Neurological outcomes after surgery for spinal metastases in symptomatic patients: Does the type of decompression play a role? A comparison between different strategies in a 10-year experience

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\textbf{Article info}

\textbf{Article history:}
Received 27 September 2020
Revised 30 October 2020
Accepted 2 November 2020
Available online 10 November 2020

\textbf{Keywords:}
Spinal metastases
Separation surgery
Minimal invasive spine surgery
Circumferential decompression
Metastatic epidural compression

\textbf{Abstract}

\textbf{Introduction:} The impact of neurological deficits plays a role of inestimable importance in patients with a neoplastic disease. The role of surgery for the management of symptomatic spinal cord compression (SSCC) cannot be overemphasized, as surgery represents often the first and paramount step in patients presenting with motor deficits. The traditional paradigm of simple bilateral laminectomy for the treatment of spinal cord compression has been reviewed. The need to achieve a proper circumferential decompression of the spinal sac has been progressively highlighted in combination with the development of the more comprehensive and multidisciplinary concept of separation surgery.

\textbf{Objective:} The aim of this paper is to analyze different strategies of decompression, while evaluating whether circumferential/anterior decompression is able to guarantee a better control and restoration of neurological functions in patients with motor impairment, if compared to traditional posterior decompression.

\textbf{Materials and methods:} This is a retrospective observational study investigating symptomatic patients that underwent surgical treatment for spinal metastases at author’s Institutions from January 2010 to June 2019. Data recorded concerned patient demographics, tumor histology, peri-operative and follow-up neurological status (ASIA), ambulation ability, stability (SINS), grade (ESCC) and source of epidural compression and type of decompression (anterior/anterior-lateral (AD); posterior/posterior-lateral (PD/PDL); circumferential (CD)).

\textbf{Results:} A total number of 84 patients was included. AD/CD patients showed higher chance of neurological improvement and reduced rates of worsening compared to PD/PDL group (94.1%/100% vs 60.4%; 11.8% vs 45.8% respectively). Univariate logistic regression identified immediate post-operative improvement to be a significant protective factor for worsening at last follow-up. Stratifying patients for site of compression and considering anterior and circumferential groups, immediate post-operative neurological improvement was mostly associated with AD and CD (p 0.011 and 0.025 respectively). Walking at last follow up was influenced by post-operative maintenance of ambulation (p 0.001).

\textbf{Conclusion:} The necessity to remove the epidural metastatic compression from its source should be considered of paramount importance. Since the majority of spinal cord compression involves firstly the ventral part of the sac, CD/AD are associated with better neurological outcomes and should be achieved in case of circumferential or anterior/anterolateral compression.

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\textbf{Abbreviations:} HRQoL, health-related quality of life; SSCC, symptomatic spinal cord compression; ASIA, American Spinal Injury Association Impairment Scale; SINS, spinal instability neoplastic score; ESCC, epidural spinal cord compression scale; ASCC, anterior spinal cord compression; P-ISC, anterior lateral spinal cord compression; PSCC, posterior spinal cord compression; CSCC, circumferential spinal cord compression; PDL, postero-lateral decompression; AD, anterior decompression; CD, circumferential decompression; IONM, intraoperative neurophysiological monitoring; RT, radiotherapy; MIS, minimally invasive surgical; cEBRT, conventional external beam radiation therapy.

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https://doi.org/10.1016/j.jbo.2020.100340
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1. Introduction

The impact of neurological deficits plays a role of inestimable importance in patients with a neoplastic disease. Evidence showed that neurological deficits caused by spinal cord compression are associated with reduced life expectancy and Health-Related Quality of Life (HRQoL) [1,2,3]. Recently, a prospective, multi-centric, international study has analyzed how neurological deficits could impact functional status, HRQoL, and overall survival [4]. Results showed that patients with neurological deficits have reduced overall survival and worse HRQoL and that the need for an early diagnosis is of paramount importance. These findings place the emphasis on how surgeons, radiation oncologists and oncologists could preserve or restore the integrity of the spinal cord. The role of surgery for the management of symptomatic spinal cord compression (SSCC) cannot be overemphasized, as surgery represents often the first and paramount step in patients presenting with motor deficits [5]. In the last decades, only few papers focused on differences among various types of decompression that could be achieved without considering the type and source of neoplastic compression of the spinal cord [6,7,8]. The majority of SSCC cases involves firstly the ventral part of the sac since metastases usually origin within the vertebral body [9]. Hence, regardless of the surgical approach, the need to achieve a proper circumferential decompression of the spinal sac has been progressively highlighted in combination with the development of the more comprehensive and multidisciplinary concept of separation surgery [10,11]. Then, the traditional paradigm of simple bilateral laminectomy for the treatment of spinal cord compression has been reviewed. The aim of this paper is to analyze different strategies of decompression, while evaluating whether circumferential/anterior decompression is able to guarantee a better control and restoration of neurological functions in patients with motor impairment, if compared to traditional posterior decompression.

