed for an average period ranged 9.7–42.7 months and 10 were followed for a median period ranged 3.1–79.2 months. After treatment, the average survival time was ranged 6–27 months, and median survival time was ranged 3–77 months as reported in 8 and 42 studies respectively. Survival rates at 6, 12, 24, 36, 48 and 60 months for various types of primary tumors were calculated and presented in

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**Fig. 2**

(a) Number of studies and patients for each type of primary tumor; (b) Distribution of spinal metastatic location; diffused patients include those presented with three or four sections of spinal metastases; (c) Therapeutic modalities provided for patients; (d) Overall survival rate for primary tumor; (e) Prognostic effect of factors included in revised Tokuhashi Score. (Note: NI = not identified; PCa = prostate cancer; NSCLC = non-small cell lung cancer; BCa = breast cancer; RCC = renal cell cancer; HCC = hepatocellular carcinoma; TCa = thyroid cancer; LC = lung cancer; NPC = nasopharyngeal carcinoma; RT = radiotherapy; CMT = chemotherapy; HT = hormonal therapy; IT = immunotherapy; BP = bisphosphonates; EBRT = external-beam radiation therapy; SRS = stereotactic radiosurgery; RI = radioisotopes; DS = decompression surgery; SF = spinal fusion; TGT = targeted therapy; PS = performance status; met. = metastases; Neu. = neurological)
Fig. 2d. Overall, thyroid cancer had the highest survival rate, followed by prostate cancer/ breast cancer, renal cell cancer and mixed cancer, and non-small cell lung cancer and hepatocellular carcinoma lived for the shortest life span.

**Qualitative data summary on prognostic factors**
Numbers of studies that showed significance and non-significance for each prognostic factor are presented in Fig. 2e. Performance status was analyzed in 42 articles and 30 (71.4%) supported it as a significant factor. Prediction value of bone metastasis was involved in 35 studies, and 14 (40.0%) reported statistical significance. Number of involved vertebrae was analyzed in 44 studies, and 8 (18.2%) studies drew significant conclusions. As for visceral metastasis, 26 (63.4%) studies regarded it as a significant predictor.

**Quantitative data synthesis**
Prognostic effects of five factors (primary tumor type number of involved vertebrae and mixed cancer, and non-small cell lung cancer and hepatocellular carcinoma lived for the shortest life span.

**Table 3** Results of quantitative meta-analyses

| Prognostic factor                      | No. of studies | No. of patients | Pooled effect size (HR) | CI 95% | I² (%) | Effect model | Z test (P value) | Excluded studies by sensitivity analysis | Publication bias (P value) |
|----------------------------------------|----------------|-----------------|-------------------------|--------|--------|--------------|-----------------|------------------------------------------|--------------------------|
| KPS(10-40 VS.50-70) [9, 38, 71]        | 3              | 479             | 1.27                    | (0.89, 1.79) | 19.8 Fixed | 0.186³       | 0                            | 1.000                      | 0.188                   |
| KPS(10-40 VS.80-100) [11, 26, 38, 76] | 4              | 377             | 3.46                    | (1.83, 6.57) | 0.0 Fixed | < 0.001     | 3 [9, 71, 79] | 0.308                      | 0.404                   |
| KPS(50-70 VS.80-100) [26, 75, 78, 79] | 4              | 455             | 2.47                    | (1.83, 3.32) | 0.0 Fixed | < 0.001     | 0                            | 1.000                      | 0.834                   |
| KPS(10-70 VS.80-100) [30, 31, 32-35, 46] | 6             | 1307            | 1.94                    | (1.68, 2.25) | 7.0 Fixed | < 0.001     | 0                            | 0.133                      | 0.214                   |
| ECOC(1-2 VS.3–4) [19, 37, 40, 43, 64, 66, 75] | 7             | 887             | 2.22                    | (1.82, 2.71) | 23.0 Fixed | < 0.001     | 4 [29, 32, 60, 72] | 0.548                      | 0.345                   |
| Extraspinal bone metastases [9, 19, 26, 29, 32, 34, 38, 43, 47, 60, 70] | 11            | 3831            | 1.37                    | (1.23, 1.52) | 38.5 Fixed | < 0.001     | 0                            | 0.755                      | 0.819                   |
| No. of involved vertebrae (≥2 VS.1) [26, 34, 37, 41, 52, 60] | 6              | 450             | 1.22                    | (0.96, 1.56) | 31.9 Fixed | 0.102³      | 0                            | 1.000                      | 0.434                   |
| No. of involved vertebrae (≥3 VS.1–2) [8, 19, 29, 31, 38, 43, 53, 63, 75] | 9              | 1292            | 1.34                    | (1.17, 1.53) | 29.7 Fixed | < 0.001     | 0                            | 0.118                      | 0.046⁶                   |
| Visceral metastases [9, 19, 26, 30, 31, 33, 34, 38, 44, 46, 47, 52, 53, 56, 58, 60, 66, 76] | 18            | 1779            | 1.83                    | (1.59, 2.09) | 43.9 Fixed | < 0.001     | 7 [28, 29, 32, 33, 35, 43, 74, 72] | 0.880                      | 0.969                   |
| Ambulatory status [8, 19, 26, 28–32, 36, 37, 41, 43, 51, 53, 60, 63, 69, 71, 75] | 20            | 4456            | 1.80                    | (1.52, 2.13) | 52.8 Random | < 0.001     | 0                            | 0.922                      | 0.953                   |
| Frankel (C-D VS. E) [34, 46, 49, 53, 76] | 6              | 631             | 1.41                    | (1.10, 1.81) | 39.5 Fixed | 0.006       | 0                            | 0.707                      | 0.967                   |

