Surgical Oncology 27 (2018) 7–10

Contents lists available at ScienceDirect

Surgical Oncology

journal homepage: www.elsevier.com/locate/suronc

Prediction of survival in patients with symptomatic spinal metastases: Comparison between the Tokuhashi score and expert oncologists

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ARTICLE INFO

Article history:
Received 21 April 2017
Received in revised form
16 May 2017
Accepted 1 November 2017

Keywords:
Survival prediction
Spinal metastases
Multidisciplinary

ABSTRACT

Background: Existing scoring systems have suboptimal accuracy in prognosticating patients with spinal metastases. Currently, there is no superior method in predicting survival. This study aims to compare the accuracy of survival prediction by expert oncologists versus the revised Tokuhashi scores with actual survivals in a cohort of symptomatic spinal metastases patients.

Methods: All patients who underwent surgical treatment for metastatic spinal tumours in a tertiary hospital between January 2011 to December 2015 were reviewed. Each patient's data was reconstructed into an anonymised clinical scenario and presented independently to five blinded attending oncologists with at least three years' post fellowship experience. They were surveyed for survival prediction twice at no less than four weeks' interval apart; the test-retest reliability was examined. The agreement of their prognostication and modified Tokuhashi scores were compared with actual survivals.

Results: Fifty-five patients were included during the study period. The mean age at presentation was 61.1 years (range, 41 to 79), and mean actual survival was 21.6 months (range, 1 to 68). Cohen's kappa agreement with actual survival was higher by oncologists' estimation (0.52) than by revised Tokuhashi score prediction (0.31) ($p = 0.018$). Intra-class correlation showed high inter-reliability (0.71) between the five oncologists and a high test-retest reliability (0.69) between both rounds of the survey.

Conclusion: This study showed that expert oncologists provided more accurate survival prediction than revised Tokuhashi scores in patients with spinal metastases. Future studies are required to identify factors in their assessment that led to improved accuracy.

1. Introduction

Surgical treatment, in combination with radiotherapy and chemotherapy, has been shown to improve outcome such as survival and neurological status in patients with spinal metastases [1–4]. However, because surgeries for this group of patients are associated with significant morbidity and mortality [5,6], only those patients whose anticipated improvement in quality of life outweighs the potential risks are considered for surgical intervention. Careful consideration of the life expectancy is key in the decision-making.

Several scoring systems have been proposed to predict survival time in patients with spinal metastases [7–10], amongst which the revised Tokuhashi score is the most widely used [8,11]. When Tokuhashi first published the results of his scoring system in 2005, the predictive value reached 82.5% [8], and became invaluable in surgical decision-making and informed consent [12]. However, with the advancement of cancer treatment in the modern era, particularly in patients where targeted therapies are available, life expectancy has improved significantly compared with the original cohort of study participants from the 1990s. Accordingly, the accuracy of the revised Tokuhashi score in predicting survival has deteriorated with time. Using more recent cohorts of patients with specific primary tumour groups, it has been found that this scoring system is now suboptimal in predicting survivals [13–19]. Nonetheless, no superior method in determining survival in this group of patients has been proposed.

The aim of this study was to assess the accuracy of

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https://doi.org/10.1016/j.suronc.2017.11.001
0960-7404/

prognostication by five blinded attending oncologists and the revised Tokuhashi score compared with actual survivals in patients with spinal metastases.

2. Materials and methods

A retrospective review of all consecutive patients who underwent spinal metastasis surgery at a tertiary referral centre in Hong Kong between 2011 and 2015 was conducted. Inclusion criteria were established metastatic spinal disease at the time of surgery or confirmed postoperatively, and complete follow-up data. Exclusion criteria were primary spinal tumour and patients younger than 18 years of age. This study was approved by our local institutional review board.

The following data for each patient were recorded: age and gender, circumstances of spinal metastasis diagnosis, details of primary tumour if known including time of diagnosis, site, histological type, biomarkers, previous course of treatment, imaging findings, variables needed to compute the revised Tokuhashi scores, indications for surgery, details of surgical treatment, and survival data.

Each patient's data was reconstructed into an anonymised clinical scenario simulating a discussion in a multidisciplinary team meeting for spinal tumour. The scenario included the following categories of information according to the NOMS framework [20].

