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ORIGINAL ARTICLE

More help than harm: surgery for metastatic spinal cord compression is associated with more favorable overall survival within a propensity score analysis

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Abstract

Purpose Indication for surgical decompression in metastatic spinal cord compression (MSCC) is often based on prognostic scores such as the modified Bauer score (mBs), with favorable prognosis suggestive of surgery and poor prognosis of non-surgical management. This study aimed to clarify if (1) surgery may directly affect overall survival (OS) aside from short-term neurologic outcome, (2) explore whether selected patient subgroups with poor mBs might still benefit from surgery, and (3) gauge putative adverse effects of surgery on short-term oncologic outcomes.

Methods Single-center propensity score analyses with inverse-probability-of-treatment-weights (IPTW) of OS and short-term neurologic outcomes in MSCC patients treated with or without surgery between 2007 and 2020.

Results Among 398 patients with MSCC, 194 (49%) underwent surgery. During a median follow-up of 5.8 years, 355 patients (89%) died. MBs was the most important predictor for spine surgery ($p < 0.0001$) and the strongest predictor of favorable OS ($p < 0.0001$). Surgery was associated with improved OS after accounting for selection bias with the IPTW method ($p = 0.021$) and emerged as the strongest determinant of short-term neurological improvement ($p < 0.0001$). Exploratory analyses delineated a subgroup of patients with an mBs of 1 point who still benefited from surgery, and surgery did not result in a higher risk of short-term oncologic disease progression.

Conclusion This propensity score analysis corroborates the concept that spine surgery for MSCC associates with more favorable neurological and OS outcomes. Selected patients with poor prognosis might also benefit from surgery, suggesting that even those with low mBs may be considered for this intervention.

Keywords Spinal metastasis · Spinal surgery · Survival · Progression · Neurologic function

Introduction

Spinal metastases occur in 40% of cancer patients, and in up to 20% of these cases further progression to symptomatic metastatic spinal cord compression (MSCC) may occur [1, 2]. While spinal decompression surgery and stabilization is an established treatment strategy for MSCC, selection of patients who will benefit from surgery is challenging in clinical practice, since any patient-individual treatment strategy must provide the maximum

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palliative and minimum operative morbidity effect [3]. In this context, the Modified Bauer score (mBs) to predict overall survival (OS) provides a rational selection basis for a proper treatment strategy based on the sum of four simple variables (assigning one point each for: no visceral metastases, no lung cancer, solitary skeletal metastases, and the tumor entities breast, kidney, lymphoma, and myeloma) [4, 5]. Recommendations range from extensive surgery for patients with beneficial prognosis (mBs: 3–4 points), limited surgery for moderate prognosis (mBs: 2 points), and non-operative supportive care for patients with poor prognosis [mBs: 0–1 point(s)] [6].

This allocation naturally results in a selection bias, as patients with a favorable prognosis prediction are more likely to be selected for surgery. While the beneficial effect of surgical decompression and stabilization on neurologic outcome in MSCC has been demonstrated in a prospective randomized setting and a meta-analysis [7, 8], and the correlation between low disease load with long time post-operative survival has been proven prospectively [9], the question whether surgery itself might directly affect clinical outcome and prognosis, probably even in patients with unfavorable mBs scores, remains unclear. As decompression surgery in MSCC is an established and recommended technique in patients with good prognosis, performing a randomized controlled trial to examine overall survival outcomes of treatment with and without spine surgery is challenging from an ethical standpoint. On the other hand, in clinical practice, patients may undergo surgery despite their mBs stratification being indicative of poor prognosis or be treated without surgery in case of beneficial prognosis. In this setting of a non-randomized treatment allocation, propensity score analysis on observational data is an accepted method to minimize the mentioned selection bias and explore which patients could directly benefit from decompressive surgery [10, 11].

While the benefit of surgery on neurologic outcomes in MSCC is less debated, an ongoing discussion revolves around potential adverse effects of spine surgery on oncologic outcomes. It is not unplausible that in a metastatic cancer patient with high burden of malignant disease, a surgical intervention might have the potential to weaken a patient's condition, which in turn might trigger disease progression [12].

Therefore, we conducted this study to clarify if (1) aside from earlier reported neurological improvement, surgery for MSCC may also directly affect OS, (2) explore whether certain patients in whom surgery is not primarily recommended based on prognostic scores might benefit from surgery, and (3) gauge putative adverse effects of surgery on short-term oncologic outcomes.

Methods

Ethics statement

This study was approved by the local Institutional Ethical Review Board (IRB) (Reference number: EK-Nr. 30-252 ex 17/18) and performed in accordance with relevant guidelines and regulations; informed consent for later retrospective analysis of their data was obtained from all participants.

Study population

All referrals ($n = 1788$) to a single orthopedic surgery department for evaluation of radiologically confirmed spinal metastases between 2007 and 2020 were retrospectively included in this study (Supplementary Fig. 1). Case history and clinical follow-up were retrieved from the hospital's intern, and associated centers' data systems using keyword identification of all written examination reports, complete follow-up on all-cause mortality for all patients' data/dates were received from insurance data. Demographic data and cancer specific medical history (first diagnosis and entity; date of any new metastasis; spinal metastasis including location, date, fracture; onset of MSCC, neurologic impairment (Frankel scale A-D) and recovery (at least Frankel scale D; or E if D initially) within the first 6 weeks of decision, mBs, date of decision and surgery and/or radiation) were collected from all patients. No patients with intradural metastases were included in this study.

