

Time to Surgical Treatment for Metastatic Spinal Disease: Identification of Delay Intervals

Global Spine Journal
2023, Vol. 13(2) 316–323
© The Author(s) 2021
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/2192568221994787
journals.sagepub.com/home/gsj



Floris R. van Tol, MD¹, Anne L. Versteeg, MD, PhD^{2,3},
Helena M. Verkooijen, MD, PhD⁴, F. Cumhur Öner, MD, PhD¹,
and Jorrit-J Verlaan, MD, PhD¹

Abstract

Study Design: Retrospective cohort study

Objectives: Minimizing delays in referral, diagnosis and treatment of patients with symptomatic spinal metastases is important for optimal treatment outcomes. The primary objective of this study was to investigate several forms of delay from the onset of symptoms until surgical treatment of spinal metastases for patients with and without a known preexisting malignancy.

Methods: All patients receiving surgical treatment for spinal metastases in a single tertiary spine center were identified. Referral patterns were reconstructed and the total delay was divided into 4 categories: patient delay (onset of symptoms until medical consultation), diagnostic delay (medical consultation until diagnosis), referral delay (diagnosis until referral to spine surgeon) and treatment delay (referral spine to surgeon until treatment). These intervals were compared between patients with and without a known preexisting malignancy.

Results: The median total delay was 99 days, patient delay 19 days, diagnostic delay 21,5 days, referral delay 7 days, treatment delay 8 days and diagnosis and treatment delay combined 18,5 days. No difference in total delay was observed between patients with and without a known preexisting malignancy. Total delay was not significantly associated with patient age, sex, oncological history, tumor prognosis and spinal level of the tumor.

Conclusions: Patients with symptomatic spinal metastases experience considerable delays, even after metastatic spinal disease has been diagnosed, regardless of a preexisting malignancy. By identifying and eliminating the causes of these delays, diagnosis, referral and treatment may be expedited leading to improved patient outcome.

Keywords

tumor, tumors, metastases

Introduction

Metastatic spinal disease is one of the most debilitating complications of cancer. The incidence of spinal metastases, currently affecting approximately 20% of all oncological patients, is increasing rapidly due to improvements in palliative cancer care.^{1–4} One of the most important factors for achieving satisfactory treatment outcome is timely recognition of symptomatic spinal metastases.⁵ Previous studies have shown that delayed treatment is associated with both unfavorable surgical outcomes, including increased amounts of blood loss, longer operating times, and a higher incidence of complications, and unfavorable long-term clinical outcomes such as poor functional performance, impaired quality of life, and

¹ Department of Orthopedic Surgery, University Medical Center Utrecht, The Netherlands

² Department of Radiation Oncology, University Medical Center Utrecht, The Netherlands

³ University of Toronto, Canada

⁴ Division of Imaging and Oncology, University Medical Center Utrecht, The Netherlands

Corresponding Author:

Jorrit J. Verlaan, Department of Orthopedics, University Medical Center Utrecht, P.O. Box 85500 (G05.228), 3508 GA Utrecht, The Netherlands.
Email: j.j.verlaan@umcutrecht.nl



Creative Commons Non Commercial No Derivs CC BY-NC-ND: This article is distributed under the terms of the Creative Commons Attribution-Non Commercial-NoDerivs 4.0 License (<https://creativecommons.org/licenses/by-nc-nd/4.0/>) which permits non-commercial use, reproduction and distribution of the work as published without adaptation or alteration, without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).

reduced survival.^{6,7} Reducing delays in referral, diagnosis and definitive treatment of patients with spinal metastases may therefore improve patient outcome considerably.⁸

In principle all neurologic injuries caused by spinal metastases in patients with known malignancies could be viewed as potentially preventable complications. To identify targets for reducing delays in referrals of patients with spinal metastases, an understanding of the referral patterns is required. Previous studies have analyzed referral patterns in patients with spinal metastases, however these studies were limited to patients with symptomatic metastatic spinal cord compression (MSCC).⁹⁻¹⁴ Analyzing referral patterns in patients with MSCC may yield a skewed representation, because the onset of MSCC is generally regarded as a medical emergency accelerating the referral process substantially. Secondly, spinal metastases should preferably be identified long before the onset of MSCC. To better understand referral patterns of patients with symptomatic spinal metastases it is essential to also analyze patients without neurological symptoms who require (surgical) treatment. Moreover, the absence or presence of a preexisting malignancy will doubtlessly play a meaningful role in the risk assessment for metastatic spinal disease and the subsequent referral patterns, warranting separate analysis for these 2 patient groups. Lastly, no prior study has continued referral pattern analysis after the diagnosis was made. It might be possible that substantial delays still occur after the diagnosis but prior to treatment.

The primary objective of this study was to reconstruct referral patterns in patients surgically treated for symptomatic spinal metastases and to assess the total delay experienced from onset of symptoms until the initiation of treatment. As a secondary objective, we aimed to investigate the relative contribution of different types of delay to the total experienced delay and compare these separate intervals between patients with and without a known preexisting malignancy.