2. Materials and methods

This is a retrospective observational study investigating patients that underwent surgical treatment for spinal metastases at author’s Institutions from January 2010 to June 2019. Data were extracted from a prospectively collected database including: age, sex, histotype of primitive tumor, number and time of occurrence of the spinal metastases, spine level involved by the lesions, pre and post-operative neurological evaluation according to American Spinal Injury Association impairment scale (ASIA), Spinal Instability Neoplastic Score (SINS) [12], anatomical extension of vertebral involvement, epidural compression grade according to described Epidural Spinal Cord Compression Scale (ESCC) [13], type of surgical treatment, extension of decompression surgery, type of fixation if performed, radiotherapy protocol and neurological evaluation at the last follow up. Clinical and radiological data were obtained at time of admission and at follow-up clinic evaluation by fully trained neurosurgeons of the Department. A consent was obtained to use clinical information for research purposes.

2.1. Inclusion criteria were

- Surgical treatment of spinal localization of malignant neoplasm in adult patients, including both solid and hematopoietic tumors in patients with motor deficits (at least 1 point for at least 1 limb according to the MRC scale);
- Availability of at least 3 months follow-up with all recorded data;
- Pre-existing conditions that could independently prejudice the neurological status of the patient or its evaluation (neurological disease, neuropathies, other pathological/traumatic vertebral or skeletal fractures at different levels, brain events)
- Occurrence after treatment or during the follow-up of post-surgical and/or post radiation and/or post systemic treatment complications and/or systemic adverse events that could impair the neurological evaluation of the patient
- Pre-existing or occurrence in the post-operative period of skeletal metastases or other vertebral bone metastases with epidural compression that could impair neurological assessment
- Post-surgical treatment with Stereotactic Spinal Radiosurgery (SSRS), since circumferential decompression before SSRS is mandatory (separation surgery) in order to create a proper ablative target [14].

2.2. Exclusion criteria were

- Post-surgical treatment with Stereotactic Spinal Radiosurgery (SSRS), since circumferential decompression before SSRS is mandatory (separation surgery) in order to create a proper ablative target [14].
- Pre-existing or occurrence in the post-operative period of skeletal metastases or other vertebral bone metastases with epidural compression that could impair neurological assessment
- Post-surgical treatment with Stereotactic Spinal Radiosurgery (SSRS), since circumferential decompression before SSRS is mandatory (separation surgery) in order to create a proper ablative target [14].

2.3. Radiological/surgical evaluation

In this analysis SSCC was described considering bone involvement and anatomical site of epidural compression on MRI defining 5 different types: anterior (ASCC), antero-lateral (A-lSCC), Postero-lateral (P-ISCC), Posterior (PSCC) and Circumferential (CSCC) (Table 1).

Different surgical techniques have been adopted during the analyzed period, in combination with the development of new findings in spinal metastases management (see discussion). Many procedures, at the beginning of the investigation period, consisted in pure posterior or postero-lateral decompression regardless of the source of neoplastic active compression. In the last years authors started performing circumferential/anterior decompression in case of thoracolumbar locations affected by ASCC, A-lSCC or CSCC. Procedures have been then categorized (see Table 1 for details): Posterior Decompression (PD), Postero-Lateral Decompression (PLD), Anterior Decompression (AD), Circumferential decompression (CD). Intraoperative neurophysiological monitoring (IONM) have always been used during surgery [15]. Throughout the years many technological adjuncts helped surgeons in maximizing the safety and efficacy of the procedures. Then auxiliary technology has been used in the last years to decrease surgical morbidity while performing more aggressive procedures, like 3D-HD endoscope assistance for thoracic ventral separation [16], intraoperative CT based navigation system to guide tumor debulking [16] or intraoperative Ultrasound to verify the achievement of a proper decompression [17] (Fig. 1). As about surgical approaches to decompress the ventral sac, the anterior per-carotid route was the choice in cervical locations (Fig. 2). In thoracolumbar metastases the transpedicular approach was usually preferred in order to obtain a proper ventral separation with partial removal of the vertebral body. If a total corpectomy was planned, surgery was mostly performed with the retro-pleuric or retro-peritoneal approach followed by posterior fixation. Fixation was performed in cases of mechanical instability, both overt or potential, according to the SINS score. For transpedicular fixation, titanium or carbon-fiber screws have been used throughout the years. Heterologous bone graft, PEEK cages and Titanium or Carbon fiber plates have been used for anterior fixation and replacement when needed [18].

