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ORIGINAL ARTICLE

Evaluation of the relevance of surgery in a retrospective case series of patients who underwent the surgical treatment of a symptomatic spine metastasis from lung cancer

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Abstract
Background The management of spine metastases is an increasing concern for spine surgeons. When considering surgery, it is crucial to ensure that its iatrogenic effects will not exceed its potential benefits, particularly in frail patients with short life expectancy. Among all prognostic factors, the primary site of cancer is the most important, lung cancer being the poorest. Although surgery has shown its effectiveness in the management of spine metastases, there is a lack of studies focusing on lung cancer alone.
Purpose To assess the effectiveness and safety of surgery in the management of symptomatic spine metastases from lung cancer.
Methods We retrospectively reviewed all patients ($n = 53$) who underwent surgery for spine metastasis from lung cancer at the Lille University Hospital between January 2005 and December 2011. Patients for whom surgery was effective to restore or preserve ambulation, to relieve pain, and to ensure stability without severe complication were considered "surgical success".
Results No patient was lost to follow-up and vital status data were available for all patients. The median survival was 2.1 months and was not influenced by the surgical success ($p = 0.1766$). We reported seven major complications in seven patients, including three epidural haematoma, two massive pulmonary embolisms and two deaths from cardiopulmonary failure. The surgical success rate was 49 % and on univariate analysis, the factors that have influenced the postoperative outcome were the KPS ($p < 0.001$), the Frankel grade ($p = 0.0217$) and the delay between the cancer diagnosis and the occurrence of spine metastases ($p = 0.0216$).
Conclusion A strict patient selection is required to limit the iatrogenic effect of surgery, which may alter the quality of life of these frail patients with limited life expectancy.

Keywords Metastasis · Lung cancer · Spinal cord compression · Complications · Surgical success

Introduction

The spine is the third most common site of metastases following lung and liver. Approximatively 50–70 % of patients with solid cancer will develop spine metastases during the course of the disease. Lung, breast and prostate are the more common primary sites, reflecting both their high prevalence and their predilection to the bones [1]. The management of spine metastases is a growing concern for spine surgeons, due to the improvement of care that leads to an extended survival of cancer patients [1, 2]. Except in rare cases, the treatment may be palliative rather than curative, especially for patients with short- or mid-term life expectancy. Due to the high variability of clinical and radiological presentations, the treatment strategy should be ideally defined in a multidisciplinary fashion, providing the treatment the best suited to each particular situation, in order to preserve or, whenever possible, improve the patients' quality of life [3]. Within the therapeutic arsenal, surgery has clearly demonstrated its usefulness to achieve pain relief, spinal cord

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decompression and to ensure stabilization of the involved vertebrae [3, 4]. However, surgery is associated with high morbidity and complication rates, especially in patients with numerous neoplasm-associated comorbidities, which can delay the initiation of adjuvant therapy and affect the patient outcome. This consideration is particularly true for patients with a limited life expectancy for whom the drawbacks of surgical treatment are likely to exceed its potential benefits [5, 6]. Thus, it is essential to better assess the patients' life expectancy, when considering surgery for spine metastases. The Tokuhashi score [7], which is the most widely used, takes into consideration six parameters such as general condition, severity of palsy, number of spine metastases, number of extraspinal bone metastases and metastases to major internal organs. Among all, the primary site of cancer is the most important prognostic factor, lung cancer being the poorest. Many other scoring systems have been proposed; all reported that the prognosis of spine metastases from lung cancer was poor [8]. Although surgery has shown its effectiveness in the management of spine metastases, there is a lack of studies focusing on lung cancer alone. Therefore, benefits of surgical management for spine metastases from lung cancer remain unclear.

Methods

Inclusion criteria

Using the coding process, we reviewed the medical records of the 523 patients who underwent surgery for the treatment of a spinal tumor in the Lille University Hospital between January 2005 and December 2011. We excluded patients who underwent excisional surgery for a solitary spine metastasis or for a primitive spine tumor. In total, 450 patients underwent a palliative surgery for symptomatic thoracolumbar spine metastases. Primary cancer was the lung in 53 patients who were included in this study.

Data collection

Age, sex, Karnofsky Performance Status (KPS), clinical signs, radiological findings, histopathological results and the delay between the lung cancer diagnosis and the occurrence of spine metastases have been systematically recorded in the medical records. Preoperative pain and neurological status were, respectively, measured using the VAS scale and the Frankel grade [9]. The revised Tokuhashi score [7] and the Spinal Instability Neoplasic score [10] were retrospectively measured (Table 1). Operative parameters (blood loss, operative time), length of hospital stay and the ability for the patient to leave the hospital were also reported.