Methods

All patients who received surgical treatment for spinal metastases between March 2009 and January 2019 in a single tertiary spine center (in The Netherlands) were eligible for inclusion. Patients with spinal tumors from hematological malignancies were also eligible due to the broad similarities in clinical presentation and surgical treatment compared to spinal metastases originating from solid tumors. The ethics review board (METC Utrecht, protocol no. 17-695/C) approved a waiver of informed consent for this observational, retrospective cohort study.

Indications for surgical intervention included intractable pain, mechanical instability or neurological deficits. Patients with a life expectancy of at least 3 months were deemed eligible for surgical treatment.¹⁵ All treating spine surgeons adhered to generally accepted principles for surgical treatment of patients with spinal metastases, combining common scoring systems (currently NOMS: ASIA/Frankel classification for neurological status combined with Bilsky score for degree of epidural compression; Bollen classification for prognosis; SINS for spinal stability and KPS for general patient

condition).¹⁵⁻¹⁷ Furthermore, a uniform treatment strategy was achieved by a weekly multidisciplinary “spine meeting” between spine surgeons and radiation oncologists. Demographic data, tumor histology, EQ-5D score, Karnofsky Performance Score, VAS-pain score, neurological status, the presence of other metastases and the number of affected spinal levels were collected. The clinical profile of the primary tumor was classified as favorable, moderate or unfavorable, based on up-to-date median overall survival, similar to the biological tumor profile used by the Bollen classification.¹⁸

For each patient, the referral timeline was reconstructed from the onset of first symptoms (probably) caused by the spinal metastases until definitive treatment using data from the patients’ electronic medical records. For any previously diagnosed malignancy, the date of diagnosis, histological type and preexisting presence of spinal metastases were collected. Hereafter, the onset and type of the presenting symptom(s) and the date the patient first contacted any health-care provider were noted. For each health-care provider involved in the referral pattern the following parameters were extracted separately: date of consultation, medical specialty, type of care (*i.e.* primary, secondary or tertiary), the neurological status (Frankel-score) and ambulatory state (5-point Likert scale from fully ambulant to bedridden), date of diagnosis of spinal metastases (if applicable) and in case of a referral, the date, medical specialty and type of care (*i.e.* primary, secondary or tertiary) of the specialty referred to.

The overall delay throughout the referral pattern was divided into 4 distinct intervals: patient delay, diagnostic delay, referral delay and treatment delay. Patient delay was defined as the time between the onset of first symptoms caused by the spinal metastases (*i.e.* new back pain or neurological symptoms) and the first time a patient contacted any health-care provider for these symptoms. Diagnostic delay was defined as the time between the first time the patient contacted any health-care provider and the diagnosis of metastatic spinal disease. Referral delay was defined as the time between the diagnosis of metastatic spinal disease and referral to the spine surgeon. Treatment delay was defined as the time between referral to the spine surgeon and surgical treatment of the patient. The referral patterns were reconstructed using the hospital’s electronic health-records. In case of missing data, the patients’ general practitioners were contacted by phone to complete the referral patterns. It is mandatory for all health care providers in the Netherlands to provide the family doctor with a report of any medical consultation performed. Therefore, health records possessed by the general practitioner could be used for additional reconstruction of the referral patterns.

Due to the retrospective nature of this study, the exact date of a particular event (*e.g.* the onset of symptoms, a medical consultation, a referral date etc.) could not always be retrieved reliably. In the case where an approximation was written down (*i.e.* “several days,” “last year” etc.) decision rules were developed to allow for consistent date approximation. These decision rules, along with other general considerations on how to interpret incomplete data, were described in a Standard

Operating Procedure (SOP) to promote data consistency. The SOP provided decision rules on quantifying date approximations such as “several days” or “3–4 months,” how to handle missing data (e.g. when no onset of complaints could be found, the onset of complaints should be synchronized with the first visit to a health-care provider) and a data extraction format.

Preoperative baseline parameters were compared between patients with and without a previously known malignancy. Patient delay, diagnostic delay, referral delay, treatment delay and total delay were extracted from the reconstructed referral patterns and compared between patients with and without a known malignancy.

Statistical Analysis

For continuous data, means, standard deviations (SD) and, in the case of non-normally distributed data, medians and interquartile range (IQR) were used. For categorical data frequencies were used. To compare the 2 patient groups (presence vs absence of a known preexisting malignancy) at baseline, unpaired t-tests were used for continuous data and Chi-squared tests for categorical data. To compare the different delay intervals, unpaired t-tests were used. Because most of the intervals were left-skewed, log-transformed values were used for these t-tests. To independently analyze prognostic factors for the total delay, a multivariable linear regression analysis was used with total experienced delay as the dependent parameter. In the case of continuous independent parameters, a regular regression coefficient was presented. In the case of categorical independent parameters, a reference category was chosen and each non-reference category received its own coefficient in relation to the reference category. Significance for all tests was accepted at $P < 0.05$. All analyses were performed using IBM SPSS Statistics for Macintosh, Version 24.0 (Armonk, NY: IBM Corp).