MSCC and institutional standard procedure

Patients with symptomatic MSCC with neurologic impairment ($n = 398$) and timepoint of onset of symptom were identified from our data system. A decision (A) decompressive surgery with dorsal stabilization and subsequent recommendation of radiation (B) no surgery, recommendation of radiation was documented in all cases. According to our clinic internal protocol, this decision was based on the calculated mBs, time since onset of neurologic impairment, general health state, and patients' consent to surgery. Extent of surgical intervention was performed according to mBs recommendation in most cases [6]. Radiation was recommended in all MSCC cases, if residual radiation dose was available for the region involved.

Statistical methods

All statistical analyses were performed by FP with Stata (Windows version 17.0, Stata Corp., Houston, TX, USA). Continuous variables were reported as medians [25th–75th percentile] and count data as absolute frequencies (column

%). The distribution of variables between two or more other variables was assessed with rank-sum tests, χ^2-tests, and Fisher's exact tests, as appropriate. Risks of death-from-any-cause (overall survival) and progression-free survival were estimated with 1-Kaplan–Meier estimators, compared between two or more groups with log-rank tests, and modeled with uni- and multivariable Cox regression models. Risks of radiographic disease progression were estimated with competing risk cumulative incidence estimators accounting for death-from-any-cause as the competing event of interest, compared between two or more groups with Gray's test, and modeled with Fine and Gray competing risk regression models. Predictors of spine surgery were examined with logistic regression. The magnitude of difference in the distribution of variables between patients with and without spine surgery was quantified with standardized mean differences (SMDs). Propensity score analyses were performed with inverse-probability-of-treatment-weights (IPTW), and balance diagnostics were performed as previously described. The propensity score model was developed on multiply imputed data (chained equations algorithm, 10 imputation datasets, separate imputation models for continuous, binary, and ordinal variables) including all ten available variables of the dataset, whereas other analyses were done according to the complete-case principle. The full analysis code is available on reasonable request from FP (florian.posch@medunigraz.at).

Results

Study cohort

Of 1778 referrals to our department for orthopedic evaluation of radiologically confirmed spinal metastases, 398 patients had symptomatic MSCC with neurologic impairment (Table 1). Median age was 66 years [25th–75th percentile: 56–74], and 144 patients (36%) were female. The most frequent tumor entities were prostate, lung, and breast cancer. During a median follow-up of 5.8 years according to the reverse Kaplan–Meier estimator and 0.5 years according to the median of observation times, 355 patients (89%) died. This corresponded to 3-month, 6-month, 12-month, and 3-year all-cause mortality of 34% (95%CI 30–39), 51% (95%CI 46–56), 64% (95%CI 59–69), and 85% (95%CI 81–88), respectively (Supplementary Fig. 2).

Spine surgery for symptomatic MSCC with neurologic impairment

One-hundred-ninety-four patients (49%) were treated with spine surgery, whereas the remaining 204 patients were treated non-surgically. The most important predictor of spine surgery was the mBs; twenty-eight percent, 34%, 52%, 64%, and 81% of patients with mBs of 0, 1, 2, 3, and 4 points were treated with surgery, respectively ($p < 0.0001$). Other predictors of spine surgery were younger age, a pathologic fracture, and selected tumor entities (e.g., breast cancer, renal cancer, endocrine cancer), whereas brain metastases or a new metastatic site in the 3 prior months were associated with lower odds of spine surgery (Table 2).

Predictors of overall survival outcomes

A low mBs emerged as the strongest predictor for an adverse survival experience. In detail, 6-month mortality estimates were 82%, 75%, 46%, 32%, and 0% in patients with mBs of 0, 1, 2, 3, and 4 points, respectively (log-rank $p < 0.0001$, Fig. 1). In further univariable analysis, factors associated with more favorable survival were younger age, selected tumor entities (e.g., breast cancer, sarcoma, and renal cell cancer), no brain metastases, no new metastatic sites within the preceding 3 months, and treatment with spine surgery (Table 3).

Overall survival outcomes with spine surgery versus non-surgical management–Propensity score analysis

Patients who were treated with spine surgery had more favorable survival outcomes than patients being treated non-surgically (6-month mortality: 46% vs. 81%, log-rank $p < 0.0001$, Hazard ratio (HR) = 0.43, 95%CI 0.34–0.54, $p < 0.0001$, Fig. 2A). However, spine surgery was associated with many favorable prognostic factors for survival such as a higher mBs (Table 1). The association between spine surgery and lower mortality prevailed after accounting for the mBs in stratified analysis (stratified log-rank $p < 0.0001$) as well as multivariable analysis (HR for all-cause death for spine surgery adjusted for the mBs = 0.57, 0.45–0.72, $p < 0.0001$). Nonetheless, we still anticipated bias in comparing outcomes between patients with and without spine surgery due to the non-random indication of this procedure in our retrospective study. To control this anticipated selection bias, we performed a propensity score analysis. The propensity score model (Supplementary Table 1) included all ten variables available to us, and the resulting propensity score covered the whole probability range from 0 to 1 (Supplementary Fig. 3A). The resulting IPTW (Supplementary Fig. 3B) led to a considerable reduction in standardized mean differences and statistical significances between patients who were treated with and without spine surgery including in the most important prognostic variables such as the mBs and brain metastases (Supplementary Fig. 4, Table 1). In IPTW-analysis, spine surgery was still associated with more favorable survival outcomes (IPTW-adjusted log-rank $p = 0.021$, Fig. 2B, IPTW-Adjusted HR for death with spine surgery = 0.68, 0.49–0.94, $p = 0.021$).