Note: *Pooled effect sizes were considered to be non-significant statistically (P value was more than 0.05 by Z test); A significant publication bias was existed according to Egger’s test and the nonparametric trim and fill method was performed to rectify the bias.
is shown in Table 4. Patients with KPS 10–40/50–70 and patients with single/double involved vertebrae were merged together and the total score of the RTS was not changed which was added up to 15.

**Discussion**

The primary aim of the treatment on spinal metastasis is to attain the optimal relief on symptoms of MSCC (e.g., intractable pain and neurological deficit), restore or maintain spinal stability and improving the quality of life by various individualized therapeutic options. A number of prognostic scoring systems have been established to assist clinicians in predicting prognosis, such as Tokuhashi [3, 4], Tomita [6] and Enkaoua [82]. To achieve the optimal remission of symptoms, surgeons must consider patients’ life expectancy. However, most of the scores present sources of
Table 4 A remodified Version of Revised Tokuhashi Score

| System | Score |
|--------|-------|
| General condition (Karnofsky Performance Status, KPS)
  Poor and moderate (KPS 10–70) | 0 |
  Good (KPS 80–100) | 2 |
| Extraspinal bone metastases
  ≥3 | 0 |
  1–2 | 1 |
  0 | 2 |
| No. of metastases in the vertebral body
  ≥2 | 0 |
  1 | 2 |
| Metastases to the major internal organs
  Unremovable | 0 |
  Removable | 1 |
  No metastases | 2 |
| Primary site of the cancer
  Lung, osteosarcoma, stomach, bladder, esophagus, pancreas | 0 |
  Liver, gallbladder, unidentified | 1 |
  Others | 2 |
  Kidney, uterus | 3 |
  Rectum | 4 |
  Thyroid, breast, prostate, carcinoid tumor | 5 |
| Neurological Status
  Complete (Frankel A, B) | 0 |
  Incomplete (Frankel C, D) | 1 |
  None (Frankel E) | 2 |

Note: This remodified version of RTS was raised according to results in the meta-analyses and remodifications on the cut-off of KPS (a) and number of involved vertebrae (b) were conducted for the scoring system. The patients with KPS 10–40/50–70 and patients with single/double involved vertebrae were merged together.

In bias in patient selection and involve conflicting factors. According to RTS, performance status, bone metastasis, number of involved vertebrae, visceral metastasis, primary tumor and spinal cord palsy are significant to predict patients’ overall survival [3, 4]. Current study identified the role of factors included in RTS in predicting overall survival in patients with spinal metastases.