Results

In total, 307 patients, including 175 patients without a known preexisting malignancy and 132 patients with a known malignancy were included in the analyses (Figure 1). No differences were observed between the 2 groups at the time of treatment in terms of mean patient age (62.0 vs 61.8 years), EQ-5D score (0.38 vs 0.36), median Karnofsky Performance Score (KPS 70 vs 70), the presence of other metastases (28.2% vs 27.9%), and the number of affected levels (one affected level in 47.1% vs 47.3%). The percentage of males was significantly lower in patients with a known preexisting malignancy (47.1% vs 62.8%). Furthermore, breast cancer was more prevalent in patients with a known malignancy (27.6% vs 7.0%) and lung cancer (9.2% vs 20.2%) and hematological malignancies (8.6% vs 41.1%) in patients without a known malignancy. Mainly due to the high prevalence of hematological malignancies, the biological tumor favorability was higher in patients without a previously known malignancy. In patients with a known

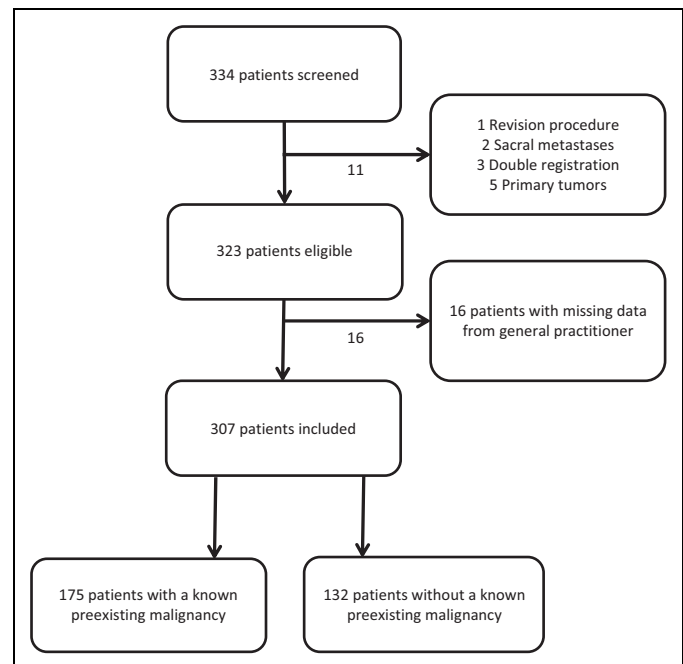


Figure 1. Flowchart of patient inclusion. The inclusion of all eligible patients followed by the 3 Categorization into 2 separate groups: 1) Patients with a known preexisting malignancy and 4 2) patients without a known preexisting malignancy.

malignancy, significantly less patients had sensorimotor disturbances (Frankel A-D, 31.5% vs 46.5%) (Table 1).

Delay Intervals

Overall, patients had a median total delay of 99 days (14 weeks) from the onset of symptoms associated with spinal metastases, until definitive treatment. Overall, median patient delay was 19 days, diagnostic delay 21,5 days, referral delay 7 days and treatment delay 8 days. The median for referral and treatment delay combined was 18,5 days (Figure 2). Comparing patients with and without a known malignancy, median patient delay was 14 vs 25 days ($P = 0.001$), diagnostic delay 15 vs 34 days ($P = 0.002$), referral delay 9,5 vs 4 days ($P < 0.001$), treatment delay 11 vs 5 days ($P < 0.001$), referral and treatment delay combined 21 vs 13 days (0.834) and total delay 99 vs 99,5 days ($P = 0.077$) (Figure 3). Multivariable linear regression analysis showed that total delay was not significantly associated with patient age, sex, oncological history, spinal level of the tumor and tumor prognosis (Table 2).

Discussion

In the current study, referral patterns of 307 patients surgically treated for symptomatic spinal metastases were reconstructed and subsequently analyzed. The median total delay (representing the time from first symptoms until definitive treatment) for all patients was more than 3 months (99 days). According to our results patient delay is only the second largest contributor to total delay, as considerable delays also occur while patients

Table 1. Pre-Treatment Baseline Characteristics for Patients With and Without a Preexisting Malignancy.