Outcomes measure

We investigated whether surgery was safe and effective to preserve or restore patient autonomy, relieve pain and provide spine stability.

- Functional outcome: we measured the Frankel grade preoperatively, at discharge and at 1 month. Patients, whose surgery succeeded in restoring and/or preserving their autonomy durably (Frankel D/E), were considered as good results.
- Pain: we measured pain (back and radicular) preoperatively, postoperatively and at 1 month. Patients, who experienced a decrease in VAS of at least two points without increase of pain medication, were considered as good results.
- Spine stability: we assessed whether surgery was effective to preserve or restore stability, enabling patients to stand without brace. We considered as good results patients who harbored overt instability, for whom surgery has achieved effective stabilization. Patients with posterior epidural involvement, who underwent a single laminectomy, were also considered as good results if surgery has not led to iatrogenic instability and if the patient has not experienced further instability from tumor progression.
- Complications: complications have been carefully addressed and classified using the Clavien-Dindo classification [11]. Complications equal or superior to grade IIIb were considered as severe (Table 2).

Statistical analysis

First, descriptive analyses have been performed. Numerical parameters have been described as mean and standard deviations, categorical parameters as frequencies. Then, bivariate analysis has been realized: comparisons of numerical parameters, according to success, were performed using the Wilcoxon non-parametric test, comparisons of frequencies using the Chi square or Fisher exact test.

Survival estimates have been computed using the Kaplan–Meier method. Comparison of survival curves has been performed using the log-rank test.

Statistical analyses have been performed using the SAS V9.4 software (SAS Institute, Cary, NC, USA).

Results

No patient was lost to follow-up and vital status data were available for all patients.

Table 1 Main classifications

Type	Definition
a: Frankel classification	
A	Complete: no motor or sensory function
B	Incomplete: sensory present, motor function absent
C	Incomplete: sensory present, motor function present but not useful (grade 2 or 3/5)
D	Incomplete: sensory present, motor function present and useful (grade 4/5)
E	Normal sensory and motor function

Characteristic	Score
b: Tokuhashi scoring system[a–c]	
General condition (Karnofsky)	
Poor (10–40 %)	0
Moderate (50–70 %)	1
Good (80–100 %)	2
Number of extra spinal bone metastases	
>2	0
1–2	1
0	2
Number of spine metastases	
>2	0
2	1
1	2
Metastases to major organs	
Unremovable	0
Removable	1
None	2
Primary site	
Lung, stomach, oesophagus, pancreas	0
Liver, gall bladder, unknown	1
Others	2
Kidney, uterus	3
Rectum	4
Breast, prostate, thyroid, carcinoid	5
Palsy	
Complete (Frankel A or B)	0
Incomplete (Frankel C or D)	1
None (Frankel E)	2

Parameter	Score
c: Spinal Neoplastic Instability Score[d–f]	
Location	
Junctional (C0–C2, C7–T2, T11–L1, L5–S1)	3
Mobile spine (C3–C7, L2–L4)	2
Semirigid (T3–T10)	1
Rigid (S2–S5)	0
Pain	
Continue	3
Occasional	1
None	0
Bone lesion	
Lytic	2
Mixed	1
Blastic	0
Radiographic alignment	
Subluxation/translation	4
Deformity (scoliosis, kyphosis)	2
Normal	0
Vertebral body collapse	
>50 %	3
<50 %	2
No collapse but >50 % body involved	1
None	0
Posterolateral involvement	
Bilateral	3
Unilateral	1
None	0

Interpretation

[a] Score $\leq$ 8: life expectancy $<$ 6 months

[b] 9 $\leq$ score $<$ 12: life expectancy 6–12 months

[c] Score $\geq$ 12: life expectancy $>$ 12 months (excisional)

Interpretation

[d] 0–6: stable

[e] 7–12: potentially unstable

[f] 13–18: unstable

Table 2 The Clavien-Dindo classification

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for treatment except antiemetics, antipyretics, analgesics, and electrolytes
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I
Grade III	Requiring intervention
IIIa	Not under general anesthesia
IIIb	Under general anesthesia
Grade IV	Life threatening complication requiring ICU management
Grade V	Death of the patient

