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ORIGINAL ARTICLE

Application of the NSE score (Neurology-Stability-Epidural compression assessment) to establish the need for surgery in spinal metastases of elderly patients: a multicenter investigation

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Abstract

Purpose This retropective multicentric study aims to investigate the clinical applicability of the NSE score in the elderly, to verify the role of this tool as an easy help for decision making also for this class of patients.

Methods All elderly patients (> 65 years) suffering from spinal metastases undergoing surgical or non-surgical treatment at the authors' Institutions between 2015 and 2022 were recruited. An agreement group (AG) and non-agreement group (NAG) were identified accordingly to the agreement between the NSE score indication and the performed treatment. Neurological status and axial pain were evaluated for both groups at follow-up (3 and 6 months). The same analysis was conducted specifically grouping patients older than 75 years.

Results A strong association with improvement or preservation of clinical status ($p < 0.001$) at follow-up was obtained in AG. The association was not statistically significant in NAG at the 3-month follow-up (p 1.00 and 0.07 respectively) and at 6 months (p 0.293 and 0.09 respectively). The group of patients over 75 years old showed similar results in terms of statistical association between the agreement group and better outcomes.

Conclusion Far from the need or the aim to build dogmatic algorithms, the goal of preserving a proper performance status plays a key role in a modern oncological management: functional outcomes of the multicentric study group showed that the NSE score represents a reliable tool to establish the need for surgery also for elderly patients.

Keywords Spinal metastases · NSE score · Separation surgery · Spinal instability · Epidural compression

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Introduction

Both general human lifespan and that of patients with neoplastic disease increased in the last decades, together with the advancements in global health care and treatments for cancer [1]. Therefore, many surgical treatment paradigms shifted in order to re-consider the necessity of care in elderly patients [2].

In these terms, since spine is one of the main locations of metastases in human malignancies, the burden of spinal metastatic disease in elderly patients has markedly grown for spine surgeons, radiotherapists and oncologists [3–5]. On the one hand there is the need to avoid surgical complications which could result in fatal outcomes in frail patients; on the other hand, the necessity to ensure a proper local control even for years had to be taken into account nowadays because of extended life expectancy and of new technologies and innovations for cancer therapy [6–10].

In 2020 a new score (NSE score) was proposed to assess the need for surgery and validated in adult population suffering from spinal metastases (Fig. 1) [11]. This score analyzed three main points: neurological assessment, stability of the spine and epidural compression in patients suitable for surgery according to American Society of Anaesthesiologists (ASA) score < 4 and the Eastern Cooperative Oncology Group (ECOG) score < 3. The results of the retrospective application of the score showed how patients with agreement presented the best clinical outcomes in terms of neurological status and axial pain, even in the absence of histological diagnosis before treatment and without considering survival estimation. However, its efficacy in an elderly patient population that may present to surgeon's attention with multiple comorbidities, alterations in bone metabolism, and a more fragile condition remains undefined.

This multicentric study aims to investigate the clinical applicability of the NSE score in the elderly, to verify the role of this tool as an easy help for decision making also for these patients and then to strengthen evidence about modern milestones in the assessment and treatment of spinal metastatic disease.

Neurology		**S**tability *SINS score*		**E**pidural compression *ESCC scale (Bilsky Scale)*	
No deficits or Complete cord >72h	0	SINS 0-6 (Stable)	0	Types 0-1a-1b	0
Non motor radicular	1	SINS 7-12 (Potentially Unstable)	3	Type 1c	1
Motor Radicular or Mechanic radicular	3	SINS 13-18 (Unstable)	5	Type 2	3
Complete cord <72h	4			Type 3	3
Incomplete cord or Cauda Equina Syndrome	5				
ASA<4; ECOG<3					
0-2 NO SURGERY		**3-4 GREY ZONE**		**5+ SURGERY**	

Fig. 1 The NSE score

Patients and methods

This is a retrospective multicentric observational study analyzing data of elderly patients suffering from spinal metastases undergoing surgical or non-surgical treatment at the authors' Institutions between 2015 and 2022. Patients were treated according to general principles of care during the study period after multidisciplinary evaluations, following also surgical or patients' preferences [11–13]. An informed consent was signed for clinical and surgical procedures. A specific consent was not required for this study and Institutional Review Board approval was not sought due to the retrospective nature of the study.