	Known preexisting malignancy n = 175	Unknown preexisting malignancy n = 132	P-value
Mean age, years (SD)	62.0 (11.9)	61.8 (11.6)	0.910
Gender, male (%)	82 (47.1%)	81 (62.8%)	0.007
Tumor Histology, n (%)			<0.001
Breast	48 (27.6%)	9 (7.0%)	
Gastrointestinal	16 (9.2%)	5 (3.9%)	
Lung	16 (9.2%)	26 (20.2%)	
Hematological malignancy	15 (8.6%)	53 (41.1%)	
Prostate	17 (9.8%)	13 (10.1%)	
Renal	23 (13.3%)	10 (7.8%)	
Other	25 (14.3%)	6 (4.5%)	
Unknown	12 (6.9%)	4 (3.1%)	
Tumor favorability, n (%)			<0.001
Favorable	23 (13.5%)	53 (42.4%)	
Moderate	74 (43.3%)	24 (19.2%)	
Unfavorable	74 (43.3%)	48 (38.4%)	
EQ5D, mean (SD)	0.38 (0.32)	0.36 (0.30)	0.565
KPS, median* (IQR)	70 (50-80)	70 (50-80)	0.882
VAS pain, mean (SD)	5.2 (2.4)	4.5 (2.5)	0.022
Frankel on entry, n (%)			0.035
A	0	2 (1.6%)	
B	4 (2.3%)	3 (2.3%)	
C	12 (6.9%)	15 (11.6%)	
D	37 (21.3%)	40 (31.0%)	
E	121 (69.5%)	69 (53.5%)	
Mobility on entry, n (%)			0.062
Normal	108 (62.1%)	68 (52.7%)	
Uses one crutch	3 (1.7%)	0	
Uses walker or 2 crutches	11 (6.3%)	10 (7.8%)	
Confined to wheelchair	12 (6.9%)	5 (3.4%)	
Confined to bed	40 (23.0%)	46 (35.7%)	
Other metastases, n (%)			0.961
Yes	49 (28.2%)	36 (27.9%)	
No	125 (71.8%)	93 (72.1%)	
Spinal level n (%)			0.129
Cervical	13 (8.1%)	12 (11.1%)	
Cervicothoracic	10 (6.2%)	8 (7.4%)	
Thoracic	66 (41.0%)	50 (46.3%)	
Thoracolumbar	20 (12.4%)	12 (11.1%)	
Lumbar	39 (24.2%)	16 (14.8%)	
Diffuse	13 (8.1%)	10 (9.3%)	
Number of affected levels n (%)			0.678
1	82 (47.1%)	61 (47.3%)	
2	31 (18.8%)	19 (14.7%)	
3	24 (13.8%)	15 (11.6%)	
≥4	37 (21.3%)	35 (26.4%)	

*Karnofsky Performance Score.

are under medical attention throughout the ensuing referral chain. A previously known malignancy was associated with shorter patient and diagnostic delay, however longer referral and treatment delay, resulting in a total delay comparable to patients without a previously known malignancy. In other words, oncological patients developing new back pain do not

seem to advance faster through the overall referral chain than patients without a preexisting cancer diagnosis, suggesting a paucity in awareness or sense of urgency for metastatic spinal disease in known oncological patients among Dutch health-care providers. As has been shown in previous studies, earlier treatment will likely result in patients being more fit for (surgical) intervention, ultimately leading to better patient outcome.^{6,7,19} The data presented in this study provides several targets for minimizing delay in patients with spinal metastases, thereby potentially enhancing the clinical outlook for better pre- and postoperative status.

Non-malignant back pain is one of the most prevalent conditions in middle-aged people and commonly regarded as self-limiting.²⁰ Symptoms caused by spinal metastases are generally difficult to distinguish from symptoms caused by non-malignant back pain and are therefore often subjected to a wait-and-see policy.²¹ Consequently, patients with spinal metastases are at risk for delays in their diagnosis, referral and treatment, particularly in the absence of a previously diagnosed malignancy.^{22,23} The incidence of malignant spinal disease in all patients with lower back pain is described to be as low as 0.7%.²⁴ However, in 4.9% of all patients with compression fractures the fracture is of a pathological nature.²⁵ In specialized spine centers, 5.9% of patients presenting with non-mechanical back pain without movement restrictions are subsequently diagnosed with metastatic disease.²⁶ Specifically in oncological patients, an estimated 92.5% of pain complaints is related to tumor involvement.²⁷ A previous study analyzing oncological patients with new onset back pain found that 60% of patients without abnormalities on neurological examination still showed radiologic evidence of spinal metastases.²⁸ Consequently, even though the incidence of metastatic spinal disease in the general population is relatively low, the incidence increases as patients enter hospital care, particularly in those patients who are already known to have a malignancy. It is important for health care providers in secondary and tertiary care to acknowledge the relatively high prevalence of metastatic spinal disease among patients with back pain.

In our study, the overall delay for all patients was 99 days from the onset of symptoms until treatment, which is slightly longer than overall delays described in studies performed by Husband⁹ (75 days) and Levack et al.¹⁰ (90 days). In the current study patients without MSCC at the time of treatment were also included, in contrast to Levack et al. and Husband, who included only patients with MSCC. The referral process is often accelerated after the onset of neurological deficits, commonly regarded as a medical emergency, explaining the longer total delay in patients presenting without neurological deficits. In our study, a median patient delay of 19 days was observed, which is similar to the median patient delay of 18 days observed by Levack et al.¹⁰ Another study investigating time to radiotherapeutic treatment showed that patient delay was the biggest contributor (64%) to a total delay of 12 days.¹⁴ In a study by Guzik, patients noticing a decline in their neurological status still showed a mean patient delay of 4 days from the onset of neurological deterioration.¹³ Patient delay may be