Prognostic effect of factors

General condition

Rades [43] compared overall survival of patients with Eastern Cooperative Oncology Group (ECOG) performance status 1–2 and 3–4, and the former group was presented with a significant higher survival. Van der Linden [9] and Bartels [62] also included performance status in their prognostic scores. Generally, patients with better performance status could tolerate more invasive therapeutic modalities, which would extend patients’ survival. However, some other studies did not consider performance status as a significant predictor. Leithner [26] supposed some other factors, such as arising of visceral metastasis and severe neurological deficit, would also make patients debilitated, and further decreased patients’ performance status, but these patients might be favourable in otherwise general condition to tolerate invasive therapy. In current study, performance status was identified to be a significant predictor for all except comparison between KPS 10–40 and 50–70 (P = 0.186). Thus, in general, performance status could be identified to be a reliable predictor. Similar to the results of the previous studies [9, 38, 71], we thought that the cut-off of KPS should not included KPS 10–40/50–70 as patients were both too debilitated to be cured from invasive therapies.

Extraspinal bone metastases and number of involved vertebrae

Rades [32] found that bone metastasis was significant in predicting prognosis of patients treated with radiotherapy. In study of Chong [31], patients with ≤2 column involved had a significant longer overall survival than the ones with >2 column involved. Generally, the two factors were often related to biological behaviour of invasion, spread and proliferation, which indicates advanced stages of cancer. In addition, added number of involved vertebrae would increase the difficulty of treatment and probability of occurrence of complications. Meanwhile, many studies presented non-significant results on prognosis effect of the two factors, such as van der Linden [9]. And Tomita Score adopted bone metastasis but not number of spinal metastases [6]. In current study, extraspinal bone metastases and number of involved vertebrae (≥3 VS. 1–2) were confirmed to be significant factors, but number of involved vertebrae (multiple VS. single) was of non-significance. Overall, we think that the two factors are reliable but the cut-off of number of involved vertebrae should not included single/multiple spinal metastases, and use of >1 vertebrae as cutoff is less effective for predicting survival than use of >2 vertebrae.

Visceral metastases

In scores of Tomita [6], van der Linden [9] and Enkaoua [82], visceral metastasis is included as a predictor. Rades [29] found that not only arising of visceral metastases with ≥2 sites had a poorer prognosis than arising of 0–1 site, patients with and without metastasis also had a diverse survival. Generally, visceral metastases is considered as a significant factor due to 3 reasons: (1) it is often related to an advanced stage of cancer; (2) it may increase number of complications; (3) it deliver more metastatic burden to patients than spinal metastasis. However, Bollen [35] found that visceral metastasis was not a significant factor for all but patients with favourable primary tumor types, and
patients with moderate and unfavourable profile of primary tumors were of very poor prognosis that prognostic effects of visceral metastases were weakened. Regardless of existed controversies, our meta-analysis identified visceral metastases as a significant predictor ($P < 0.001$).

**Histology of primary tumor**

As reported by Arrigo [28], primary tumor was a robust predictor in spinal metastasis. Yeung [80] also found that primary tumor types by RTS was a significant predictor overall. Nevertheless, a minority of studies presented a non-significance on the prognostic effect of primary tumor [19, 31, 36]. As reported in study of Lee [45], discrepancy of survival among different primary tumors were not significant. And they insisted that it's due to some advanced adjuvant therapeutic modalities that make patients with primary tumor of high malignancy lived a longer survival. In current study, we figured that thyroid cancer had the highest survival rate, followed by prostate/ breast cancer, renal cell cancer and mixed cancer, and non-small cell lung cancer and hepatocellular carcinoma lived for the shorted life span, which was in accordance with RTS [4].

**Neurological status**

Sioutos [5] and Enkaoua [82] included neurological deficit in their scores. Rades [22] and Tang [37] also accepted ambulatory status as a significant factor, since patients with neurological deficit might become too deteriorated to tolerate more aggressive surgical procedures and adjuvant therapies, and more severe complications would arise among paraplegic patients. However, there were also many studies that did not adopt neurological status as a predictor based on their cohorts such as Tomita Score [6]. They insisted that neurological deficit could be improved through appropriate treatment, which would bring about a longer survival. Van der Linden [9] speculated that symptom of myeloplegia could just reflect the location and volume of lesions but not the biological behaviour. In current study, both of ambulatory status and arising of neurological deficit before treatment were confirmed to be significant, which was in accordance with RTS [4].