2.4. Post-operative evaluations

Patient evaluations were assessed at discharge and at follow-up. The standard Modified Research Council (MRC) scale for
muscles strength was adopted. Neurological improvement was recorded when patients recovered at least 1 point at at least 1 limb according to the MRC scale. Neurological worsening was registered when patients lost at least 1 point at at least 1 limb.

2.5. Statistical analysis

Descriptive statistics were reported as a median, mean and standard deviation for continuous variables. Comparison of proportions were performed with Chi-squared test for categorical variables and, when needed (>20% of values <=5 and/or presence of values < 1), with Cramer’s Phi and V coefficients to verify association between variables. Univariate/Multivariate logistic regression was performed in order to define relationships between dependent and independent variables. Statistical significance was defined with a p-value < or = 0.05. All statistical analyses were performed using SPSS Statistics software (IBM SPSS Statistics for Windows, Version 24.0; IBM Corp., Armonk, New York, USA).

3. Results

A total number of 84 patients (M:F 70.2%:29.8%) was considered after retrospective evaluation of inclusion/exclusion criteria from a total case series of 321 cases. Mean age reported was 66.5 years (SD 10.8; median 69). Descriptive data are summarized in Table 2. Considering the anatomical site of epidural compression, CSCC and Al-SCC resulted the most common finding (44.0% and 27.4% respectively). Posterior/postero-lateral decompression was performed in 48 patients (57.1%), while anterior and circumferential decompression were achieved in 17 (20.2%) and 19 (22.6%) cases respectively. Fixation was performed in 78 patients (92.9%,) and body replacement in 26 cases (30.9%). Radiotherapy (cEBRT) was always performed after surgery (Mean 4 weeks). Used protocols were 8 Gy in one fraction (54.3%), 20 Gy in 5 fractions (25.6%), 30 Gy in 10 fractions (20.1%) without significative difference among different type of decompression performed.

According to neurological assessment, 84 patients reported a pre-operative neurological deficit. Immediate post-operative evaluation (carried out at discharge from our department) reported neurological improvement in 64 patients (76.2%), stability in 19 patients (22.6%), while in 1 case (1.2%) a worsening was observed (Table 2). At follow-up (Mean 10.8 months) a deterioration of neurological status was recorded in 28.6% of all the cases (24 patients). The most common timing of deterioration was registered within 3–12 months after surgery (3–6, 20.4%; 6–12, 18.3%). (Table 2).

Table 1
Anatomical site of spinal cord compression.

| Spinal cord compression | Description |
|-------------------------|-------------|
| Anterior Spinal Cord Compression (ASCC) | Anterior elements (vertebral body and ligamentous structures) involvement anterior epidural space occupation; |
| Antero-lateral Spinal Cord Compression (Al-SCC) | Vertebral body and pedicle involvement anterior and lateral epidural space occupation; |
| Postero-lateral Spinal Cord Compression (Pl-SCC) | Posterior elements (lamina, spinous process, transversus process, facet joint and ligamentous structures) and pedicle involvement posterior and lateral epidural space occupation; |
| Posterior Spinal Cord Compression (PSCC) | Posterior elements involvement posterior epidural space occupation; |
| Circumferential Spinal Cord Compression (CSCC) | Vertebral body, pedicle and posterior elements involvement (unilateral or bilateral) anterior, lateral and posterior epidural space occupation |

Fig. 1. Thoracic lung cancer metastasis (A-G). A 63 years old woman presented to the authors attention with mechanical back pain. (A) Sagittal T2w MRI and (B) CT scan showing an osteolytic T8 metastatic lesion with ventral Bilsky grade 2 epidural compression and mechanical instability (SINS score 12). (C) A navigated CD was performed and (D) 3D endoscope was used to better achieve ventral decompression of the dural sac; (D) one level above and below the pathological vertebra was fixed using carbon fiber/PEEK system. (F) Post-operative myelo-CT scan showing CD with restored CSF space around the cord (separation surgery). (G-H) Post-operative CT scan showing CD (H) and partial vertebral body removal without the need for anterior column reconstruction.
3.1. Analysis

The type of surgical decompression was associated with different neurological outcomes in the immediate post-operative period and at follow-up. In the post-op evaluation, AD/CD patients showed higher chance of neurological improvement and reduced rates of worsening compared to PD/PLD group (94.1%/100% vs 60.4%; 11.8% vs 45.8%). Moreover, considering only patients with neurological improvement immediately after surgery, the chance of worsening resulted to be significantly higher for PD/PDL patients compared to AD and CD groups (37.9% vs 12.5% and 0%, p 0.004) (Table 3).