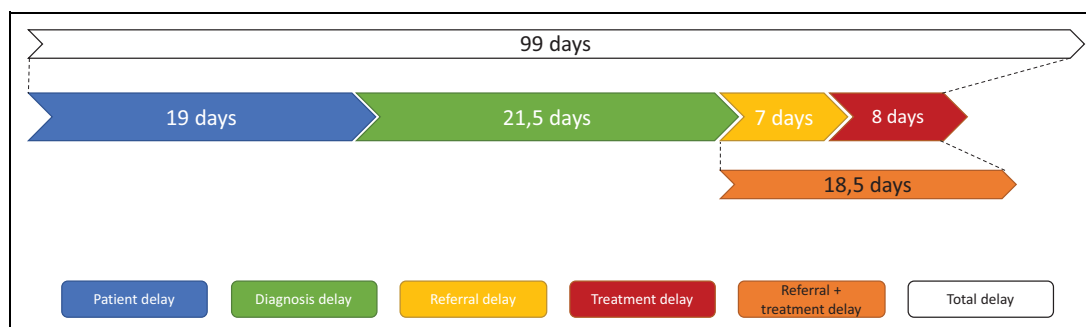


Figure 2. Delay intervals for all patients. Median number of days of patient delay (onset of symptoms to medical consultation), diagnostic delay (medical consultation to diagnosis), referral delay (diagnosis to referral spine surgeon), treatment delay (referral spine surgeon to treatment), referral and treatment delay combined and total delay.

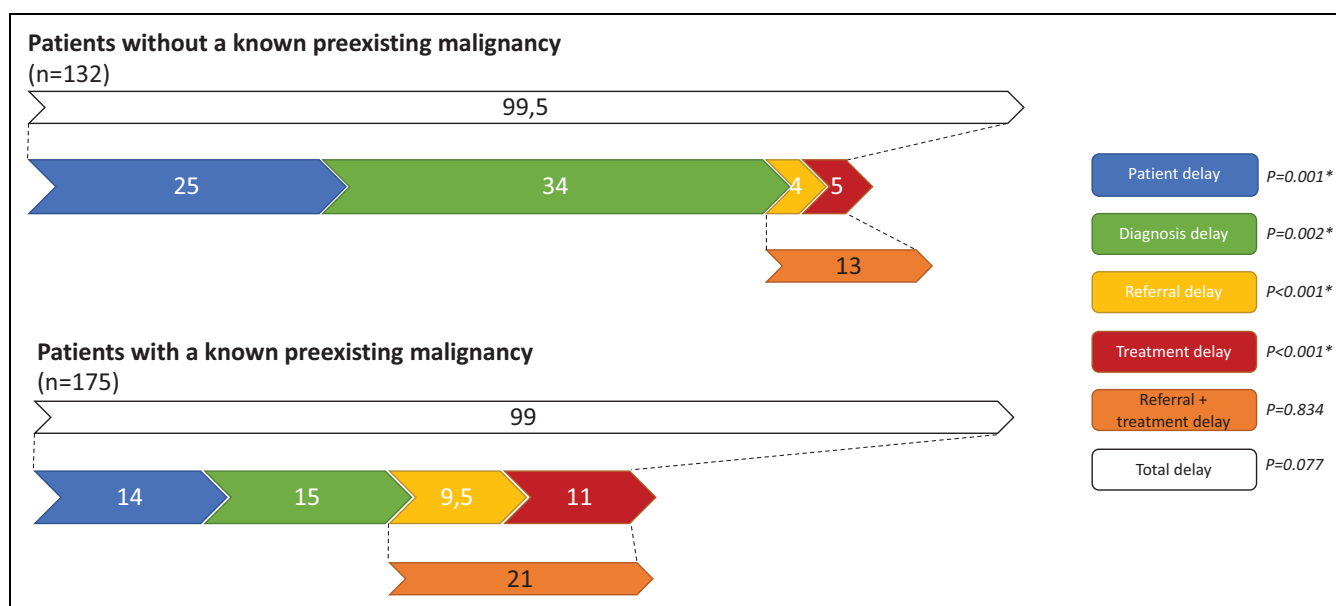


Figure 3. Delay intervals for patients with and without a known preexisting malignancy. Median number of days of patient delay (onset of symptoms to medical consultation), diagnostic delay (medical consultation to diagnosis), referral delay (diagnosis to referral spine surgeon), treatment delay (referral spine surgeon to treatment), referral and treatment delay combined and total delay for patients with and without a preexisting malignancy.

reduced by patient education or self-assessment tools, however this will always remain a challenge, especially in patients unaware or in repudiation of any underlying malignancy. In the current study, the largest contributor to total delay was diagnostic delay with a median of 21.5 days, slightly longer than the previously reported 15 days by Levack et al.¹⁰ Another study by Bach et al. showed that even after presentation with symptoms indicative of MSCC, patients still experienced a mean diagnostic delay of 23 days.²⁹ Timely diagnosis remains a significant challenge in patients with spinal metastases, apparently even in the presence of progressive neurological symptoms. Nonetheless, timely treatment is largely dependent on timely diagnosis, making diagnostic delay one of the most important targets for optimization and shortening of the referral chain. For example, educating general practitioners and/or other health-care providers on the importance of red flags, especially a preexisting

cancer diagnosis, when assessing patients with back pain or lowering MRI/CT thresholds for oncological patients with back pain may lead to a reduction in diagnostic delay.