**Remodification on the revised Tokuhashi score**

Tokuhashi Scoring was developed for the preoperative evaluation on the prognosis of metastatic spinal tumors and has been used clinically with minor revisions [3, 4]. For the revised score, consistency rate between the predicted prognosis from the criteria of the total scores and the actual survival was proved to be as high as 86.4% in the 118 patients evaluated prospectively after 1998 [4]. Yamashita [79] identified the relation between the revised Tokuhashi score and actual survival of 85 patients and found that actual survival matched the predicted survival in 67 (79%) of 85 patients. Thus, RTS was found to be very effective to predict survival. Nevertheless, some studies identified the RTS as a less predictive and practicable prognostic system [10, 83]. Gakhar [83] found that RTS was only significantly accurate in group of patients with expected survival of more than 12 months but not in groups with less than 1 months or between 6 to 12 months. According to current study, in general, factors of RTS were all valuable in predicting survival as many studies had verified [65, 71]. While more accurate prognosis may be obtained if remodifications were made on the cut-off of KPS and number of involved vertebrae were conducted for the scoring system in future. Considering the results of quantitative pooling, we thought that patients with KPS 10–40/50–70 and patients with single/double involved vertebrae should be merged together.

Though RTS was proved to be practicable and accurate for predicting the life expectancy of patients with spinal metastasis in plenty of former studies as well as the current study, it was also limited since it had only analyzed the prognostic effect of preoperative characteristics. The RTS has been used for a long term after it was first established in 1990 and revised in 2005. But to our knowledge, the significant predictors for spinal metastasis have been changed over the time, especially after some effective adjuvant interventions, such as target or chemical therapies have been applied to the clinical treatment. The patients’ life expectancy have been obviously altered in some specific tumor types in the recent years. For instance, after the introduction of the anti-VEGF antibody Bevacizumab combined with a Cisplatin-containing regimen was used in nonsquamous NSCLC, and the patients’ progression-free survival was significantly improved [82]. In the study of Horn et al., [83] it was also demonstrated that Bevacizumab (more than 14 months) significantly improved the overall survival of patients with adenocarcinoma compared standard therapy (10 months). Hence, apart from the factors that has been involved in the RTS, we propose establishing new scores or new revisions on RTS in the future to sufficiently consider the effect of modern therapeutic modalities, which would further increase the accuracy and prognostic capacity on predicting the patients’ survival.

**Limitations of this study**

Our study nonetheless has limitations. Firstly, primary articles included were published with design of retrospective cohorts dominantly, and only an average value of 7.8 ± 1.0 stars for NOS was presented which would cause some potential bias. It may be due to few prospective cohort studies have been carried out till now. Anyhow, majority of studies were of an acceptable quality and none was showed to be with high risk of bias (NOS ≤ 5 stars). Secondly, the studies included in this work lacked information on either one or more RTS parameter(s) as few studies had completely
contained and reported the data about each of the parameter, which would lead to an inevitable bias. What’s more, current study could only evaluate and verify the prognostic effects of the factors in Tokuhashi Score, but we did not assess the accuracy of predicted survival time for patients with various levels of Tokuhashi scores.

**Conclusion**

Factors included in RTS were all significant on prognostic predicting for patients with spinal metastasis and should be considered when choosing the appropriate treatment modality. What’s more, we believe that more accurate prognosis may be obtained by merging patients with KPS 10–40/KPS 50–70 and patients with single/double involved vertebrae together. Using the modified RTS, patients present with a low score are predicted to live a short period and some palliative therapies should be applied, while patients should be treated with invasive procedures when present with a high RTS score. Additionally, we suggest that more sufficiently considering on the effect of modern therapies is necessary for developing new scores in the future, as adjuvant interventions have significantly altered the patients’ life expectancy in the recent years.

**Additional file**

Additional file 1: Appendix 1. Searching strategies used for the literature retrieving. (DOCX 13 kb)

**Abbreviations**

CI: confidence interval; ECOG: Eastern Cooperative Oncology Group; HR: hazard ratio; MSCC: metastatic spinal cord compression; NOS: the Newcastle-Ottawa Scale; PS: performance status; RTS: revised Tokuhashi Score

**Acknowledgments**

Not applicable.

**Funding**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Availability of data and materials**

The authors declare that all the data supporting the findings of this study are available within the article and its supplementary information files.