Population

The main demographical data are summarized in Table 3. Fifty-three patients have been included in this study. There were 45 men and 8 women with a mean age at diagnosis of 59.2 years (range 36–78 years). The mean KPS was 74.3 (range 60–90). With regard to the Tokuhashi score, 44 patients (83 %) had a score inferior or equal to 8 while 9 patients (17 %) had a score between 9 and 11. The time from lung cancer diagnosis to occurrence of bone metastasis was less than 1 month in 21 patients, between 1 and 6 months in 18 patients, between 6 months and 1 year in 10 patients and more than 1 year in 4 patients. The major histological types of the primary site were adenocarcinoma (31 patients), followed by squamous cell carcinoma (nine patients), small cell carcinoma (eight patients), large cell carcinoma (four patients), and undifferentiated carcinoma (one patient). According to the SINS, seven patients had a stable lesion (0–6), 35 patients had a potentially unstable lesion (7–12) and 11 patients had an unstable lesion (13–18).

Operative parameters

The affected levels were the upper cervical spine (C1–C2) in 2 patients, the lower cervical spine (C3–C7) in 7 patients, the upper thoracic spine (T1–T6) in 22 patients, the lower thoracic spine (T7–T12) in 13 patients and the lumbar spine (L1–L5) in nine patients. Twenty-five patients underwent spinal cord decompression only, while 28 patients underwent both decompression and spinal stabilization. There was a strong correlation between the surgical stabilization and the SINS ($p = 0.0001$). Indeed, all patients with an unstable lesion have benefited from surgical stabilization. Conversely, no patient with a stable lesion underwent surgical stabilization.

Table 3 Main demographical data

Variable	Mean value	p value[b]
Age (range)	59.2 (range 36–78)	0.0990
Sex		0.4672
Male (%)	45 (84.9 %)	
Female (%)	8 (15.1 %)	
Karnofsky performance status (range)	74.3 (range 60–90)	**<0.0001**
Delay LC/SM[a]		**0.0216**
<1 month	21 (39.6 %)	
1–6 months	18 (34.0 %)	
6 months to 1 year	10 (18.9 %)	
>1 year	4 (7.5 %)	
Histology		0.3477
Adenocarcinoma (%)	31 (58.5 %)	
Squamous cell carcinoma (%)	9 (17.0 %)	
Small cell carcinoma (%)	8 (15.1 %)	
Large cell carcinoma (%)	4 (7.5 %)	
Undifferentiated (%)	1 (1.9 %)	
Level		0.3526
Upper cervical spine (C1–C2)	2 (3.8 %)	
Lower cervical spine (C3–C7)	7 (13.2 %)	
Upper thoracic spine (T1–T6)	22 (41.5 %)	
Lower thoracic spine (T7–T12)	13 (24.5 %)	
Lumbar spine (L1–L5)	9 (17.0 %)	
Frankel		**0.0217**
A	3 (5.7 %)	
B	10 (18.9 %)	
C	14 (26.4 %)	
D	11 (20.7 %)	
E	15 (28.3 %)	

Bold values are statistically significant at $p < 0.05$

[a] Delay between lung cancer diagnosis and occurrence of spine metastasis

[b] Univariate analysis of factors that may have influenced the "Surgical success"

The mean operative time was 120 min (range 40–220 min) and the mean estimated blood loss was 840 ml (100–3200 ml). Five patients required blood transfusion during or immediately after the surgery.

Outcome

Regarding functional outcome, surgery was effective in preserving or restoring durably the ability to ambulate for 36 patients (67.9 %). Note that three patients who where ambulatory preoperatively worsened their neurological condition (Table 4). Regarding pain control, surgery was effective in decreasing pain durably and significantly (without increasing pain medication) in 37 patients (69.8 %). No patients reported significantly and sustainably increase of pain in relation to surgery. Regarding spinal stability, surgery was considered effective for 44 patients (83.0 %). Postoperative CT-scan demonstrated solid hardware anchorage in the 28 patients who underwent spinal stabilization. Surgery was also effective for 16 of the 25 patients who underwent decompression only, as they have shown no new clinical or radiological signs of instability during follow-up. Nine patients (17 %), who underwent decompression surgery, have presented clinical and radiological signs of instability related to local tumor progression, which required the wearing of an orthosis. Finally, seven patients presented severe complications (grade - ≥ IIIb). Three patients presented an epidural haematoma that required reoperation and was responsible for durable neurological decline (loss of ambulation). Two patients presented massive pulmonary embolism requiring prolonged ICU management (grade IV). Two patients presented cardiopulmonary failure resulting in death (grade V).