Considering immediate post-operative neurological improvement among patients belonging to the PD group, no differences were found within different anatomical sites of epidural compression (p 0.578). However, the majority of patients that did not report neurological improvement, suffered from ASCC and/or AL-SCC or CSCC (52.6% and 36.8% respectively). The same results were confirmed analyzing neurological status at the last follow-up (p 0.989).

Patients were then stratified according to different anatomical site of epidural compression considering its previous suggested role. Post-operative neurological improvement was evaluated according to surgical decompression type (Table 4). Considering ASCC/Al-SCC and Circumferential groups, immediate post-operative neurological improvement was mostly associated with AD and CD (p 0.011 and 0.025 respectively) This analysis was not feasible in the PCSS/P-lCSS group because posterior or posterolateral decompression were obviously the only operations performed in these cases.

These findings were later confirmed at follow-up (p 0.035 and 0.013 respectively).

Then, association between neurological improvement in the immediate post-operative period and neurological worsening at the last follow up was recorded (Table 5). No neurological worsening at the last follow up was recorded in 51 patients (79.7%) among patients with post-operative neurological improvement, while neurological worsening was observed in 55% of cases belonging to the no post-operative neurological improvement group (p 0.004). This association was confirmed by univariate logistic regression that showed higher probability to not observe neurological worsening at the last follow up for patients that have registered a neurological improvement in the immediate post-operative period (Nagelkerke R-squared 0.136, Exp(B) 0.209; p 0.004) (Table 5).

The same analysis was also performed stratifying patients according to surgical decompression type performed and no statistically significative associations were found.

Ultimately, ambulation ability was analyzed. Among patients that presented with ambulation impairment, 11 patients (61.1%) were able to walk in the immediate post-operative period (p 0.001). Moreover, the multivariate logistic regressing analysis reported that the pre-operative ambulation ability resulted to be the only significative factor influencing the post-operative ability to walk (Nagelkerke 0.460; Exp(B) 41.28; p 0.001) (Table 6). The same analysis was performed evaluating the ability to walk at the last follow up and the multivariate logistic regression showed that post-operative ambulation ability resulted to be the only factor affecting this outcome (Nagelkerke 0.575; Exp(B) 87.32; p 0.001) (Table 6).
The management of spinal metastases has undergone multiple transformations in the last ten decades [19]. In the first half of the 20th century the standard of treatment was represented by posterior surgery via laminectomy in order to decompress the spinal cord. Nevertheless, this approach was limited especially by the impossibility to reach the ventral aspect of the dural sac removing cord. Furthermore, the absence of spinal instrumentation did not address problems related to spinal instability. This is why with the advent of Radiotherapy (RT) in the ‘50s–’70s, surgery was progressively abandoned: neurological and pain outcomes of RT were not inferior and the risks of surgery did not constitute an issue [20,21,22]. The re-establishment of surgery took place in the ‘80s–’90s with the development of A) instrumented fixation able to treat instability and mechanical pain; B) safe anterior approaches to enable for more aggressive debulking. In the 2005 the paramount randomized trial by Patchell et al. showed how the combination between decompressive surgery and RT led to better outcomes if compared to RT alone, then becoming the standard of treatment [5]. The advent of Minimally Invasive Surgical (MIS) techniques developed for degenerative surgery [23,24], as well as the advancements in RT (SSRS) and chemotherapy (targeted therapies) have further implemented the need for a multidisciplinary and comprehensive approach [23,25].

Given this, the treatment of patients with SSCC poses a unique challenge. The restoration of a proper clinical status in a metastatic patient is mandatory to maintain a proper quality of life while avoiding to reduce the overall survival [4]. The treatment of symptomatic spinal cord compression still remains mainly a surgical issue, at first, since surgery is able to rescue quickly the spinal cord when necessary [26–29]. Nevertheless, evidence addressing neurological outcomes following different type of surgical decompression are lacking so far. Available studies focused on comparisons among surgical techniques (laminectomy vs anterior corpectomy vs posterolateral corpectomy) rather than decompressive strategies. Furthermore, little attention has been given to the source of compression [30].