**Authors’ contributions**

XYG: methodology, validation, formal analysis, investigation, data curation, writing-original draft, writing-reviewing and editing, project administration. LDX: investigation, writing-reviewing and editing. HJC: conceptualization, methodology, validation, investigation, writing-reviewing and editing. LYH: methodology, validation, investigation, writing-reviewing and editing. WJF: conceptualization, methodology and validation. JFT: formal analysis, investigation and data curation. HKC: writing original draft. YL: writing-reviewing and editing. ZH: validation and investigation. XM: project administration, supervision. ZHR: investigation and data curation. All authors read and approved the final manuscript.

**Ethics approval and consent to participate**

Not applicable.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

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Received: 18 April 2018 Accepted: 27 November 2018

Published online: 13 December 2018

**References**

1. Byrne TN. Spinal cord compression from epidural metastases. N Engl J Med. 1992;327:614–9.
2. Jacobs WB, Perrin RG. Evaluation and treatment of spinal metastases: an overview. Neurosurg Focus. 2001;11:e10.
3. Tokuhashi Y, Matsuaki H, Tomyama S, Kawano H, Ohnaka S. Scoring system for the preoperative evaluation of metastatic spine tumor prognosis. Spine. 1990;15:1110–3.
4. Tokuhashi Y, Matsuaki H, Oda H, Oshima M, Ryu J. A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. Spine. 2005;30:2186–91.
5. Sioutos PJ, Arbab E, Meshualam CF, Galicich JH. Spinal metastases from solid tumors. Analysis of factors affecting survival. Cancer. 1995;76:61453–9.
6. Tomita K, Kawahara N, Kobayashi T, et al. Surgical strategy for spinal metastases. Spine (Phila Pa 1976). 2001;26(3):298–306.
7. Bauer HC, Wedin R. Survival after surgery for spinal and extremity metastases. Prognostic factors in 241 patients. Acta Orthop Scand. 1995;66:143–6.
8. North RB, Larocca VR, Schwartz J, et al. Surgical management of spinal metastases: analysis of prognostic factors during a 10-year experience. J Neurosurg. Spine. 2005;2:564–73.
9. Van der Linden YM, Dijkstra SP, Vonk EJ, et al. Prediction of survival in patients with metastases in the spinal column. Results based on a randomized trial of radiotherapy. Cancer. 2005;103:320–8.
10. Quraishi NA, Manoharan SR, Arealis G, et al. Accuracy of the revised Tokuhashi score in predicting survival in patients with metastatic spinal cord compression (MSCC). Eur Spine J. 2013;22(Suppl 1):S21–6.
11. Pointillart V, Vital JM, Salimi R, et al. Survival prognostic factors and clinical outcomes in patients with spinal metastases. J Cancer Res Clin Oncol. 2011; 137(5):849–56.
12. Wells GA, Shea B, O’Connell D et al. Newcastle-Ottawa Quality Assessment scale Cohort Studies. 2012. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
13. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ. 2003;327:557–60.
14. Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315:629–34.
15. Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics. 2000;56:455–63.
16. Lei M, Liu Y, Yan L, et al. A validated preoperative score predicting survival and functional outcome in lung cancer patients operated with posterior decompression and stabilization for metastatic spinal cord compression. Eur Spine J. 2016;25(12):3971–8.
17. Lei M, Liu Y, Liu S, et al. Individual strategy for lung cancer patients with metastatic spinal cord compression. Eur Spine J. 2016;25(5):728–34.
18. Lei M, Liu Y, Tang C, et al. Prediction of survival prognosis after surgery in patients with symptomatic metastatic spinal cord compression from non-small cell lung cancer. BMC Cancer. 2015;15:853.
19. Rades D, Hutenlocher S, Evers JN, et al. Do elderly patients benefit from surgery in addition to radiotherapy for treatment of metastatic spinal cord compression. Strahlenether Onkol. 2012;188(5):424–30.
