Spinal metastasis with neurologic deficits

Outcome of late surgery in patients primarily deemed not suitable for surgery

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Background and purpose — A significant number of patients with spinal metastases are treated non-surgically, but may need surgical treatment at a later stage due to progression of symptoms. Therefore, we investigated the need for late surgical decompression in patients with spinal metastasis who were initially deemed as non-surgical candidates, as well as the outcome of late surgery.

Patients and methods — 116 patients who were referred to the orthopedic oncology department between 2002 and 2011 due to spinal metastasis with neurologic symptoms were deemed to be non-surgical candidates. The primary reason was minor neurologic deficits in 40 patients (M) and short survival (S) in 76 patients.

Results — 8 patients underwent a late operation due to progression of the neurologic symptoms, all of them belonged to group M. M-patients with a modified Bauer score of less than 2 had both an inferior survival as well as a higher risk for late surgery. Postoperative improvement in neurologic function was noted in 5/8 operated patients, whilst 2 patients had stationary symptoms and 1 deteriorated.

Interpretation — The need for late surgery arises in a minority of patients with spinal metastasis primarily treated non-surgically, and only in patients with minor neurologic compromise rather than poor general condition. An established prognostic score (modified Bauer) can be used to guide decision-making. Late surgical decompression is effective in restoring the neurologic status

Radiotherapy has been the standard treatment for decades in cases of neurologic deficits due to spinal metastasis (SM) as early studies did not show any benefit of surgery (Young et al. 1980, Dea and Fisher 2014). There has been a shift in the management of SM in the past 20 years, since data from both retrospective and prospective studies have demonstrated a superior outcome of combined surgical decompression and radiotherapy as compared with radiotherapy only (Sundaresan et al. 1995, Harrington 1997, Patchell et al. 2005, Falicov et al. 2006, Ibrahim et al. 2008, Quan et al. 2011).

However, surgical treatment is not offered to all patients. Surgery is generally not justified in patients with short expected survival, although it is hard to define who is terminally ill. Some may even overcome a period of poor condition due to optimal supportive care. Some SM patients have a favorable oncological prognosis due to modern treatment but present with minor neurologic deficits. Thus, there may be a progression of the neurologic symptoms of SM patients initially regarded as non-candidates for surgery. It is unknown how many of these patients need to undergo late surgery, if there are any factors associated with a higher risk for late surgery, and whether the outcome of this intervention is comparable to that of primary decompression. We investigated the incidence and outcome of late surgical decompression in 116 consecutive patients who were referred to our tertiary center with a query regarding surgical intervention due to SM with neurologic deficits, but were initially not operated on.

Patients and methods

We reviewed the prospectively collected database of our department and identified 360 patients between 2002 and 2011 who were referred with a query regarding their suitability for surgery because of SM with neurologic deficits. Of these, 116 (81 male) were deemed as inappropriate for surgery. Our primary indication for surgery is significant neurologic deficits (Jansson and Bauer 2006), but factors such as the condition of the patient, expected survival, and the number of lumbar levels

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engaged by the tumor, as well as the expected morbidity of surgical decompression, are also taken into account. Decision was individualized and taken by 1 or more senior grade consultants with informed consent of the patient, relying on clinical judgment rather than the use of a formal scoring system with exact predetermined criteria. The decision not to operate was mainly based on the absence of significant neurologic compromise, i.e. Frankel D or near normal neurology, despite a good prognosis in 40 (34%) patients (minor neurology, group M). Short expected survival and poor overall condition, multi-level tumor, or a combination of the above was noted in 76 (66%) patients (short-survival group S).

Mean age at referral was 68 (28–89) years and mean follow-up was 15 months. At last follow-up 3 patients were still alive. The majority of patients in the S-group (n = 34) had prostate cancer, whereas 12 had lung cancer, 7 breast cancer, 5 renal cancer, and 18 had other malignancies. In the M-group, 15 patients had prostate cancer, 6 myeloma, 4 breast cancer, 3 lung cancer, and 2 had other malignancies. 94 patients presented with compression of the thoracic spine, 19 of the lumbar, and 3 of the cervical spine. Imaging was by MRI or CT. A pathological fracture was documented in 21 patients. 9% of the patients had a Frankel A score at admittance, 9% Frankel B, 26% Frankel C, 35% Frankel D, and 22% Frankel E. Of the patients belonging to the M-group, 20 had Frankel-D status at diagnosis and 20 only minor deficits, which were best classified to the Frankel E grade. Of patients in the S-group, 10 had Frankel A status at diagnosis, 10 Frankel B, 28 Frankel C, 22 Frankel D and 6 Frankel E. All but 5 patients had had postoperative radiotherapy (3 because of poor general condition and 2 because adjuvant treatment relied on systemic chemotherapy). Postoperative radiotherapy was given after wound healing (3–6 weeks). In half of the patients the given dose was 20 Gy (4 Gy x 5), in 20% 16 Gy (8 Gy x 2), in 18% the dose exceeded 20 Gy (the most common being 30 Gy given in 10 fractions) and in 12% of cases a single dose of 8 Gy was given.