Table 1 Baseline characteristics of the study population ($n = 398$)

Variable	n (%miss.)	Overall ($n = 398$)	No surgery ($n = 204$)	Surgery ($n = 194$)	p	p_{IPTW}
Age (years)	392 (2%)	66 [56–74]	67 [57–75]	64 [56–73]	**0.040**	0.810
Female sex	398 (0%)	144 (36%)	65 (32%)	79 (41%)	0.067	0.723
Tumor entity	398 (0%)	/	/	/	0.093	0.654
Melanoma	/	13 (3%)	9 (4%)	4 (2%)	0.261	0.901
Breast	/	62 (16%)	26 (13%)	36 (19%)	0.110	0.788
Lung	/	72 (18%)	47 (23%)	25 (13%)	**0.009**	0.665
GI	/	28 (7%)	16 (8%)	12 (6%)	0.518	0.479
ENT	/	4 (1%)	2 (1%)	2 (1%)	0.999	0.836
Sarcoma	/	10 (3%)	2 (1%)	8 (4%)	0.057	**0.030**
Renal	/	42 (11%)	17 (8%)	25 (13%)	0.139	0.359
Prostate	/	84 (21%)	47 (23%)	37 (19%)	0.332	0.503
Lymphoma/leukemia	/	8 (2%)	4 (2%)	4 (2%)	0.999	0.109
MUO	/	18 (5%)	10 (5%)	8 (4%)	0.709	0.750
Gynecologic	/	4 (1%)	2 (1%)	2 (1%)	0.999	0.644
Myeloma	/	27 (7%)	10 (5%)	17 (9%)	0.126	0.508
Endocrine	/	8 (2%)	2 (1%)	6 (3%)	0.133	0.113
Bladder/urothelial	/	10 (3%)	6 (3%)	4 (2%)	0.752	0.810
Others	/	8 (2%)	4 (2%)	4 (2%)	0.999	0.369
Modified Bauer score	349 (12%)	/	/	/	**< 0.0001**	0.973
0 points	/	39 (11%)	28 (16%)	11 (6%)	**0.007**	0.435
1 point	/	91 (26%)	60 (34%)	31 (18%)	**0.001**	0.727
2 points	/	125 (36%)	60 (34%)	65 (38%)	0.402	0.984
3 points	/	73 (21%)	26 (15%)	47 (27%)	**0.004**	0.854
4 points	/	21 (6%)	4 (2%)	17 (10%)	**0.006**	0.510
Pathologic fracture	321 (19%)	133 (41%)	56 (34%)	77 (50%)	**0.003**	0.629
Brain metastases	398 (0%)	33 (8%)	28 (14%)	5 (3%)	**< 0.0001**	0.983
Metastasis location: cervical spine	363 (9%)	136 (37%)	75 (39%)	61 (36%)	0.505	0.849
Metastasis location: thoracic spine	390 (2%)	317 (81%)	163 (81%)	154 (81%)	0.922	0.952
Metastasis location: lumbar spine	380 (10%)	267 (70%)	147 (74%)	120 (67%)	0.146	0.964
Extravertebral bone metastases	337 (15%)	180 (53%)	99 (61%)	81 (47%)	**0.009**	0.826
New metastatic site within 3 months	398 (0%)	164 (41%)	99 (49%)	65 (34%)	**0.002**	0.740
Time between cancer diagnosis and decision ≥ 2 years (= Metachronous interval)	398 (0%)	173 (43%)	87 (43%)	86 (44%)	0.735	0.884

Distribution overall and by spine surgery status. Continuous variables (e.g., age) are reported as medians [25th–75th percentile], whereas count data (e.g., female sex) are reported as absolute frequencies (%). n (%miss.) report the number of patients with fully observed data for the respective variable (% missing)

p values < 0.05 are indicated in bold font

p values from rank-sum tests; χ^2 Tests, and Fisher's exact tests, as appropriate; P_{IPTW} p values obtained by linear regression and univariable logistic regression after weighting these models with the inverse probability of treatment weight (IPTW); *GI* Gastrointestinal; *ENT* Ear Nose Throat; *MUO* Metastasis of unknown origin

Subanalysis–Survival outcomes analyses by modified Bauer score

In subanalysis, spine surgery appeared to be associated with favorable overall survival across all mBs groups except in those patients with a mBs of 0 points (p for interaction = 0.058, Fig. 3). Also, in patients with a mBs of 1 point ($n = 91$), patients who were treated with spine surgery ($n = 31$) experienced a more favorable OS prognosis than patients not treated with spine surgery (1-year mortality: 63% vs. 92%, log-rank $p = 0.0003$, Fig. 4). This suggested that there may be a subgroup within this mBs group that may benefit from spine surgery. To further delineate those patients, we explored predictors of OS in patients with an mBs of 1 point (Table 4). Here, lower age, female sex, non-genitourinary malignancies, and no new metastatic sites within the preceding 3 months emerged as variables

Table 2 Univariable predictors of spine surgery ($n = 398$)