In 2016 Molina et al. conducted an extensive review of the literature about clinical outcomes of only posterior approaches for symptomatic metastatic spine disease. In terms of neurological improvement, corpectomy following the transpedicular or the consto-transversectomy approach did not show better results compared to laminectomy although able to reduce the recurrence rate. However, important limitations were due to a) the extensive variation in the scales used to report outcomes; b) the small number of patients in some of the considered studies; c) overlapping of data; d) the presence, mainly, of case series and cohorts without comparison groups; More importantly, the source of compression was not considered. In the available literature, the reductive garb of the surgical approach (laminectomy vs corpectomy) has probably masked the issue given by the need to remove the compression directly from its source. With the advent of SSRS, the need for direct surgical removal of the tumor compressing the dura emerged and was considered mandatory in order to create a target for the radiation beam (also known as Separation Surgery). The use of cEBRT after surgery, although not affected by the presence of high-grade compression like in case of SSRS, should not enable the surgeon to neglect the need for a proper decompression, especially in radio-resistant tumor. In the literature, comparisons between posterior and anterior decompression have usually investigated complications, costs and quality outcomes with controversial results, and often considering only the surgical approach (laminectomy vs corpectomy). The profile of complications of more aggressive approaches could vary according to the appropriateness of surgical indication, the systemic status of the patient, and above all the skills/experience of the surgeon. This could explain why these studies reported different results leaving the debate open.

In this study surgical approaches were not considered as the focus of the investigation: the analysis was conceived according to the type of decompression of the circumference of spinal cord and, above all, the source of compression. As known, spinal metastases usually origin within the vertebral body and cord compression involves the ventral part of the sac. Furthermore, the majority of recurrence are described to origin within the vertebral body rather than from the posterior elements. Moreover, the local control obtained with cEBRT is strongly related to the tumor volume, indeed, the bigger the tumor, the lower the rate of local control [14]. This could explain why CD/AD demonstrated to be more effective in terms of local control and cEBRT was not affected by the presence of tumor, being considered effective even in the presence of high-grade compression. However, in comparison with some metastases like cervicomedullary neurinomas or pituitary adenomas, the control obtained with cEBRT was not effective in the presence of high-grade compression [29,30].

Table 2

| Type of surgery | n | % |
|-----------------|---|---|
| Posterior/Postero-lateral decompression | 17 | 20.2% |
| Anterior decompression | 19 | 22.6% |
| Circumferential decompression | 78 | 92.9% |
| Anterior Fixation | 22 | 28.2% |
| Posterior Fixation | 56 | 71.7% |
| No fixation | 22 | 7.1% |
| Complications | 8 | 11.9% |
| Blood loss(ml) (mean value) | 580.5 |
| Neurological Assessment | |
| Immediate Post-Operative Period | |
| Neurological Improvement | 64 | 76.2% |
| No Neurological Improvement | 20 | 23.8% |
| Last Follow Up Evaluation | |
| Neurological Worsening | 24 | 28.6% |
| No Neurological Worsening | 60 | 71.4% |

4. Discussion

Discussion
pression: in case of CSCC, ASCC or A-lSCC, a direct removal of the tumor responsible for the epidural impingement resulted in better clinical outcomes (Table 4). The type of decompression resulted to be a key factor in the logistic regression in order to ensure a stable neurological restoration and patients who reported a post-operative improvement were more likely to avoid a worsening in

| Immediate Post-operative Period | Neurological Improvement (%) | No Neurological Improvement (%) |
|-------------------------------|-------------------------------|-------------------------------|
| Anterior                      | 16 (94.1)                    | 1 (5.9)                       |
| Posterior/Postero-lateral     | 29 (60.4)                    | 19 (39.6)                     |
| Circumferential               | 19 (100)                     | 0 (0)                         |

| Last Follow-Up Evaluation     | Neurological Improvement (%) | No Neurological Improvement (%) |
|-------------------------------|-------------------------------|-------------------------------|
| Anterior                      | 15 (88.2)                    | 2 (11.8)                      |
| Posterior/Postero-lateral     | 26 (54.2)                    | 22 (45.8)                     |
| Circumferential               | 19 (100)                     | 0 (0)                         |

| Patients that reported neurological improvement in the immediate post-operative period | No Neurological Worsening (%) | Neurological Worsening (%) |
|---------------------------------------------|-------------------------------|----------------------------|
| Anterior                      | 14 (87.5)                    | 2 (12.5)                    |
| Posterior/Postero-lateral     | 18 (62.1)                    | 11 (37.9)                   |
| Circumferential               | 19 (100)                     | 0 (0)                       |

| Immediate Post-operative Period | Neurological Improvement (%) | No Neurological Improvement (%) |
|-------------------------------|-------------------------------|-------------------------------|
| ASCC and Al-SCC               | Neurological Improvement (%) | No Neurological Improvement (%) |
| Anterior                      | 15 (93.8)                    | 1 (6.3)                       |
| Posterior/Postero-lateral     | 11 (52.4)                    | 10 (47.6)                    |
| Circumferential               | 3 (100)                      | 0 (0)                        |