A total of 32 patients were able to leave the hospital and return home after surgery. Factors that demonstrated value in predicting the ability of patients to leave hospital were the KPS ($p = 0.0156$), the Tokuhashi score ($p = 0.039$), the Frankel scale ($p = 0.0087$) and the occurrence of a major complication ($p = 0.012$).

Table 4 Functional outcomes

Preop	Postop					
	A	B	C	D	E	
A	1	1		*1*		3
B		4	1	*5*		10
C		1	6	*5*	*2*	14
D	1			*5*	*5*	11
E		2			*13*	15
	2	8	7	16	20	53

Patients for whom surgery has enabled to preserve or restore ambulation are highlighted in italics

Success rate

If we consider as good results patients for whom surgery was effective to restore or preserve ambulation, to relieve pain, and to ensure stability without severe complication, the success rate was 49 % (Table 5). However, if we consider as good results patients for whom surgery was effective to restore or maintain ambulation and relieve pain without severe complication, regardless of stability, the success rate was 52.8 %. Finally, only taking into account the functional outcome and complications regardless of pain and stability, the success rate was 64.2 %. On univariate analysis, the factors influencing the postoperative outcome were the KPS ($p < 0.001$), the Frankel grade ($p = 0.0217$) and the delay between the cancer diagnosis and the occurrence of spine metastases ($p = 0.0216$). Age, sex, histology and level were not statistically significant factors in predicting postoperative outcome.

Survival

The median survival was 11 weeks (range 3–110; SD = 5.585) for patients who were considered "surgical success" and 8 weeks (range 0–140; SD = 5.269) for patients for whom surgery was not considered successful (Fig. 1). The difference was not statistically significant ($p = 0.1766$). In this population the revised Tokuhashi score has not demonstrated accuracy to predict survival ($p = 0.7994$).

Discussion

Despite their high incidence, there is still no consensus regarding ideal management of symptomatic spine metastases [12]. For decades, radiotherapy has been considered

Table 5 Measurement of surgical success rate

Preserve/restore ambulation	Pain relief	Stability	No severe complication	Number of patients (%)
√	√	√	√	26 (49 %)
√	√		√	28 (52.8 %)
√			√	34 (64.2 %)
√				36 (67.9 %)

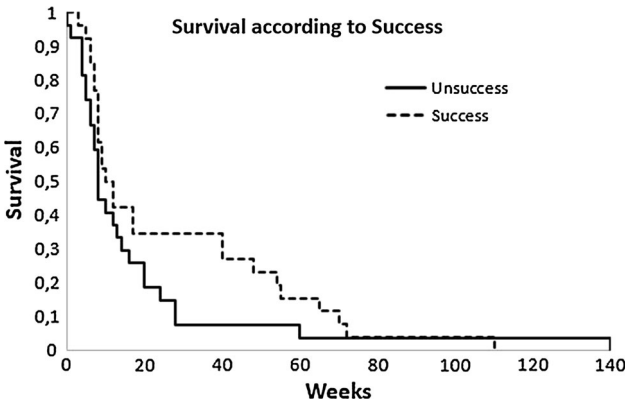

Fig. 1 Kaplan–Meier plot of overall survival time (weeks) for patients who were considered "surgical success" (*red line*) and for patients for whom surgery was not considered successful (*blue line*)