Variable	Odds ratio (OR)	95%CI	*p*
Age (per 5 years increase)	0.92	0.85–1.00	**0.043**
Female sex	1.47	0.97–2.22	0.067
Tumor entity	/	/	/
Melanoma	0.84	0.23–2.99	0.782
Breast	2.60	1.29–5.24	**0.007**
Lung	Ref.	Ref.	Ref.
GI	1.41	0.58–3.44	0.450
ENT	1.88	0.25–14.16	0.540
Sarcoma	7.52	1.48–38.14	**0.015**
Renal	2.76	1.26–6.06	**0.011**
Prostate	1.48	0.77–2.83	0.236
Lymphoma/leukemia	1.88	0.43–8.16	0.399
MUO	1.50	0.53–4.29	0.446
Gyne	1.88	0.25–14.16	0.540
Myeloma	3.20	1.27–8.02	0.540
Endocrine	5.64	1.06–30.03	**0.043**
Bladder/urothelial	1.25	0.32–4.86	0.744
Others	1.88	0.43–8.16	0.399
Modified Bauer Score	/	/	/
0 points	Ref.	Ref.	Ref.
1 point	1.32	0.58–2.99	0.513
2 points	2.76	1.26–6.02	**0.011**
3 points	4.60	1.97–10.72	**< 0.0001**
4 points	10.82	2.97–39.43	**< 0.0001**
Pathologic fracture	1.98	1.26–3.11	**0.003**
Brain metastases	0.17	0.06–0.44	**< 0.0001**
Metastasis location: cervical spine	0.87	0.56–1.33	0.505
Metastasis location: thoracic spine	1.03	0.62–1.71	0.922
Metastasis location: lumbar spine	0.72	0.46–1.12	0.146
Extravertebral bone metastases	0.56	0.37–0.87	**0.0009**
New metastatic site within 3 months	0.53	0.36–0.80	**0.002**
Time between cancer diagnosis and decision ≥ 2 years	1.07	0.72–1.59	0.735

Data were obtained with univariable logistic regression models

p values < 0.05 are indicated in bold font

OR Odds ratio; *95%CI* 95% confidence interval; *p* Wald test *p* value; *Ref.* Reference category; *GI* Gastrointestinal; *ENT* Ear Nose Throat; *MUO* Metastasis of unknown origin

for delineating patients with an mBs of 1 point and a more favorable OS prognosis.

Subanalysis–Progression of disease after surgery

One-hundred-and-five patients experienced radiographic disease progression after spine surgery. The risk of radiographic disease progression was significantly higher in patients undergoing spine surgery than in patients treated without spine surgery (6-month competing risk cumulative incidences: 20.9% vs. 11.8%, Gray's test $p = 0.016$, Supplementary Fig. 5A), and this association weakened after adjusting for the mBs (Subdistribution hazard ratio (SHR) for radiographic disease progression with spine surgery adjusted for mBs = 1.51, 0.86–2.64, $p = 0.151$). Given the more favorable OS with spine surgery reported above, this association likely indicated reverse causality. We therefore performed a joint analysis of radiographic progression and mortality [i.e., progression-free survival (PFS)], in which spine surgery was associated with more favorable PFS (6-month risk of radiographic progression or death: 46.4% vs. 74.9%, log-rank $p < 0.0001$, HR for radiographic progression or death with spine surgery = 0.45, 0.34–0.58, $p < 0.0001$, Supplementary Fig. 5B).

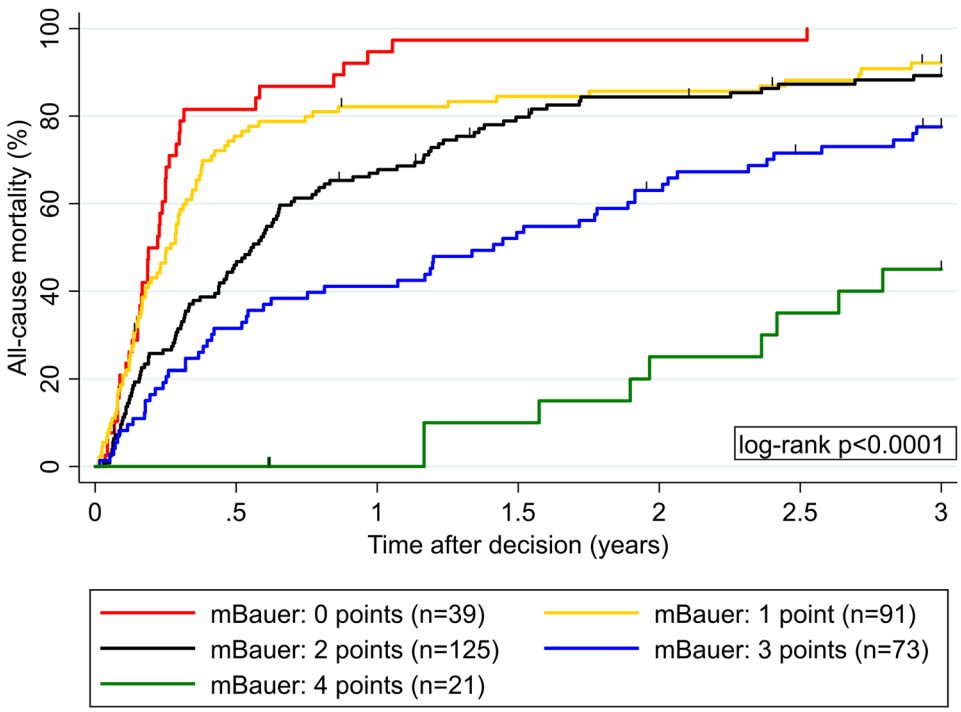

Fig. 1 Risk of death-from-any-cause according to the modified Bauer score. Curves were obtained with 1-Kaplan–Meier estimators. Vertical ticks on the curves represent censored observations. The modified Bauer score externally validates as a strong prognostic factor for mortality in patients with malignant spinal cord compression