| Last Follow-Up Evaluation     | Neurological Improvement (%) | No Neurological Improvement (%) |
|-------------------------------|-------------------------------|-------------------------------|
| ASCC and Al-SCC               | Neurological Improvement (%) | No Neurological Improvement (%) |
| Anterior                      | 14 (87.5)                    | 2 (12.5)                      |
| Posterior/Postero-lateral     | 11 (52.4)                    | 10 (47.6)                    |
| Circumferential               | 3 (100)                      | 0 (0)                        |

| ASCC and Al-SCC               | Neurological Improvement (%) | No Neurological Improvement (%) |
| Anterior                      | 14 (87.5)                    | 2 (12.5)                      |
| Posterior/Postero-lateral     | 11 (52.4)                    | 10 (47.6)                    |
| Circumferential               | 3 (100)                      | 0 (0)                        |

| ASCC and Al-SCC               | Neurological Improvement (%) | No Neurological Improvement (%) |
| Anterior                      | 14 (87.5)                    | 2 (12.5)                      |
| Posterior/Postero-lateral     | 11 (52.4)                    | 10 (47.6)                    |
| Circumferential               | 3 (100)                      | 0 (0)                        |

| PSCC and Pl-SCC               | Neurological Improvement (%) | No Neurological Improvement (%) |
| Anterior                      | 1 (100)                      | 0 (0)                         |
| Posterior/Postero-lateral     | 13 (65.0)                    | 7 (35.0)                     |
| Circumferential               | 16 (100)                     | 0 (0)                        |

| Last Follow-Up Evaluation     | Neurological Improvement (%) | No Neurological Improvement (%) |
|-------------------------------|-------------------------------|-------------------------------|
| PSCC and Pl-SCC               | Neurological Improvement (%) | No Neurological Improvement (%) |
| Anterior                      | 1 (100)                      | 0 (0)                         |
| Posterior/Postero-lateral     | 12 (60.0)                    | 8 (40.0)                     |
| Circumferential               | 16 (100)                     | 0 (0)                        |
the follow-up (Table 5). As remarked by multiple studies [11,31] the pre-operative ambulatory assessment was the only factor affecting the post-operative ambulatory ability in the multivariate logistic regression, confirming that the preservation of the neurological status in a patient with cancer can not be overemphasized (Table 6).

Table 5
Neurological status at the last follow-up evaluation according to observed neurological improvement in the immediate post-operative period.

| No Neurological Worsening (%) | Neurological Worsening (%) |
|-------------------------------|---------------------------|
| Post-operative Neurological Improvement | 51 (79.7) | 13 (20.3) |
| No Post-operative Neurological Improvement | 9 (45.0) | 11 (55.0) |

Univariate Logistic Regression
Type of Decompression
Nagelkerke R-squared 0.136
Exp (B) 0.209 p value 0.004

Table 6
A) Ambulation assessment in the immediate post-operative period. The multivariate logistic regression showed that pre-operative ambulation was the only factor affecting the possibility to maintain ambulation during follow up.

| Immediate post-operative ambulation assessment | Post-operative Ambulatory (%) | No Post-operative Ambulatory (%) |
|----------------------------------------------|-------------------------------|---------------------------------|
| No Pre-operative Ambulatory | 11 (61.1) | 7 (38.9) |
| Pre-operative Ambulatory | 65 (98.5) | 1 (1.5) |

Multivariate Logistic Regression
Type of Decompression Nagelkerke R-squared 0.460
Type of Epidural Compression 1.419 0.624
Pre-operative ambulation ability 0.614 0.197

| Post-operative ambulation assessment at last follow up | Last Follow Up Ambulatory (%) | No Last Follow Up Ambulatory (%) |
|------------------------------------------------------|-------------------------------|---------------------------------|
| No-Post-operative Ambulatory | 2 (25.0) | 6 (75.0) |
| Post-operative Ambulatory | 74 (97.4) | 2 (2.6) |

Multivariate Logistic Regression
Type of Decompression Nagelkerke R-squared 0.575
Type of Epidural Compression 1.34 0.524
Pre-operative ambulation ability 2.27 0.530

5. Limitations

The retrospective nature of this study represents its main limitation. Although our results showed a strong association between circumferential decompression and better outcomes, one should investigate also the role of the improvement of standard of care for neoplastic patients through the years, as well as of technological advancements for surgical procedures. Furthermore, there is no stratification for patients according to their primitive cancer or systemic status. That said, ethical issues make it difficult the planning of an ad hoc prospective analysis and/trial, and this paper analysis could represent a solid preliminary analysis while contributing to enrich the existing knowledge.

6. Conclusion

Regardless of the approach, which should be tailored to the single patient trying to reduce at best the profile of risks, the necessity to remove the compression of the sac from its source is of paramount importance. CD/AD are associated with better neurological outcomes in case of circumferential or anterior/anterolateral compression.