Operated patients were allowed to mobilize without any restrictions. Routine antibiotic and antithrombotic prophylaxis were given. Neurologic deficits were evaluated according to the Frankel scale. To evaluate the mean neurologic outcome, patients were given an arithmetic score (Frankel A arbitrarily corresponding to 1 and E to 5), and the result after treatment was calculated by subtracting the first score from the last. The neurologic outcome was assessed at 2 time-points, the first at a median of 3 (1–70) weeks after referral, and the second at a median of 17 (1–636) weeks. Similar neurologic outcome was noted between the first and the second time-point. The Bauer score (Bauer and Wedin 1995), as modified by Leithner, was used in survival analysis (Leithner et al. 2008).

Statistics

Statistics analysis was carried out using SPSS software (version 20; SPSS Inc, Chicago, IL, USA) and Stata (version 13; StataCorp, College Station. TX, USA). Categorical variables were studied using the chi-square ($\chi 2$) test. The Kaplan–Meier method was used for survival analyses and comparisons were done using the log-rank test. End-points were death and the incidence of secondary surgical decompression. Since the Kaplan–Meier method is based on the assumption of non-informative censoring, which is not fulfilled when studying the late surgery rate, the result was validated using competitive risk analysis with the method of Pepe and Mori. All tests were double-sided, and a p-value of ≤ 0.05 was considered significant. 95% confidence intervals are presented in parentheses. Confidence intervals are given in order to better describe the inferential uncertainty. The core facility of the Statistics Department of the Karolinska Institute was consulted in the analysis of the data.

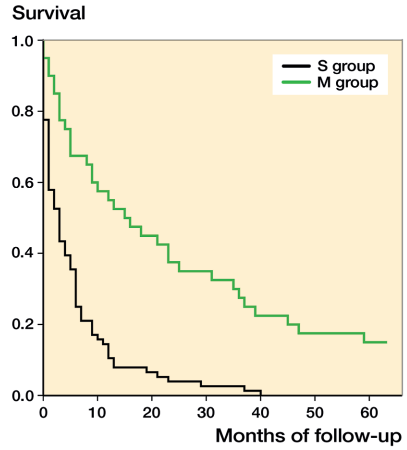

Figure 1. Kaplan–Meier curve of overall survival of 116 patients initially treated non-surgically due to spinal metastasis. Main indications for conservative treatment were either absence of significant neurologic compromise while oncological prognosis was good (M-group), or poor prognosis and overall condition, widespread disease, or a combination of the above (S-group). Median overall survival of patients in the S-group was 3 months (CI 2–5), whereas median overall survival of patients in the M-group was 15 months (CI 6–24), p < 0.001.

Ethics, funding, and potential conflicts of interest

The study fulfilled Institutional Review Board requirements. The authors did not receive any funding and declare no potential conflicts of interest.

Results

Oncological outcome of all patients

The median overall survival of the 116 patients was 5.4 (3.2–6.8) months: two-thirds of the patients were alive after 3 months, half after 6 months, and one-third after 12 months. Only 3 of the 116 patients were alive at last follow-up. Patients in M-group had a median survival of 15 (6–24) months, whereas these in S-group had a median survival of 3 (1–5) months ($p < 0.001$) (Figure 1). The 3-month and 12-month sur-

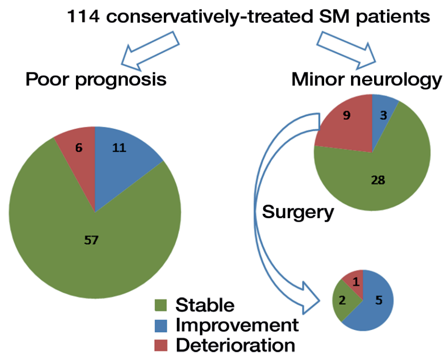

Figure 2. Flowchart showing the neurologic outcome of 114/116 patients with spinal metastasis who were initially treated non-surgically because of either absence of significant neurologic compromise whilst oncological prognosis is good (minor neurology), or poor prognosis and condition, widespread disease, or a combination of the above (poor prognosis). Neurologic status at a median of 2.5 weeks according to Frankel score: stable, improvement, or deterioration.

vival for M-patients was 85% and 58% respectively. Among S-patients, the 3 month-survival rate was 53%, and only 14% survived for 12 months.