The primary goal of surgery was the restoration or the preservation of patients' neurological status and their related quality of the life for the remaining lifetime. For this reason, the analysis evaluated functional outcomes while no analysis has been made on overall survival.

The inclusion and exclusion criteria were defined as follow:

Inclusion criteria

- Age ≥ 65 years [14];
- A diagnosis of a malignant neoplasm with a treated location of spinal metastases, including both solid and hematopoietic tumors;
- Minimum follow up of 3 months;
- ASA < 4 and for patients who underwent surgery.
- ECOG < 3 based on clinical condition before the onset of symptoms related to spinal cord compression.
- Complete availability of pre-operative radiological data (CT and MRI) evaluated by expert neurosurgeons and radiologists.
- Complete availability of clinical data during post-operative period and follow-up.

Exclusion criteria

- Patients suffering from traumatic and/or osteoporotic fractures or other pre-existing conditions that could impair neurological evaluation (i.e., neuropathies, musculoskeletal disorders, brain events).
- Occurrence during follow-up of post-radiations and/or post-systemic treatment complication that could impair post-surgical evaluation (i.e., infections, myocardial infarction, venous thromboembolism, kidney failure, pulmonary diseases, liver failure);
- pre-existing conditions or occurrence after treatment of events able to influence the neurological evaluation of the patient (neurological diseases, traumatic/pathological vertebral fractures at other levels, neuropathies, brain traumatic or non-traumatic events), and/or of bony events able to compromise the evaluation of axial radicular pain (spine traumatic or pathological fractures at other levels, skeletal metastases);
- Presence of more than 1 spinal metastases with high grade epidural compression and/or with Spinal Instability Neoplastic Score (SINS) > 6 [15].

Data collection

Data included: sex, age, histology of primary tumor, pre-operative and post-operative ECOG score, pre-operative and post-operative pain assessment, anesthesiological risk evaluation according to ASA classification, pre-operative and post-operative neurological evaluation, need for surgical treatment according to Neurological Stability Epidural compression (NSE) score, stability evaluation according to SINS score, the entity of epidural compression according to the Epidural Spinal Cord Compression scale (ESCC or Bilsky scale) [16], the location of compression, type of surgical decompression, type of fixation when performed and clinical and radiological evaluation at follow up.

NSE score

For a detailed description of the score and its rationale the authors remind to its first validation study [11]. The score was built on three main items: clinical neurological status, spine stability, and epidural compression evaluation. Neurological status was graded between 0 and 5 in order to classify conditions in ascending order of severity but taking into account a potential recoverability (Fig. 1). Stability was evaluated according to the SINS score [15], given more points to overt unstable spine requiring fixation. Epidural compression was classified according to the ESCC scale, in ascending order of severity with risk of neurological deficit and necessity of at least separation surgery. Indications according to NSE score are summarized as follows:

- **NSE score < 3**: surgery is not recommended.
- **NSE score of 3 or 4** identified a grey zone in which both surgery or radiation/systemic treatments alone could be considered, depending above all on the type of tumor (if known), availability of tools like SRS, clinical and general status [11].
- **NSE score > 5**: surgery should be required.

Grouping, neurological status and pain assessment

Firstly, patients were divided into two groups according to the agreement between the NSE score indication and the performed treatment; therefore, the agreement group (AG) and the non-agreement group (NAG) were identified. The two groups were separately evaluated according to both neurological and axial pain status before and after the treatment at follow up (3 and 6 months). The same analysis was made for patients in the grey zone (NSE score of 3 or 4). The same evaluation was then made further stratifying the study population on patients older than 75 years.

Neurological status during follow up was considered as stable, improved or worsened, on the basis of strength increase or decrease of minimum 1 point on the MRC scale at at least 1 limb. Pain control, instead, was defined with NRS scale, considering the use of drugs as well in order to mitigate potential subjective bias given by the fluctuation of cancer pain and according to the WHO Analgesic Ladder [17]. Thus, the following categories were considered: (a) worsened assuming opioids; (b) improved assuming opioids; (c) worsened without opioids; (d) improved without opioids; (e) pain relief; (f) stable. Neurological status and pain assessments were both analyzed at 3 and at 6 months after treatment in both AG e NAG groups.