Ethical committee approval

All clinical and radiological data were collected and retrospective analyzed. This study does not require any variations in patient’s treatment and no formal ethics committee approval was
required. All procedures performed for this study were in accordance with the ethical standard of author's Institution and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Data availability statement

Data not publicly available due to ethical/privacy restrictions. Due to the nature of this research, participants of this study did not agree for their data to be shared publicly, so supporting data is not available.

Funding

None.

CRediT authorship contribution statement

F. Cofano: Conceptualization, Methodology, Investigation, Supervision, Writing. G. Di Perna: Conceptualization, Formal analysis, Data curation. A. Alberti: Data curation, Formal analysis. B.M. Baldassarre: Data curation. M. Ajello: Investigation. N. Marenco: Investigation. F. Tartara: Supervision. F. Zenga: Validation. D. Garbossa: Supervision, Validation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] D. Prasad, D. Schiff, Malignant spinal cord compression, Lancet Oncol. 6 (2005) 15–24.
[2] M.G. Fehlings, A. Nater, L. Tetreault, et al., Survival and clinical outcomes in surgically treated patients with metastatic epidural spinal cord compression: results of the prospective multicenter AOSpine study, J. Clin. Oncol. 34 (2016) 268–276.
[3] O. Barzilai, I. Lauffer, Y. Yamada, et al., Integrating evidence-based medicine for treatment of spinal metastases into a decision framework: neurologic, oncologic, mechanical stability, and systemic disease, J. Clin. Oncol. 35 (2017) 2419–2427.
[4] O. Barzilai, A.L. Versteeg, C.R. Goodwin, A. Sahgal, L.D. Rhines, D.M. Scibua, et al., Association of neurologic deficits with surgical outcomes and health-related quality of life after treatment for metastatic epidural spinal cord compression, Cancer (2019).
[5] R.A. Patchell, R.A. Tibbs, W.F. Regine, R. Payne, S. Saris, R.J. Kryscio, et al., Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial, Lancet 366 (9486) (2005) 643–648.
[6] N.A. Quarishi, G. Arealis, K.M. Salem, S. Purushothamdas, K.L. Edwards, B.M. Boszczyk, The surgical management of metastatic spinal tumors based on an Epidural Spinal Cord Compression (ESCC) scale, Spine J. 15 (8) (2015) 1738–1743.
[7] T.D. Azad, K. Varshneya, A.L. Ho, A. Veeravagu, D.M. Scibua, J.K. Ratliff, Laminectomy versus corpectomy for spinal metastatic disease-complications, costs, and quality outcomes, World Neurosurg. 131 (2019) e468–e473.
[8] D. Bakar, J.E. Tanenbaum, K. Phan, V.J. Alentado, M.P. Steinmetz, E.C. Benzel, et al., Decompression surgery for spinal metastases: a systematic review, Neurosurg. Focus 41 (2) (2016) E2.
[9] C. Maccario, M.S. Spinelli, S. Mauro, C. Perisano, C. Graci, M.A. Rosa, Physiopathology of spine metastasis, Int. J. Surg. Oncol. 2011 (2011). https://doi.org/10.1155/2011/107969 107969.
[10] I. Lauffer, D.G. Rubin, E. Lis, B.W. Cox, M.D. Stubblefield, Y. Yamada, et al., The NOMS framework: approach to the treatment of spinal metastatic tumors, Oncologist 18 (6) (2013) 743–751.
[11] G. Di Perna, F. Cofano, C. Mantovani, S. Badellino, N. Marenco, M. Ajello, et al., Separation surgery for metastatic epidural spinal cord compression: A qualitative review, J. Bone Oncol. 100320 (2020).
[12] C.G. Fisher, C.P. DiPaola, T.C. Ryken, M.H. Bilsky, C.J. Shaffrey, S.H. Berven, et al., A novel classification system for spinal instability in neoplastic disease: an evidence-based approach and expert consensus from the Spine Oncology Study Group, Spine (Phila Pa 1976) 35 (2010) E1221–E1229.
[13] M.H. Bilsky, I. Lauffer, D.R. Fourney, M. Groff, M.H. Schmidt, P.P. Varga, et al., Reliability analysis of the epidural spinal cord compression scale, J. Neurosurg. Spine 13 (3) (2010) 324–328.
[14] O. Barzilai, M.K. Amato, L. McLaughlin, et al., Hybrid surgery-radiosurgery therapy for metastatic epidural spinal cord compression: a prospective evaluation using patient-reported outcomes, Neurooncol. Pract. 5 (2018) 104–113.