Exploratory analysis–Short-term neurologic outcome

A subset of 71% of our cohort ($n=281$) had data on short-term neurologic outcome available (described in the Methods section). Here, any neurologic improvement was seen in 126 (75%) of the 168 patients undergoing spine surgery, and 21 (19%) of the 113 patients treated without spine surgery (χ^2 $p<0.0001$). Spine surgery and the mBs were the strongest determinants of neurologic improvement (Fig. 5, Supplementary Table 2).

Discussion

This study was motivated by the current uncertainty regarding the potential beneficial or detrimental effect of spine surgery for MSCC patients beyond the established positive effect on immediate neurological improvement. We sought to clarify this question performing an IPTW analysis on the largest cohort of MSCC patients to date, with comparable characteristics to earlier published cohorts concerning distribution of tumor entities, localization of spinal metastasis, incidence of MSCC and overall survival [2, 4]. Similar to earlier publications [4], the mBs consistently validated as an accurate tool for mortality risk stratification of MSCC patients in our cohort. Notably, our data revealed that a higher mBs was also prognostic for improved short-term neurologic outcome, externally validating the mBs as a solid tool for both assessing short-term overall survival and potential neurologic improvement, irrespective of surgical management in patients with MSCC.

As intended by this study, aside from earlier reported neurological improvement [8], our results from the IPTW analysis suggest for the first time that surgical decompression and stabilization in MSCC are associated with improved OS. Our analysis further suggests this positive OS effect even in certain patients in whom surgery is not primarily recommended based on pre-operative mBs.

A possible explanation for this finding might be the correlation of recent immobilization with pulmonary embolism and increased mortality [13]. Additionally, oncologists often indicate antineoplastic therapy based on performance status, wherefore patients with low Karnofsky indices or high Eastern Cooperative Oncology Group (ECOG) performance scores are not considered candidates for further chemotherapy [14]. Consequently, a better health status resulting from decompressive spine surgery may lead to a higher dose-density of oncologic therapy.

Although the "tumor-debulking" effect of decompressive spine surgery is likely limited, an OS benefit of spine surgery is also conceivable considering the recent literature on improved OS with metastasectomy in colorectal cancer [15] soft tissue sarcoma [16] and renal cell carcinoma [11] as well as the OS benefit of stereotactic radiotherapy in oligometastatic cancers [17].

Coming to the question, which factors beyond the mBs might still lead to a benefit from surgery in terms of improved OS, our analysis suggests that younger patient age, non-genitourinary malignancies, and no brain metastasis or

Table 3 Univariable predictors of overall survival ($n = 398$)

Variable	Hazard ratio (HR)	95%CI	*p*
Age (per 5 years increase)	1.07	1.03–1.12	**0.002**
Female sex	0.81	0.64–1.01	0.064
Tumor entity	/	/	/
Melanoma	1.05	0.57–1.95	0.869
Breast	0.43	0.30–0.62	**< 0.0001**
Lung	Ref.	Ref.	Ref.
GI	1.25	0.80–1.96	0.333
ENT	1.02	0.37–2.81	0.967
Sarcoma	0.20	0.08–0.49	**< 0.0001**
Renal	0.41	0.27–0.62	**< 0.0001**
Prostate	0.54	0.39–0.76	**< 0.0001**
Lymphoma/leukemia	0.08	0.02–0.34	**0.001**
MUO	1.10	0.64–1.87	0.734
Gyne	1.85	0.67–5.08	0.233
Myeloma	0.26	0.15–0.45	**< 0.0001**
Endocrine	0.38	0.16–0.88	**0.024**
Bladder/urothelial	1.69	0.87–3.30	0.122
Others	0.47	0.20–1.09	0.079
Modified Bauer score	/	/	/
0 points	Ref.	Ref.	Ref.
1 point	0.60	0.41–0.89	**0.011**
2 points	0.41	0.28–0.60	**< 0.0001**
3 points	0.25	0.16–0.38	**< 0.0001**
4 points	0.09	0.04–0.19	**< 0.0001**
Pathologic fracture	0.95	0.74–1.22	0.692
Brain metastases	2.59	1.78–3.77	**< 0.0001**
Metastasis location: cervical spine	1.07	0.85–1.35	0.579
Metastasis location: thoracic spine	0.94	0.71–1.24	0.651
Metastasis location: lumbar spine	1.28	1.00–1.63	0.051
Extravertebral bone metastases	1.48	1.16–1.87	**0.001**
New metastatic site within 3 months	1.36	1.10–1.70	**0.006**
Time between cancer diagnosis and decision ≥ 2 years	1.12	0.90–1.39	0.312
Spine surgery	0.43	0.34–0.54	**< 0.0001**

Data were obtained with univariable Cox regression models

p values < 0.05 are indicated in bold font

HR Hazard ratio; *95%CI* 95% confidence interval; *p* Wald test *p* value; *Ref.* Reference category; *GI* Gastrointestinal; *ENT* Ear Nose Throat; *MUO* Metastasis of unknown origin

new metastatic sites within the last 3 months additionally determined the OS experience. The detrimental OS effect of brain metastasis and short time interval since last tumor progression is in line with earlier published data from a retrospective multivariate analysis on 62 patients [18].