1) N - Neurological/functional assessment – Frankel grading of spinal cord function and Bilsky's grading of epidural spinal cord compression
2) O - Oncological assessment – primary type, histological subtype and molecular biomarkers (including EGFR/ALK mutation status of CA lung, hormonal and Her2 profile of breast cancer)
3) M - Mechanical assessment: Spinal instability neoplastic score (SINS)
4) S - Systemic assessment: serum albumin level, significant comorbidities, extra-osseous metastases status, the extent of metastases (oligometastases versus wide spread metastases), brain metastases status, the duration and types of systemic treatments used before the episode, the date of the diagnosis of metastases and the date of diagnosis of the most recent disease progression

The scenarios were presented independently to five blinded attending oncologists with at least three years' post fellowship experience. They were surveyed for survival prediction in three categories: less than six months, between six and twelve months, and more than twelve months. These same oncologists were surveyed again in no less than four weeks' interval apart with the same clinical scenarios randomised in a different order. Their predictions and the revised Tokuhashi score were compared with actual survivals.

Descriptive statistics of mean ± standard deviation (SD) were presented for continuous variables and n (%) for categorical variables. The level of agreement between actual survival and predicted survival was evaluated by computing Cohen's kappa coefficient (K). Furthermore, we computed Krippendorff's alpha coefficient (α) to measure the inter-rater agreement among the oncologists [21], and the test-retest reliability of the two rounds of oncologists' estimation was determined by intra-class correlation coefficient (ICC) using a 2-way random-effects ANOVA model and the absolute agreement definition [22,23]. ICC values ranging 0.6–0.74 and above 0.75 were considered as good and excellent reliability, respectively [24]. We implemented bootstrapping with 1000 replications to estimate the medians and the corresponding 95% confidence interval (CI). All statistical analyses were performed using R version 3.3 and statistical tests with $p < 0.05$ were considered as significant.

3. Results

Fifty-five patients fulfilled the inclusion criteria during the study period, and thirty-seven cases had complete clinical and follow-up data for analysis. There were thirteen females, and twenty-four males, with a mean age of 61.1 years (range, 41 to 70) at the time of surgery. The primary sites of tumour at presentation were lung, breast, kidney, prostate, liver, haematological, miscellaneous, and unknown origin (see Table 1). Indications for surgical intervention included metastatic spinal cord compression, spinal instability, and intractable back pain non-responsive to conservative treatment. Surgical procedures performed included open posterior decompression with internal fixation, anterior column reconstruction, and percutaneous posterior internal fixation.

Overall mean survival was 21.6 months (range, 1 to 68). Table 2 reports observed and survivals predicted by the revised Tokuhashi score. Observed median survival in the 0–8, 9–11, and 12–15 Tokuhashi score groups was 10.5 (range, 1 to 36) months, 11.5 (1–67) months and 36 (16–68) months, respectively. Survival differed significantly across the three groups ($p < 0.003$). Table 3 reports observed and survivals predicted by the five blinded attending oncologists.

The weighted K computed to assess agreement between survival predicted by the Tokuhashi score and observed survival was 0.31 (95% CI, 0.09–0.56), and that for the oncologists' estimation was 0.52 (95% CI, 0.31–0.72). According to Landis and Koch [25], this K value indicates fair agreement for the revised Tokuhashi scores, and moderate agreement for the oncologists' estimation. The difference in agreement between the two estimation methods reached statistical significance ($p = 0.018$).

The Krippendorff's alpha coefficient, which was used to assess the interobserver reliability among the five oncologists, was 0.71 (0.59–0.83), meaning there was good agreement between observers. The overall test-retest reliability of the oncologists as assessed by the ICC was 0.69 (0.59–0.78), suggesting there was fair reliability between the first and second rounds of the evaluation.

Table 4 shows the weighted K values and the ICCs (95% CI) for test-retest reliability for each oncologist in the first and second rounds of prediction.

4. Discussion

Surgical intervention followed by radiotherapy can improve ambulatory status and survival and is cost-effective in selected patients with spinal metastases [26–28]. However, correct patient selection is essential as surgery still carries significant risks and morbidities. Central to this decision process is accurate prediction of the patient's life expectancy, as it is generally accepted that patients with less than 3 months' survival may not benefit from decompressive surgery [3]. Despite its significance, survival prediction in patients with spinal metastases is still variable with numerous scoring systems proposed, including Bauer, Tokuhashi, Tomita, van der Linden and Sioutos [29]. Amongst them, the revised Tokuhashi score is the most commonly used, but its validity as a single tool in survival prediction is called into question. Recent publications applying the revised Tokuhashi scores to predict survival showed accuracy as low as 9.1% [18,19]. This has significant implications in daily clinical practice as predicted survival is one of the most important parameters that helps to guide the treatment in this group of patients. An improved tool has yet to be proposed.

There are two main types of survival predictions: temporal (the patient will live a certain amount of time) and probabilistic (the