This is the first study to separately analyze delays in the referral chain after the diagnosis of metastatic spinal disease and treatment. After patients were diagnosed, a median of 7 days was required for the patients to be referred to their definitive caregiver (in the current study: a spine surgeon), and another 8 days from referral until the initiation of treatment. In many cases, symptomatic spinal metastases require radiotherapeutic or surgical treatment which are commonly performed in specialized, tertiary care centers. Therefore, non-specialized (oncological) health-care providers may not always be familiar with the management of metastatic spinal disease and may not be aware of the preferred treatment regimen (*i.e.* systemic, radiotherapeutic, or surgical interventions),

Table 2. Multivariate Linear Regression Analysis for Total Experienced Delay.

		Delay Days (CI)	n = 254 P value
Intercept		85,6 (−7,6 to 178,9)	0.072
Age		0,5 (−0,7 to 1,8)	0.381
Sex	Female	Reference	
	Male	−15,9 (−44,5 to 12,6)	0.275
Oncological history	No preexisting malignancy	Reference	
	Preexisting malignancy	−10,5 (−40,5 to 19,9)	0.499
Level spinal tumor	Cervical	Reference	
	Cervicothoracic	68,7 (−1,5 to 138,9)	0.055
	Thoracic	−11,1 (−59,6 to 37,4)	0.654
	Thoracolumbar	−13,5 (−72,7 to 45,8)	0.656
	Lumbar	22,6 (−30,8 to 75,9)	0.407
Tumor prognosis	Diffuse	19,8 (−48,3 to 88,0)	0.568
	Favorable	Reference	
	Moderate	27,5 (−12,3 to 67,3)	0.175
	Unfavorable	8,7 (−27,1 to 44,4)	0.635

resulting in delayed and/or erroneous referrals and treatment. In the past decade, the introduction of referral tools such as the Spinal Instability Neoplastic Score (SINS) have demonstrated to assist health-care providers in adequately referring patients after diagnosis of metastatic spinal disease.^{30,31} Nonetheless, this study shows that further reductions in referral delay could be possible to further expedite treatment. Educational initiatives in a catchment area, aimed at increasing awareness and expertise on the treatment of metastatic spinal disease among the involved health-care providers, along with referral tools such as the SINS may play a vital role in optimizing referral chains.

In our study, 43% of the patients did not have a previously known malignancy, which is comparable to the 34% and the 40% reported by Husband and Levack et al., respectively. We observed no difference in total delay between patients with and without a known malignancy. In contrast, Levack et al. and Husband found a median total delay of 49 days and 60 days, respectively, for patients with a known malignancy and both studies showed a total delay of 90 days for patients without a previously diagnosed malignancy.^{9,10} Similarly, in the current study, patient delay and diagnostic delay were significantly shorter if the patient already was previously diagnosed with a malignancy. This is in line with a study by Mitera and Loblaw, where median delay from the onset of symptoms until radiotherapeutic treatment was 5.5 days for patients who suspected a relationship between the symptoms and their oncological history and 17 days for those who did not.¹⁴ As opposed to our hypothesis, median referral and treatment delay were significantly longer in patients with a known malignancy. A potential explanation for this difference can be found in previous studies showing that metachronous metastases are histologically less aggressive than synchronous metastases. As a consequence, patients with a known malignancy may be less susceptible to the occurrence of acute MSCC and subsequent acceleration of

treatment.³² Moreover, in patients with a known malignancy may be considered less alarming to be diagnosed with metastases compared with patients who were previously presumed healthy being diagnosed with malignant, metastatic disease, leading to faster referral and treatment in the latter category.

In a previous study, the mean time from the onset of symptoms until neurological deficits has been described to be as little as 7 weeks.³³ This finding clearly emphasizes the need for rapid diagnosis, referral and treatment for patients with metastatic spinal disease. Delaying treatment will increase the risk for emergency surgery, which is associated with inferior outcome, however is still preferred over postponed surgery in an emergency situation.^{34,35} In case of neurological deterioration, emergency surgery is commonly preferred within 24–48 hours to maximize the chances of neurological recovery or prevent further neurological deterioration.³⁶ This however jeopardizes the ability for health-care providers to perform an adequate work-up of patients and may lead to overtreatment of patients with unfavorable prognoses.¹⁹ Previous studies have emphasized the potential improvement of patient outcome by enhancing patient pathways.⁸ Health-care providers early in the referral chain are at a unique and high-leverage position to prevent complications and improve patient outcome by early detection and referral.³⁰

This study has several limitations. Firstly, our study included only patients who were surgically treated and not patients who underwent only radiotherapeutic or systemic tumor treatment. Because surgical patients generally have more severe or more advanced metastatic spinal disease, this may bias our results toward shorter delay intervals. Nonetheless, in the literature all previous studies have focused only on patients with MSCC. Therefore, the current study is still the best available representation of typical referral patterns in patients with spinal metastases and provides a good starting point for identifying targets in the referral chain to reduce delays with the goal to improve clinical outcome for these patients. Future studies should aim to also include non-surgically treated patients to get an even more comprehensive overview of referral patterns in patients with spinal metastases. Secondly, due to the retrospective nature of this study, not all delay intervals could be fully reconstructed without the occasional approximation of the timing of certain events throughout the referral patterns. Nonetheless, each approximation is based on the same set of decision rules as was carefully noted in an SOP. Therefore, the authors are convinced that the results from the current study were not grossly biased by the retrospective nature of this study. Lastly, the current study does not identify actual causes of the occurring delays. Future studies should use the current results as guidance to identify and address specific causes of these delay intervals, thereby expediting treatment of metastatic spinal disease.