These results demonstrate that several variables inform prognosis beyond the mBs, delineating a subgroup of patients with poor survival prediction, who still had a benefit from surgery in terms of improved OS, most significantly when they were young, female, had no genitourinary malignancy, and have had no new metastatic sites within the preceding 3 months. As an early surgical intervention within 24 h of MSCC diagnosis is an established factor for improved neurologic outcome [2], our results may also help refining surgical indication in this acute setting where comprehensive staging exams are often not available, and thus, a full mBs variable set cannot be computed.

In summary, our data suggest that the weight of prognostic considerations for the indication of decompressive surgery in MSCC may be reduced, especially in the acute

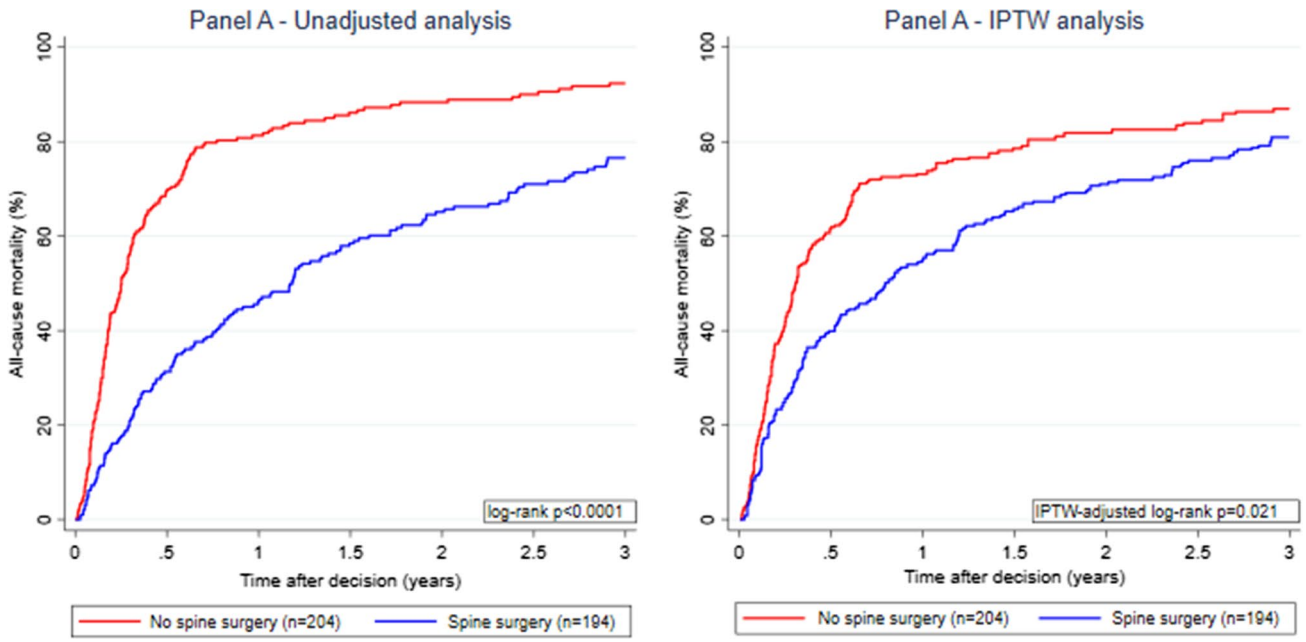

Fig. 2 Risk of death-from-any-cause according to spine surgery—Unadjusted and propensity score analysis results. Panel **A**–Unadjusted 1-Kaplan–Meier analysis. Panel **B**–1-Kaplan–Meier analysis with inverse probability of treatment weighting (ITPW, i.e., propensity score analysis. Spine surgery emerged as a predictor of a more favorable survival experience in both unadjusted analysis (Panel **A**) and after controlling for selection bias with propensity score analysis (Panel **B**)