20. Rades D, Hutenlocher S, Bajoivoic A, et al. Surgery followed by radiotherapy versus radiotherapy alone for metastatic spinal cord compression from unfavorable tumors. Int J Radiat Oncol Biol Phys. 2011;81(5):e861–8.
21. Rades D, Weber A, Karstens JH, et al. Number of extraspinal organs with metastases: a prognostic factor of survival in patients with metastatic spinal...
cord compression (MSCC) from non-small cell lung cancer (NSCLC). Anticancer Res. 2014;34(5):2503–7.
22. Rades D, Fehlauer F, Schulte R, et al. Prognostic factors for local control and survival after radiotherapy of metastatic spinal cord compression. J Clin Oncol. 2006;24(21):3388–93.
23. Patchell R, Tibbs PA, Regine WF, et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. Lancet. 2005;366:643–8.
24. Chen YJ, Chang GC, Chen HT, et al. Surgical results of metastatic spinal cord compression secondary to non-small cell lung cancer. Spine (Phila Pa 1976). 2002;31(15):E413–8.
25. Leitner A, Radl R, Gruber G, et al. Predictive value of seven preoperative prognostic scoring systems for spinal metastases. Eur Spine J. 2008;17(1):1488–95.
26. Park JH, Rhim SC, Jeon SR. Efficacy of decompression and fixation for metastatic spinal cord compression: analysis of factors prognostic for survival and postoperative ambulation. J Korean Neurosurg Soc. 2011;50(3):343–40.
27. Arting RT, Kalaniithi P, Cheng J, et al. Predictors of survival after surgical treatment of spinal metastases. Neurosurgery. 2011;68(3):674–81 discussion 681.
28. Rades D, Douglas S, Venenga T, et al. Metastatic spinal cord compression in non-small cell lung cancer patients. Prognostic factors in a series of 356 patients. Strahlenther Onkol. 2012;188(6):472–6.
29. Crnalic S, Löfvenberg R, Bergh A, et al. Predicting survival for surgery of metastatic spinal cord compression in prostate cancer: a new score. Spine (Phila Pa 1976). 2012;37(28):2168–76.
30. Leithner A, Radl R, Gruber G, et al. Predictive value of seven preoperative prognostic scoring systems for spinal metastases. Eur Spine J. 2013;22(4):657–66 discussion 666.
31. Bakker NA, Coppes MH, Vergeer RA, et al. Surgery on spinal epidural metastases (SEM) in renal cell carcinoma: a plea for a new paradigm. Spine J. 2014;14(9):2038–41.
32. Böllert L, van der Linden YM, Pondwaq W, et al. Prognostic factors associated with survival in patients with symptomatic spinal bone metastases: a retrospective cohort study of 1,943 patients. Neuro-Oncology. 2014;16(7):901–8.
33. Vanek P, Bradac O, Trebicky F, et al. Influence of the preoperative neurological status on survival after the surgical treatment of symptomatic spinal metastases with spinal cord compression. Spine (Phila Pa 1976). 2015;40(23):1824–30.
34. Tang Y, Qu J, Wu J, et al. Metastatic spinal cord compression from non-small-cell lung cancer treated with surgery and adjuvant therapies: a retrospective analysis of outcomes and prognostic factors in 116 patients. J Bone Joint Surg Am. 2015;97(17):1418–25.
35. Chen YJ, Chen HT, Hsu HC. Preoperative palsy score has no significant association with survival in non-small cell lung cancer patients with spinal metastases who undergo spinal surgery. J Orth Surg Res. 2015;10:149.
36. Meng T, Chen R, Zhong N, et al. Factors associated with improved survival following surgical treatment for metastatic prostate cancer in the spine: retrospective analysis of 29 patients in a single center. World J Surg Oncol. 2016;14(1):200.
37. Park SJ, Lee CS, Chung SS. Surgical results of metastatic spinal cord compression (MSCC) from non-small cell lung cancer (NSCLC): analysis of functional outcome, survival time, and complication. Spine J. 2016;16(3):322–8.
38. Huddart RA, Rajan B, Law M, et al. Spinal cord compression in prostate cancer: treatment outcome and prognostic factors. Radiother Oncol. 1997;44(3):229–36.
39. Williams BJ, Fox BD, Scibilla DM, et al. Surgical management of prostate cancer metastatic to the spine. J Neurosurg Spine. 2009;10(5):414–22.
40. Rades D, Douglas S, Venenga T, et al. A survival score for patients with metastatic spinal cord compression from prostate cancer. Strahlenther Onkol. 2012;188(9):802–6.