Neurologic outcome and incidence of late surgery

Of the 116 patients who were initially assessed for their suitability to undergo surgery and subsequently managed non-operatively, sufficient data for analysis of the neurologic outcome were available for 114 patients. Radiotherapy alone was efficient in retaining or even improving the neurologic function in the vast majority of patients (approximately 85% of the entire cohort). 8 patients underwent surgery at a later stage due to progression of the neurologic deficits; all them belonged to M-group ($p < 0.001$), the risk of undergoing late surgery for the M-group being 21% (Figure 2). Of the remaining 32 patients in the M-group who did not undergo late surgery, 28 had stable neurologic status, 3 improved, and 1 deteriorated.

Outcome of late surgery in the 8 patients initially not operated on

7/8 patients presented with more substantial compression at the same level, whereas 1 who received radiotherapy for cord compression at the 6th thoracic vertebra presented 4 years later with compression at the level of the 3rd thoracic vertebra and underwent laminectomy (Table 1). 5/8 patients experienced an improvement, 2/8 remained relatively stable, and 1/8 deteriorated. Of the 5 patients who benefited from surgery, ambulation was restored in 4/5. There was 1 postoperative complication, a wound break-down that required muscle transposition for coverage of the defect, which eventually healed. There were no deaths within the 30-day postoperative period.

Value of the Bauer prognostic score in predicting the risk for late surgical decompression

Prognostic scores have been widely used to estimate survival in patients with SM. Progression of a neurologic deficit may be associated with survival in 2 seemingly opposite ways: an aggressive tumor, with a poorer prognosis, may also be locally aggressive, but, on the other hand, longer survival with an indolent tumor may give it the necessary time to progress locally. We evaluated the Bauer score regarding its efficacy in estimating survival as well as risk for late surgery in M-patients. We found that a score of more than 2 was associated with superior overall survival and a lower risk for surgery (Figure 3). A separate competing-risk analysis of the rate of late surgical decompression with death being the competing event is given in Figure 4 (see Supplementary data).

Discussion

During the past 2 decades, various studies have established the advantages of surgical decompression for treatment of patients with neurologic deficits because of SM. However,

Table 1. Details and outcome of 8 patients with spinal metastasis who were initially treated non-operatively but underwent late surgery due to progression of neurologic deficits

Case	Age, sex	Histology	Level	Months to secondary surgery	Neurologic status at last follow-up	Comments
1	67, male	Prostate	Thoracic	31	Frankel B	Posterior decompression. Neurologic deterioration postoperatively
2	56, male	Prostate	Thoracic	47	Frankel E	Compression at new level. Posterior decompression. Wound dehiscence 3 weeks postoperatively
3	57, female	Breast	Thoracic	1	Frankel E	–
4	54, male	Lung	Lumbar	4	Frankel D	Posterior decompression
5	74, male	Prostate	Thoracic	2	Frankel D	Posterior decompression
6	72, male	Prostate	Thoracic	1	Frankel D	Posterior decompression
7	46, female	Breast	Thoracic	14	Frankel E	Anterior decompression and fixation
8	69, female	Lung	Lumbar	1	Frankel D	Posterior decompression and fixation