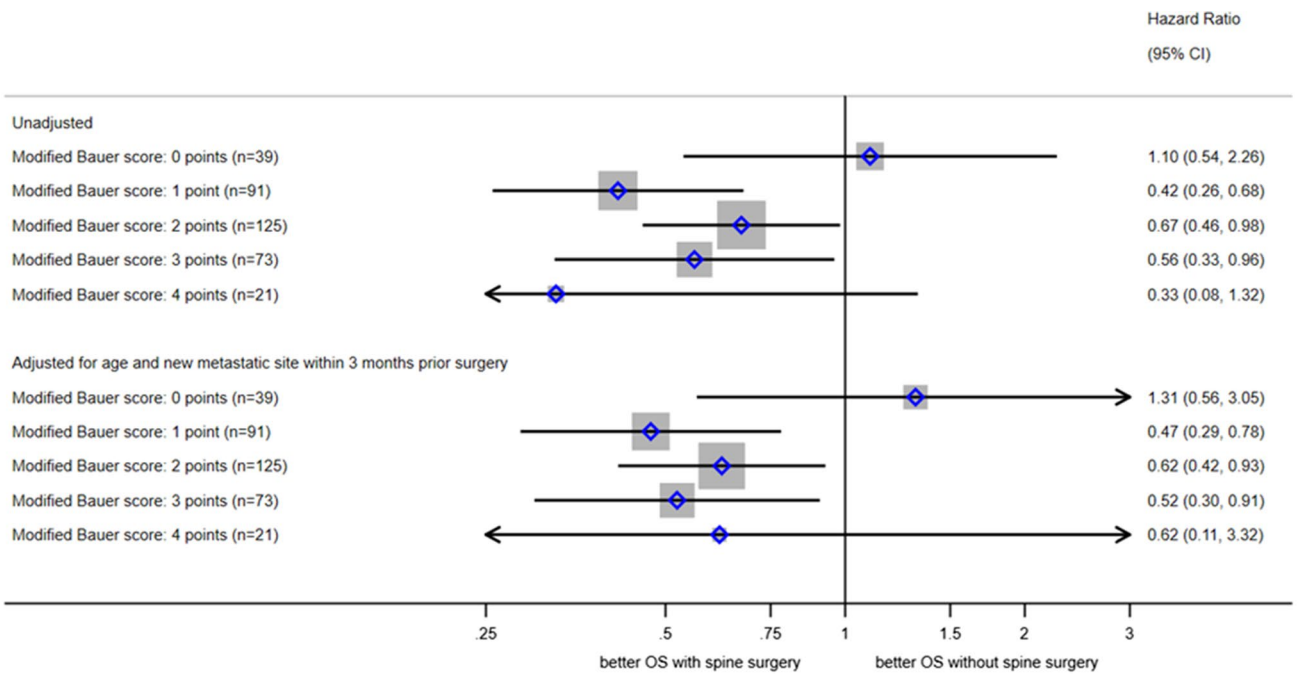

Fig. 3 Associations of spine surgery with death-from-any-cause across subgroups of the modified Bauer score. Data represent hazard ratios with 95% confidence intervals from Cox regression models. The upper panel is from an unadjusted analysis, and the lower panel from a multivariable analysis adjusting for age and any new metastatic site within 3 months prior decision. Blue diamonds are hazard ratios, and the grey boxes around these diamonds are proportional in size to the number of patients in that modified Bauer score group. The results show that spine surgery is associated with a more favorable survival experience in all modified Bauer score subgroups except the group with a modified Bauer score of 0 points

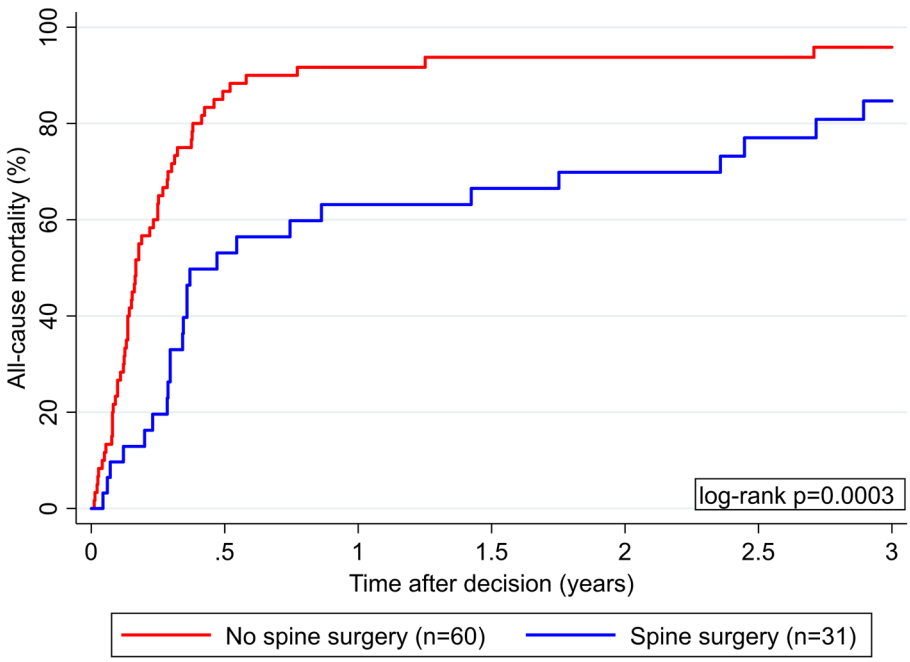

Fig. 4 Risk of death-from-any-cause according to spine surgery in patients with a modified Bauer score of 1 point ($n=91$). Curves are from 1-Kaplan–Meier estimators. The figure shows that spine surgery is associated with lower risk of death-from-any-cause within the subgroup of patients with a modified Bauer score of 1, suggesting that selected patients with a modified Bauer score of 1 may derive some overall survival benefit from spine surgery

Table 4 Univariable predictors of overall survival in the subset of patients with a modified Bauer score of 1 point ($n=91$)

Variable	Hazard ratio (HR)	95%CI	*p*
Age (per 5 years increase)	1.10	1.00–1.21	**0.040**
Female sex	0.56	0.34–0.92	**0.021**
Tumor entity	/	/	/
Lung	Ref.	Ref.	Ref.
GU	2.24	1.20–4.17	**0.011**
Others	1.50	0.89–2.54	0.126
Pathologic fracture	1.04	0.64–1.68	0.880
Brain metastases	1.27	0.65–2.47	0.480
New metastatic site within 3 months	1.69	1.08–2.65	**0.021**
Time between cancer diagnosis and decision ≥ 2 years	1.16	0.74–1.81	0.513
Spine surgery	0.42	0.26–0.68	**< 0.0001**

Data were obtained with univariable Cox regression models. The tumor entity variable had to be simplified into a three-category variable due to low numbers of individual tumor entities that would have precluded statistical modeling

p values < 0.05 are indicated in bold font

HR Hazard ratio; *95%CI* 95% confidence interval; *p* Wald test *p* value; *Ref.* Reference category; *GU* Genitourinary

setting. This is in line with recent studies, suggesting baseline performance status should take priority over expected survival in the surgical decision-making process [3, 19]. Other authors, reporting rapid improvement of quality of life and pain relief following spine surgery for MSCC, sustaining for up to 2 years after surgery [20, 21], may also support this approach.