Conclusion

In conclusion, patients with symptomatic spinal metastases experience considerable delays, even after the diagnosis of

metastatic spinal disease is established. Educating health-care providers on the urgency of treatment for metastatic spinal disease and equipping them with efficient referral tools to stimulate appropriate referrals may lead to a reduction in referral delay. Moreover, although patients with a known malignancy experience shorter patient and diagnostic delays, they also experience longer referral and treatment delays. Therefore, no differences in total delay between patients with and without a previously known malignancy were observed. Increasing awareness on the importance of a patient's oncological history in the case of back pain may also lead to a reduction in diagnostic delay. By reducing the mean total delay experienced by all patients with metastatic spinal disease, the proportion of patients with complications such as neurological deficits should decrease, thereby promoting overall patient outcome.

Nonetheless, further research is still needed to gain a more in-depth understanding of the actual causes of the delays as described in the current study. By targeting these causes, the total time to treatment can be reduced substantially, leading to improved treatment outcome for patients with symptomatic spinal metastases.

Acknowledgment

The authors would like to thank DePuy Synthes for providing the educational grant for the current study.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The current work was funded with an educational grant from DePuy Synthes.

ORCID iD

Floris R. van Tol  <https://orcid.org/0000-0003-4703-8885>

References

- Hatrick NC, Lucas JD, Timothy AR, Smith MA. The surgical treatment of metastatic disease of the spine. *Radiother Oncol*. 2000;56(3):335-339. <http://www.ncbi.nlm.nih.gov/pubmed/10974383>.
- Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. *CA Cancer J Clin*. 2017;67(1):7-30. doi:10.3322/caac.21387
- Walsh GL, Gokaslan ZL, McCutcheon IE, et al. Anterior approaches to the thoracic spine in patients with cancer: indications and results. *Ann Thorac Surg*. 1997;64(6):1611-1618. doi:10.1016/S0003-4975(97)01034-5
- Cobb III CA, Leavens ME, Eckles N. Indications for nonoperative treatment of spinal cord compression due to breast cancer. *J Neurosurg*. 1977;47(5):653-658.
- Brodowicz T, Hadji P, Niepel D, Diel I. Early identification and intervention matters: a comprehensive review of current evidence and recommendations for the monitoring of bone health in patients with cancer. *Cancer Treat Rev*. 2017;61:23-34. doi:10.1016/j.ctrv.2017.09.008
- van Tol FR, Suijkerbuijk KPM, Choi D, Verkooijen HM, Oner FC, Verlaan JJ. The importance of timely treatment for quality of life and survival in patients with symptomatic spinal metastases. *Eur Spine J*. 2020;29(12):3170-3178. doi:10.1007/s00586-020-06599-x
- van Tol FR, Choi D, Verkooijen HM, Oner FC, Verlaan JJ. Delayed presentation to a spine surgeon is the strongest predictor of poor postoperative outcome in patients surgically treated for symptomatic spinal metastases. *Spine J*. 2019;19(9):1540-1547. doi:10.1016/j.spinee.2019.04.011
- Savage P, Sharkey R, Kua T, et al. Malignant spinal cord compression: NICE guidance, improvements and challenges. *QJM*. 2014;107(4):277-282. doi:10.1093/qjmed/hct244
- Husband DJ. Malignant spinal cord compression: prospective study of delays in referral and treatment. *BMJ*. 1998;317(7150):18-21. doi:10.1136/bmj.317.7150.18
- Levack P, Graham J, Collie D, et al. Don't wait for a sensory level—Listen to the symptoms: a prospective audit of the delays in diagnosis of malignant cord compression. *Clin Oncol*. 2002;14(6):472-480. doi:10.1053/clon.2002.0098
- Lee KM, Loh Y, Shakespeare T, et al. Metastatic spinal cord compression as an oncology emergency—getting our act together. *Int J Qual Heal Care*. 2007;19(6):377-381. doi:10.1093/intqhc/mzm043
- Tsukada Y, Nakamura N, Ohde S, Akahane K, Sekiguchi K, Terahara A. Factors that delay treatment of symptomatic metastatic extradural spinal cord compression. *J Palliat Med*. 2014;18(2):107-113. doi:10.1089/jpm.2014.0099
- Guzik G. Analysis of factors delaying the surgical treatment of patients with neurological deficits in the course of spinal metastatic disease. *BMC Palliat Care*. 2018;17(1):1-6. doi:10.1186/s12904-018-0295-3
- Mitera G, Loblaw A. Delays from symptom onset to treatment in malignant spinal cord compression: quantification and effect on pre-treatment neurological status. *J Clin Oncol*. 2017;22(14 suppl):8276-8276. doi:10.1200/jco.2004.22.90140.8276
- Fisher CG, Andersson GBJ, Weinstein JN. Spine focus issue. Summary of management recommendations in spine oncology. *Spine (Phila Pa 1976)*. 2009;34(22 suppl):S2-S6. doi:10.1097/BRS.0b013e3181baae29
- Versteeg AL, Verlaan J-J, Sahgal A, et al. The spinal instability neoplastic score impact on oncologic decision-making. *Spine (Phila Pa 1976)*. 2016;41(suppl 20):S231-S237. doi:10.1097/BRS.0000000000001822
- Laufer I, Rubin DG, Lis E, et al. The NOMS framework: approach to the treatment of spinal metastatic tumors. *Oncologist*. 2013;18(6):744-751. doi:10.1634/theoncologist.2012-0293
- Bollen L, van der Linden YM, Pondaag W, et al. Prognostic factors associated with survival in patients with symptomatic spinal bone metastases: a retrospective cohort study of 1,043 patients. *Neuro Oncol*. 2014;16(7):991-998. doi:10.1093/neuonc/not318
- Verlaan JJ, Choi D, Versteeg A, et al. Characteristics of patients who survived <, 3 months or >2 years after surgery for spinal