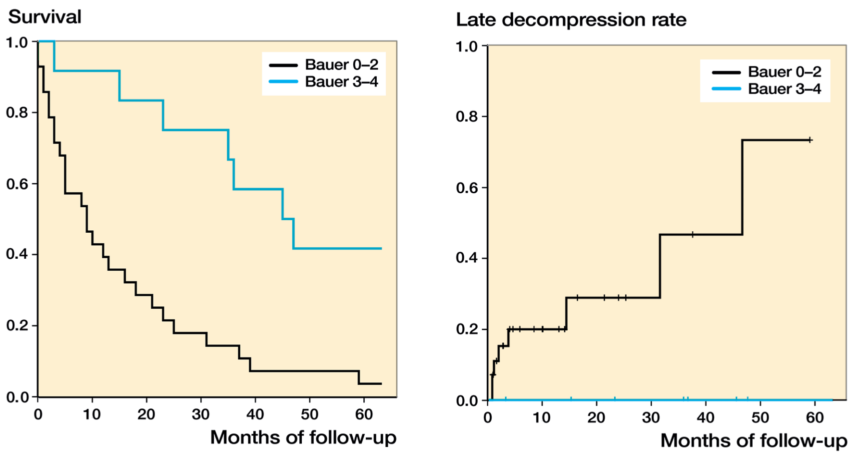

Figure 3. Kaplan–Meier curve of overall survival (left panel) in 40 patients who were initially treated non-surgically for spinal metastasis, due to absence of significant neurologic deficits while oncological prognosis was good (M-group). Median overall survival of patients with Bauer score 0–2 was 9 months (CI 3–6), whereas in those with Bauer score 3–4 this was 45 months (CI 26–64). Kaplan–Meier curve of incidence of late surgery (right panel) in the same patients, depending on their Bauer score (p = 0.006).

in everyday clinical praxis the management of the individual patient remains a challenge. Many factors such as the degree and duration of the neurologic deficits, presence of compression at more than 1 level, the radiosensitivity of the tumor, and the volume of the soft-tissue component causing compression, the condition and expected survival of the patient, and how extensive the spinal metastasis is should be considered (Dea and Fisher 2014). Survival prognostic tools have been described and may help in decision-taking, since many of them also provide guidelines regarding optimal treatment (Tokuhashi et al. 1990, Bauer and Wedin 1995, Tomita et al. 2001, Leithner et al. 2008).

Treatment choice is thus a complex individualized approach. We have always considered the presence of significant neurologic deficits as the primary indication for surgery (Jansson and Bauer 2006). Nonetheless, a significant proportion of these patients, approximately one-third according to our experience, are deemed as non-candidates for surgery. The presence of only minor neurologic deficits despite a good prognosis was the main reason in approximately 1/3 patients (M-group), whereas approximately 2/3 patients (S-group) were not operated because of a dismal prognosis.

The management of a patient belonging to the M-group is a dilemma, especially in cases where there is a moderate epidural soft-tissue component and the neoplasm is radioresistant. Some authors advocate an aggressive en bloc resection in selected patients with solitary spinal metastasis and a good prognosis, especially in the case of certain histological diagnoses (Boland et al. 1982, Chataigner and Onimus 2000). However, the value of this approach has been disputed by others (Bilsky et al. 2009). Undoubtedly, initial non-operative treatment may eventually result in progression of the neurologic symptoms, necessitating late surgical intervention. In our series, late surgery was needed in approximately 1 out of 5 M-patients. We consider this to be an acceptable proportion, especially in view of the effect of radiotherapy as a sole treatment in preserving or even improving function in over 80% of the M-group. It should be noted that the oncological outcome of the M-group was poor, with a median overall survival of 12 months, which explains the low incidence of secondary surgical intervention. Importantly, the outcome of late surgery was good, comparable to that achieved after primary surgery (Jansson and Bauer 2006). Thus, late decompression when needed appears a safe option, although we acknowledge that the number of patients in this subgroup is not large enough to draw safe conclusions and that no direct comparison with a primarily operated group was made. A primary clinical decision not to proceed to surgery was not altered in any patient with a poor prognosis, which highlights the fact that this clinical decision is usually accurate and such patients' condition is usually irreversible.

The modified Bauer score could identify patients at risk for secondary surgery. M-patients with a superior oncological prognosis had a lower risk for late surgery, possible due to the more indolent local progression of their tumor. This characteristic obviously outweighs the fact that patients with an aggressive tumor have a shorter life-span for a secondary neurologic compromise to occur. This information is valuable for both the physician and the patient during shared decision-making.

In summary, our results show that among patients treated non-surgically because of SM with neurologic deficits, late surgical intervention may be necessary only in these who are assigned to this treatment due to minor neurologic deficits and not short expected survival, especially if they have a modified Bauer score of less than 2. However, initial non-surgical treatment is a safe option, since the overall risk is low and secondary decompression appears effective in restoring neurologic function.

Supplementary data

Figure 4 is available as supplementary data in the online version of this article, http://dx.doi.org/ 10.1080/17453674.2017.1412193

PT: Data analysis and manuscript preparation. HB: study design and manuscript review.

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