Finally, we aimed to address the ongoing discussion concerning the impact of surgical stress on tumor progression and promotion of new metastases as possible contradictors for surgical intervention in palliative patients [12, 22]. Although the risk of disease progression was significantly higher in patients undergoing spine surgery, our data indicate that this is caused by reverse causality, due to more favorable overall survival and more staging examinations performed. Indeed, a joint analysis of progression and mortality revealed that spine surgery was associated with even more favorable PFS, indicating no significant tumor-promoting effect of surgery in our MSCC cases.

One main limitation of our study is that in clinical practice, besides mBs, additional factors influence treatment decision whether decompressive surgery is indicated in acute MSCC or not. These factors may be measurable, such as burden of disease, poor performance status, severe comorbidities (e.g., renal/lung/cardiac function, dementia, anticoagulation therapy), and inoperability of a lesion, or unmeasurable, such as "clinical gestalt." As with all retrospective studies, also, our analysis may have been affected by an omission of these measured or unmeasured variables, which may have led to an over- or underestimation of the "effect" of surgery on OS and neurologic outcomes. This, in addition to the single center design of this study limits generalizability of our results. Due to the retrospective design of this study, we could solely display Frankel scale as functional postoperative performance status measurement. Since recommended radiation therapy was frequently performed

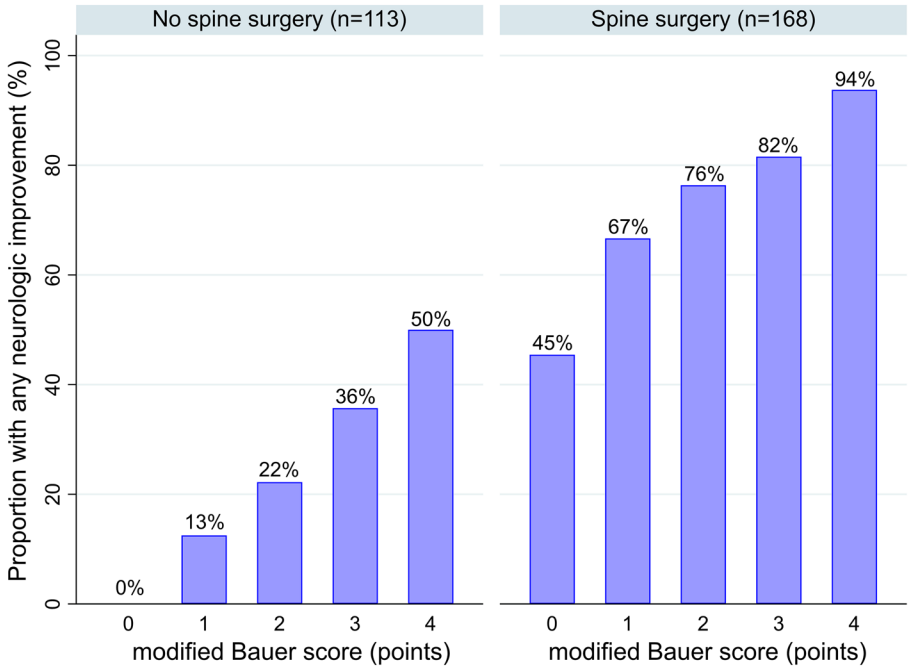

Fig. 5 Proportion of patients with any neurologic improvement—Distribution by spine surgery status and modified Bauer score. Data were only available for a subset of $n=281$ patients. The figure shows that spine surgery is associated with a higher proportion of patients with neurologic improvement, and higher-modified Bauer score is associated with a higher probability of neurologic improvement

in external centers, we could not record a complete retrospective follow-up of patients receiving radiotherapy in their remaining lifetime.

Additional studies need to be done on quality of survival rather than just survival.

Conclusion

Our results suggest that the beneficial effect of decompressive surgery in patients with MSCC is not exclusively limited to neurological symptoms, as it is also associated with more favorable OS within a propensity score analysis. Notably, we observed that selected cases with a predicted poor prognosis according to the mBs might also benefit from surgery, and these patients can be delineated based on four clinical variables. Furthermore, no convincing evidence was found that surgical intervention in MSCC impairs oncologic outcomes in terms of PFS. In summary, these results support a more liberal threshold toward a surgical approach in MSCC. Further prospective studies with additional focus on quality of life should be conducted to confirm this approach.

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Declarations

Conflict of interest The authors declare no competing financial interests. No external source of funding was used in this study.

Ethical approval This study was approved by the Institutional Ethical Review Board (Reference number: 30-252 ex 17/18) and performed in accordance with relevant guidelines and regulations.

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