41. Crnalic S, Hildingsson C, Wikström P, et al. Outcome after surgery for metastatic spinal cord compression in 54 patients with prostate cancer. Acta Orthop. 2012;83(1):180–6.
42. Lee BH, Park JO, Kim HS, et al. Perioperative complication and surgical outcome in patients with spine metastases: retrospective 200-case series in a single institute. Clin Neurol Neurosurg. 2014;122:80–6.
43. Sellin JN, Suki D, Harsh V, et al. Factors affecting survival in 43 consecutive patients after surgery for spinal metastases from thyroid carcinoma. J Neurosurg Spine. 2015;23(4):419–28.
44. Drzymalski DM, Oh WK, Werner L, et al. Predictors of survival in patients with prostate cancer and spinal metastasis. Presented at the 2009 joint spine section meeting. Clinical article. J Neurosurg Spine. 2010;13(6):789–94.
45. Tancioni F, Navaria P, Pessina F, et al. Assessment of prognostic factors in patients with metastatic epidural spinal cord compression (MESC) from solid tumor after surgery plus radiotherapy: a single institution experience. Eur Spine J. 2012;21(Suppl 1):S146–8.
46. Tsatsis CE, Suki D, Rao G, et al. Factors affecting survival in 267 consecutive patients undergoing surgery for spinal metastasis from renal cell carcinoma. J Neurosurg Spine. 2014;20(1):1108–16.
47. Pettex RJ, Spitz SM, Goodwin CR, et al. Factors associated with improved survival following surgery for renal cell carcinoma spinal metastases. Neurosurg Focus. 2016;41(2):E3.
48. Rades D, Janssens S, Kästmann L, et al. Outcomes after irradiation of epidural spinal cord compression due to metastatic thyroid Cancer. Anticancer Res. 2016;36(4):2035–9.
49. Kato S, Murakami H, Demura S, et al. The impact of complete surgical resection of spinal metastases on the survival of patients with thyroid cancer. Cancer Med. 2016;5(9):2343–9.
50. Schubba DM, Gokaslan ZL, Suk I et al. Positive and negative prognostic variables for patients undergoing spine surgery for metastatic breast cancer: the Tokuhashi score. Spine J. 2017;17(10):1659–66. Epub. 2017 May 8.
51. Walcott BP, Cveticanovich GL, Barnard ZR, et al. Surgical treatment and outcomes of metastatic breast cancer to the spine. J Clin Neurosci. 2011; 18(10):1336–9.
52. Tancioni F, Navaria P, Mancouo P, et al. Surgery followed by radiotherapy for the treatment of metastatic epidural spinal cord compression from breast cancer. Spine (Phila Pa 1976). 2011;36(20):E152–9.
53. Zadrk P, Hwang L, Ju DG, et al. Prolonged survival following aggressive treatment for metastatic breast cancer in the spine. Clin Exp Metastasis. 2011;31(1):47–55.
54. Ullman B, Naumann M, Catkalaya S et al. Prognosis scores of Tokuhashi and Tomita for patients with spinal metastases of renal cancer. Ann Surg Oncol 2006 14(2):998–1004. Epub. 2006 Nov 3.
55. Jiang L, Ouyang H, Liu X, et al. Surgical treatment of 21 patients with spinal metastases of differentiated thyroid cancer. Chin Med J. 2014; 127(23):4092–6.
56. Oliveira MF, Rotta JM, Botelho RV. Survival analysis in patients with metastatic spinal disease: the influence of surgery, histology, clinical and neurologic status. Arq Neuropsiquiatr. 2015;73(4):330–5.
57. Kataoka M, Kurisada T, Taniaka M et al. Statistical analysis of prognostic factors for survival in patients with metastatic disease. Spine J. 2016;16(3):213–9.
58. Aoode A, Forth M, Aldebeyan S, et al. The revised Tokuhashi score: analysis of parameters and assessment of its accuracy in determining survival in patient afflicted with spinal metastasis. Eur Spine J. 2018;27(4):835–840.
59. Bartels RH, Feuth T, van der Maazen R, et al. Development of a model with which to predict the life expectancy of patients with spinal epidural metastasis. Cancer. 2007;110(9):2042–9.
60. Lei M, Liu J, Liu Y, et al. Who are the best candidates for decompressive surgery and spine stabilization in patients with metastatic spinal cord compression? Spine (Phila Pa 1976). 2016;41(18):1469–76.