the mainstay treatment, as surgery has not demonstrated any clear benefit [13]. Indeed, historically surgery consisted of performing a simple laminectomy with the objective to release the pressure on the spinal cord and to reverse neurological symptoms. As 70 % of spine metastases involve the vertebral body, this strategy has led to frequent worsening of the patients' neurological condition and increasing spinal instability. With the indiscriminant use of laminectomy regardless of spine stability, surgical treatment of spine metastases remained dormant. Over the last two decades, progresses in surgical techniques and spinal instrumentations have allowed surgeons to ensure wide decompression and solid stabilization, providing efficient solutions to patients [14–16]. This led to dramatic improvement of patients' outcomes, as demonstrated by randomized controlled trials [17, 18]. Patchell et al. [18] conducted a controlled prospective trial comparing surgical treatment followed by adjuvant radiation with conventional radiation alone. This study confirmed the superiority of surgical management in terms of maintaining or regaining ambulation. Patients treated with surgery retained ambulatory longer than patients in the radiation group. In the surgical group 56 % of no ambulatory patients regained ability to walk, compared with 19 % in the radiation group. Moreover, they reported a lower analgesic and corticosteroid consumption in the surgical group. Nevertheless, many criticisms and controversies still exist regarding the benefit of surgical treatment in the palliative management of spine metastases. Detractors of surgery emphasize the relatively high morbidity rate associated with this more aggressive treatment strategy [5, 6, 19]. This concern is even more important for patients with a limited life expectancy, for whom the benefits of surgery can be surpassed by its potential side effects. Thus, it is crucial to better assess the patient's life expectancy, and many scoring systems have been developed for this purpose [7, 8]. Despite some discrepancies, they all agree that of all solid cancers, the lung has the worst prognosis among patients with spine metastases. Indeed, lung cancer has a high potential for turning into metastasis, and the diagnosis is often established late, as the symptoms in the early stages are not common [20]. Among all scoring systems, the Tokuhashi score [7] is the most widely used (Table 1). Although this score has shown its accuracy in predicting survival in patients with spine metastases of various cancers [21], it has not shown predictive value in this population of patients with lung cancer only. Indeed, the median survival was 2.1 months and was not influenced by the revised Tokuhashi score ($p = 0.7994$). Similarly, in our series, the median survival was also not influenced by the surgical success (Fig. 1). Several studies revealed similar survival times [22, 23]. However, we should be very cautious when reading these results as the survival of patients with spine metastases from lung cancer is likely to improve because of the incorporation of new therapeutic options, including specific target molecular therapies [24]. Although recent studies have already shown a slight improvement in survival thanks to these new therapies, especially in patients with EGFR mutation [25, 26], it appeared crucial to analyze the relevance of surgery in these frail patients.

Currently, the main indications for surgery are spinal cord compression, intractable pain and spinal instability [12, 27]. However, due to the high variability of clinical and radiological situations, there is still no consensus to define patients who are valuable candidates for surgery. Patients with short expected life expectancy are generally contraindicated for surgery. Similarly, patients with complete paralysis (Frankel A) evolving for more than 24 h are also contraindicated, as neurological recovery cannot be expected [28]. In our series, only three patients with complete paraplegia (Frankel A) have been operated on. Although surgeries have been performed soon (<24 h) after the onset of symptoms, only one patient experienced significant improvement enabling recovery of walking. There is still no consensus on the manner to consider a surgical success. Survival [25, 29] is not a sufficient criterion as many studies have demonstrated that survival of these patients was not influenced by their neurological status [30, 31]. In our studies, we also demonstrated that patients for whom surgery was considered successful have not experienced longer survival (Fig. 1). Many studies in this field consider as good results of patients who have presented an improvement in their neurological status at discharge [15, 16, 25, 26, 29, 30]. However, surgery should be considered effective, only if the improvement is sufficient, enabling the patient to regain ambulation durably. In our study, we decided to take into account four criteria: ambulation, pain relief, stability and absence of

major complication. After performing an individual analysis, the presence of these four criteria was required to consider a posteriori that a surgery was successful. Using these criteria, only 49 % of patients operated on have been considered as surgical success. The main prognostic factors were the KPS, the Frankel grade and the delay between the cancer diagnosis and the occurrence of spine metastases. Age, sex, histology and level were not statistically significant factors in predicting postoperative outcome. These results must be balanced by the fact that seven patients presented major complications, resulting in death for two patients and in the loss of ambulation for three patients who were ambulatory preoperatively (Table 4).

The main limitation of this study is directly related to its retrospective nature. In this study, we included only patients with symptomatic spine metastasis for whom surgery was considered suitable by the treated surgical team. Oncological treatments and EGFR mutation status may be additional prognostic factors to take into consideration [32], although they have not been considered in our study, as it was not performed routinely during the study period. Furthermore, the recent development of minimally invasive techniques of decompression and stabilization are likely to decrease the complication rate and improve patient outcomes in the future [33–36]. Similarly, percutaneous cement augmentation techniques have not been considered in our study. These techniques that are contraindicated in case of spinal cord compression are likely to ensure spinal stabilization and achieve efficient pain relief with a limited morbidity in well-selected patients, as reported by many studies [37, 38]. Despite its limitations, this study is useful because it helps to better select patients with symptomatic vertebral metastasis who are likely to really benefit from surgical treatment. It also highlights the necessity to develop a postoperative outcome score, based on the presented criteria, to homogenize the results of future studies in this field.

Conclusion

By applying various clinical criteria, more than 50 % of patients operated on for a symptomatic spine metastasis have not "really" benefited from surgery. Surgery is not recommended for patients with spine metastases from lung cancer, based on limited success and potential iatrogenic effects, which are likely to alter the quality of life of these frail patients with limited life expectancy.

Compliance with ethical standards

Conflict of interest None.

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