The same analysis was then performed in the group of patients aged over 75 years old.

Table 1 Population demographics and preoperative characteristics

Overall ($N = 101$)		
Sex	Female	33 (32.7%)
	Male	68 (67.3%)
Age at surgery	Mean (SD)	74.2 (4.7)
	Range	65.0–86.0
Elder type	Young Elderly	57 (56.0%)
	Old Elderly	44 (44.0%)
ASA Score	1	1 (1.0%)
	2	54 (53.5%)
	3	46 (45.5%)
ECOG PS	0	12 (11.9%)
	1	39 (37.6%)
	2	50 (49.5%)
Involved Spine segment	Cervical	12 (11.9%)
	Cervico-thoracic	5 (5.0%)
	Thoracic	47 (46.5%)
	Thoraco-lumbar	14 (13.9%)
	Lumbo-sacral	16 (15.8%)
SINS Score	Stable	30 (30.0%)
	Potentially Unstable	57 (57.0%)
	Unstable	13 (13.0%)
ESCC Grade	Low Grade	45 (48.0)
	High Grade	52 (52.0)
Clinical Status at Diagnosis	Neurological Deficit	49 (48.5%)
	Mechanical Pain	79 (79.0%)
NSE Score	No Surgery	31
	Grey Zone	4
	Surgery	65

Statistical analysis

Descriptive statistics were reported as 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. Statistical significance was defined with a p-value < .05. All statistical analyses were performed using Jamovi (The jamovi project (2021)". jamovi. (Version 2.2) [Computer Software]. Retrieved from https://www.jamovi.org).

Results

Descriptive results

A total number of 101 patients (68 M 33 F) met the inclusion criteria. The most common reason for exclusion was the lack of all needed data for the analysis (31/152). Mean age was 74 years (SD 4.7; range 65–86). All the descriptive data are summarized in Table 1. The most common type of tumor was non-small cell lung cancer (NSCLC) (26.7%), while the majority of remaining patients suffered from prostate cancer, breast cancer and myeloma (respectively 17.8%, 14.9% and 10.9%).

The most common location was the thoracic spine (46.5%). Patients were mainly evaluated as ASA 2 and ECOG 2 (respectively 53.5% and 48.5%). A total number of 49 patients (48.5%) had a neurological impairment before treatment. According to the SINS score, the majority of patients were potentially unstable (57%) while only the 13% resulted stable. A total number of 52 patients had high grade ESCC. 79 patients complained mechanical axial/radicular pain. Surgical treatment was required for 50 patients and, specifically, decompression only or fixation followed by posterior-lateral or circumferential decompression were the most common procedures (Table 2) [18].

An agreement between the NSE score and the treatment was recorded in 78% of patients. In case of non-agreement, the patient's preference was the most common reason for a non-surgical strategy. At last follow-up, respectively 84% and 70.1% of patients did not show a neurologic and mechanical pain worsening.

Table 2 Treatment specification and postoperative characteristics

Overall ($N = 101$)		
NSE Score	No Surgery	31
	Grey Zone	4
	Surgery	65
Treatment	Surgery alone	18 (18.0%)
	Surgery + CT/RT	39 (39.0%)
	RT	10 (10.0%)
	CT	10 (10.0%)
	CT + RT	17 (17.0%)
	No treatment	6 (6.0%)
Surgical Treatment	Fixation	3 (3.2%)
	Fixation and Posterior Decompression	11 (11.7%)
	Fixation and Postero-Lateral Decompression	10 (10.6%)
	Fixation and Anterior Decompression	2 (2.1%)
	Fixation and Circumferential Decompression	11 (11.7%)
	Posterior Decompression	13 (13.8%)
NSE-Treatment	Agreement	78 (78.0%)
	Non-agreement	22 (22.0%)
No worsening at last follow-up	Neurological status	79 (84.0%)
	Pain	68 (70.1%)

Statistical analysis

Analyzing patients of the AG, a strong statistically significant association ($p < 0.001$) was observed between improvement or preservation of neurological state and mechanical pain both at 3 and 6 months (Fig. 2; Tables 3, 4, 5 and 6). In the NAG, no statistically significant associations were found between preoperative neurologic status and mechanical pain at 3-month follow-up (p 1.00 and 0.07 respectively) and at 6 months (p 0.293 and 0.09 respectively).