61. Chang SS, Luo JC, Chao Y, et al. The clinical features and prognostic factors of hepatocellular carcinoma patients with spinal metastasis. Eur J Gastroenterol Hepatol. 2001;13(1):1341–5.
62. Chen H, Xiao J, Yang X, et al. Preoperative scoring systems and prognostic factors for patients with spinal metastases from hepatocellular carcinoma. Spine (Phila Pa 1976). 2010;35(23):E1339–46.
63. Choi C, Seong J. Predictive factors of palliative radiotherapy response and survival in patients with spinal epidural metastasis. Cancer. 2007;110(9):2042–9.
64. Moon KY, Chung CK, Jahng TA, et al. Postoperative survival and ambulatory outcome in metastatic spinal tumours: prognostic factor analysis. J Korean Neurosurg Soc. 2011;50(3):216–23.
68. Yang SB, Cho W, Chang UK. Analysis of prognostic factors relating to postoperative survival in spinal metastases. J Korean Neurosurg Soc. 2012; 51(3):27–34.
69. Helweg-Larsen S, Serensen PS, Kreiner S. Prognostic factors in metastatic spinal cord compression: a prospective study using multivariate analysis of variables influencing survival and gait function in 153 patients. Int J Radiat Oncol Biol Phys. 2000;46(3):1163–9.
70. Kumar N, Tan JI, Zaw AS, et al. Evaluation of scoring systems and prognostic factors in patients with spinal metastases from nasopharyngeal carcinoma. Spine J. 2014;14(12):2946–53.
71. Mizumoto M, Harada H, Asakura H, et al. Prognostic factors and a scoring system for survival after radiotherapy for metastases to the spinal column: a review of 544 patients at Shizuoka Cancer center hospital. Cancer. 2008; 113(10):2816–22.
72. Ogihara S, Seichi A, Hozumi T, et al. Prognostic factors for patients with spinal metastases from lung cancer. Spine (Phila Pa 1976). 2006;31(14):1585–90.
73. Rades D, Veninga T, Stalpers LJ, et al. Prognostic factors predicting functional outcomes, recurrence-free survival, and overall survival after radiotherapy for metastatic spinal cord compression in breast cancer patients. Int J Radiat Oncol Biol Phys. 2006;64(1):182–8.
74. Switlyk MD, Kongsgaard U, Skjeldal S, et al. Prognostic factors in patients with symptomatic spinal metastases and normal neurological function. Clin Oncol (R Coll Radiol). 2015;27(4):213–21.
75. Tao HM, Ye ZM, Yang DS, et al. Risk factors and prognosis of surgery for spinal metastasis. Zhonghua Zhong Liu Za Zhi. 2004;26(4):226–30.
76. Weber A, Bartscht T, Karstens JH, et al. Breast cancer patients with metastatic spinal cord compression: Number of extraspinal organs involved by metastases influences survival. Strahlenther Onkol. 2013;1–4.
77. Yamashita T, Siemenson KB, Mroz TE, et al. A prospective analysis of prognostic factors in patients with spinal metastases: use of the revised Tokuhashi score. Spine (Phila Pa 1976). 2011;36(11):910–7.
78. Yeung YN, Cheung KK, Lam TC, et al. A study of the predictive value of the modified Tokuhashi score in metastatic spinal tumour causing cord compression in a southern Chinese population. J Orthop, Trauma Rehabil. 2014;1–7.
79. Zhang D, Xu W, Liu T, et al. Surgery and prognostic factors of patients with epidural spinal cord compression caused by hepatocellular carcinoma metastases: retrospective study of 36 patients in a single center. Spine (Phila Pa 1976). 2013;38(17):E1090–5.
80. Enkaoua EA, Doursounian L, Chatellier G, et al. Vertebral metastases: a critical appreciation of the preoperative prognostic tokuhashi score in a series of 71 cases. Spine (Phila Pa 1976). 1997;22(19):2293–8.
81. Gakhar H, Swamy GN, Bommireddy R, et al. A study investigating the validity of modified Tokuhashi score to decide surgical intervention in patients with metastatic spinal cancer. Eur Spine J. 2013;22(3):565–8.
82. Sandler A, Gray R, Perry MC, et al. Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer. N Engl J Med. 2006;355(24):2542–50.
83. Horn L, Sandler A. Epidermal growth factor receptor inhibitors and antiangiogenic agents for the treatment of non-small cell lung cancer. Clin Cancer Res. 2009;15(16):5040–8.

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