- metastases: can we avoid inappropriate patient selection? *J Clin Oncol*. 2016;34(25):3054-3061. doi:10.1200/JCO.2015.65.1497
20. Woolf AD, Pfleger B. Burden of major musculoskeletal conditions. *Bull World Health Organ*. 2003;81(9):646-656.
21. Al-Qurainy R, Collis E. Metastatic spinal cord compression: diagnosis and management. *BMJ*. 2016;2539:i2539. doi:10.1136/bmj.i2539
22. Hoy D, March L, Brooks P, et al. The global burden of low back pain: estimates from the global burden of disease 2010 study. *Ann Rheum Dis*. 2014;73(6):968-974. doi:10.1136/annrheumdis-2013-204428
23. Vos T, Barber RM, Bell B, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the global burden of disease study 2013. *Lancet*. 2015;386(9995):743-800. doi:10.1016/S0140-6736(15)60692-4
24. Jarvik JG, Deyo RA. Diagnostic evaluation of low back pain with emphasis on imaging. *Ann Intern Med*. 2002;137(7):586-597.
25. Hansen EJ, Simony A, Carreon L, Andersen MO. Rate of unsuspected malignancy in patients with vertebral compression fracture undergoing percutaneous vertebroplasty. *Spine (Phila Pa 1976)*. 2016;41(6):549-552. doi:10.1097/BRS.0000000000001270
26. Cook C, Ross MD, Isaacs R, Hegedus E. Investigation of non-mechanical findings during spinal movement screening for identifying and/or ruling out metastatic cancer. *Pain Pract*. 2012;12(6):426-433. doi:10.1111/j.1533-2500.2011.00519.x
27. Caraceni A, Portenoy RK, Force T. An international survey of cancer pain characteristics and syndromes. IASP Task Force on Cancer Pain. International Association for the Study of Pain. *Pain*. 1999;82(3):263-274.
28. Rodichok LD, Harper GR, Ruckdeschel JC, et al. Early diagnosis of spinal epidural metastases. *Am J Med*. 1981;70(6):1181-1188. doi:10.1016/0002-9343(81)90825-1
29. Bach F, Larsen BH, Rohde K, et al. Metastatic spinal cord compression. *Acta Neurochir (Wien)*. 1990;107(1):37-43. doi:10.1007/BF01402610
30. Kronisch C, Balagué F, Dudler J. Fear of impending fractures: when to refer? A case-based review. *Clin Rheumatol*. 2015;34(7):1303-1309. doi:10.1007/s10067-013-2461-6
31. Versteeg AL, van der Velden JM, Verkooijen HM, et al. The effect of introducing the spinal instability neoplastic score in routine clinical practice for patients with spinal metastases. *Oncologist*. 2016;21(1):95-101. doi:10.1634/theoncologist.2015-0266
32. Bu-Ali H, Solh M, Kapur A, Mittal V. Receptor characteristics of the second tumor in synchronous versus metachronous breast cancer. *Am Surg*. 2008;74(8):702-706. doi:10.1200/jco.2008.26.15_suppl.1107
33. Kienstra GE, Terwee CB, Dekker FW, et al. Prediction of spinal epidural metastases. *Arch Neurol*. 2000;57(5):690-695. <http://www.ncbi.nlm.nih.gov/pubmed/10815135>.
34. Debono B, Braticovic C, Sabatier P, Dutertre G, Latorzeff I, Hamel O. The "Friday peak" in surgical referrals for spinal metastases: lessons not learned. A retrospective analysis of 201 consecutive cases at a tertiary center. *Acta Neurochir (Wien)*. 2019;161(6):1069-1076. doi:10.1007/s00701-019-03919-z
35. Lo WY, Yang SH. Metastatic spinal cord compression (MSCC) treated with palliative decompression: surgical timing and survival rate. *PLoS One*. 2017;12(12):1-16. doi:10.1371/journal.pone.0190342
36. Quraishi NA, Rajagopal TS, Manoharan SR, Elsayed S, Edwards KL, Boszczyk BM. Effect of timing of surgery on neurological outcome and survival in metastatic spinal cord compression. *Eur Spine J*. 2013;22(6):1383-1388. doi:10.1007/s00586-012-2635-y