[15] F. Cofano, F. Zenga, M. Mammi, R. Aliteri, N. Marenco, M. Ajello, et al., Intraoperative neurophysiological monitoring during spinal surgery: technical review in open and minimally invasive approaches, Neurosurg. Rev. 42 (2) (2019) 297–307.
[16] F. Cofano, G. Di Perna, N. Marenco, M. Ajello, A. Melcarne, F. Zenga, et al., Transpedicular 3D endoscope-assisted thoracic corpectomy for separation surgery in spinal metastases: feasibility of the technique and preliminary results of a promising experience, Neurosurg. Rev. (2019).
[17] P.D. Kelly, S.L. Zuckerman, Y. Yamada, E. Lis, M.H. Bilsky, I. Lauffer, O. Barzilai, Image guidance in spine tumor surgery, Neurosurg. Rev. 43 (3) (2020) 1007–1017.
[18] F. Cofano, G. Di Perna, M. Monticelli, N. Marenco, M. Ajello, M. Mammi, et al., Carbon fiber reinforced vs titanium implants for fixation in spinal metastases: a comparative clinical study about safety and effectiveness of the new "carbon-strategy", J. Clin. Neurosci. (2020). https://doi.org/10.1016/j.jocn.2020.03.013.
[19] N. Kumar, R. Malhotra, A.S. Zaw, K. Maharajan, N. Naresh, A. Kumar, et al., Evolution in treatment strategy for metastatic spine disease: Presently evolving modalities, Eur. J. Surg. Oncol. 43 (9) (2017) 1784–1801.
[20] D.M. Scibua, R.J. Petteys, M.B. Dekutoiski, et al., Diagnosis and management of metastatic spine disease. J. Neurosurg. Spine 13 (2010) 94–108.
[21] R.H. Bartels, Y.M. van der Linden, W.T. van der Graaf, Spinal extradural metastasis: review of current treatment options, CA Cancer J. Clin. 58 (2008) 245–259.
[22] J.S. Cole, R.A. Patchell, Metastatic epidural spinal cord compression, Lancet Neurol. 7 (2008) 459–466.
[23] P.D. Patel, J.A. Canseci, N. Houlihan, A. Gabay, G. Grasso, A.R. Vaccaro, Overview of minimally invasive spine surgery, World Neurosurg. 142 (2020) 43–56 [published online ahead of print 2020 Jun 13].
[24] N. Marenco, K. Matsuikawa, M. Monticelli, M. Ajello, P. Pacca, F. Cofano, et al., Cortical bone trajectory screw placement accuracy with a patient-matched 3-dimensional printed guide in lumbar spinal surgery: A clinical study, World Neurosurg. 130 (2019) e98–e106.
[25] F. Cofano, M. Monticelli, M. Ajello, F. Zenga, N. Marenco, G. Di Perna, et al., The targeted therapies era beyond the surgical point of view: what spine surgeons should know before approaching spinal metastases, Cancer Control. (2019), https://doi.org/10.1177/1073033X19890549.
[26] M.H. Bilsky, I. Lauffer, S. Burch, Shifting paradigms in the treatment of metastatic spine disease, Spine 34 (22 suppl) (2009) S101–S107.
[27] I. Lauffer, D.G. Rubin, E. Lis, B.W. Cox, M.D. Stubblefield, Y. Yamada, et al., The NOMS framework: approach to the treatment of spinal metastatic tumors, Oncologist 18 (6) (2013) 744–751.
[28] M. Cappuzzio, A. Gasharrini, P. Van Uruk, S. Bandiera, S. Boriani, Spinal metastasis: a retrospective study validating the treatment algorithm, Eur. Rev. Med. Pharmacol. Sci. 12 (3) (2008) 155–160.
[29] F. Cofano, G. Di Perna, F. Zenga, A. Ducati, B. Baldassarre, M. Ajello, et al., The Neurology-Stability-Epidermal compression assessment: a new score to establish the need for surgery in spinal metastases, Clin. Neurosurg. Neurosurg. (2020). https://doi.org/10.1016/j.clineuro.2020.103586.
[30] H. Uei, Y. Tokuhashi, M. Masada, Analysis of the relationship between the epidural spinal cord compression (ESCC) scale and paralysis caused by metastatic spine tumors, Spine (Phila Pa 1976) 43 (8) (2018) E448–E455.
[31] D. Tateiwa, K. Oshima, T. Nakai, et al., Clinical outcomes and significant factors in the survival rate after decompression surgery for patients who were non-ambulatory due to spinal metastases, J. Orthop. Sci. 24 (2) (2019) 347–352.
[32] D. Tateiwa, K. Oshima, T. Nakai, et al., Clinical outcomes and significant factors in the survival rate after decompression surgery for patients who were non-ambulatory due to spinal metastases, J. Orthop. Sci. 24 (2) (2019) 347–352.