Specifically, focusing on 3-month follow-up, 100% of patients without pre-treatment neurological disfunction resulted to be stable and 76.5% of patients with pre-operative disfunction showed an improvement in the AG. Results were different in the NAG where 71.4% of non-compromised patients remained stable, while the percentage of patients with pre-operative deficit showing worsening or stability were 40% and 60% respectively and no patient improved (Table 3).

Comparable results were observed at 6-month follow up: indeed, 95.1% of patients without pre-operative deficit remained stable and 65% of patients with pre-operative deficit improved after surgery in the AG (Table 4). Conversely, among patients of the NAG, 57.1% of patients without pre-operative deficit and 80% of patients with neurological deficit reported a neurological worsening, while no improvement was registered in both groups (Fig. 2). The majority of patients presenting with deficits in the AG

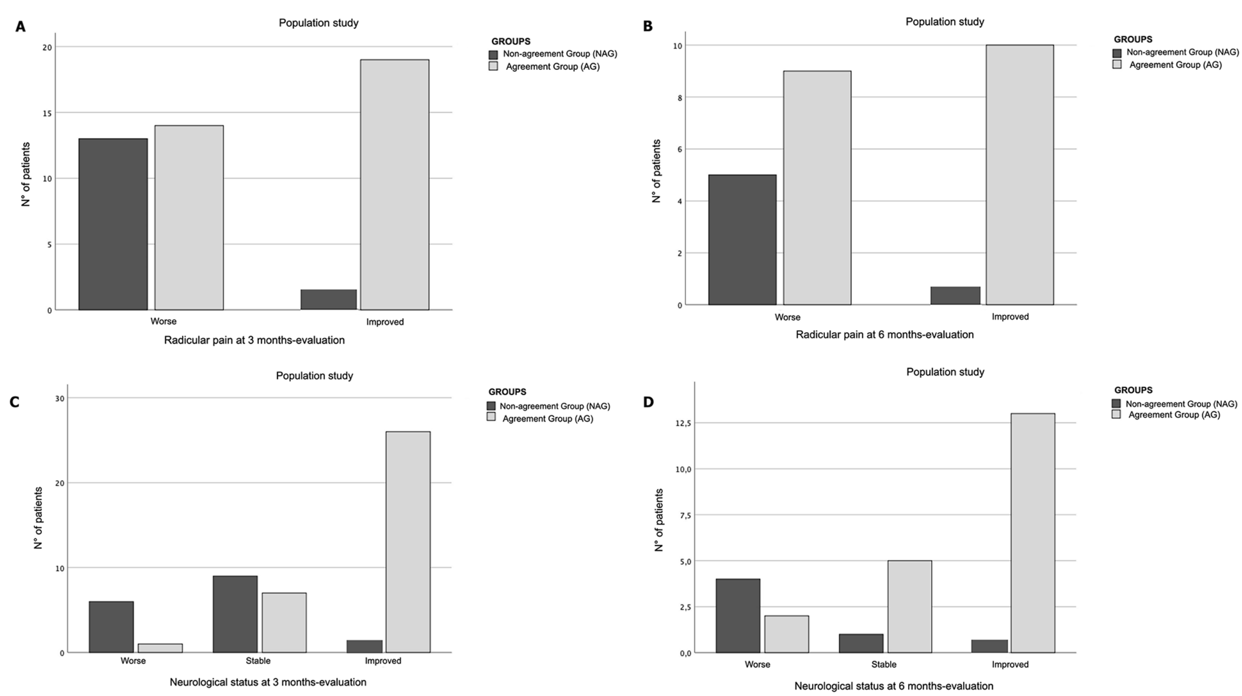

Fig. 2 The bar chart shows that the agreement-group (AG) has significant improvement in root pain at 3 (**A**) and 6 months (**B**) after the surgical procedure. The bar chart C and D shows that the agreement-group (AG) has significant improvement in neurological status (documented as the presence of worsening of at least 1 strength value according to the MSC scale) in at least 1 limb at 3 and 6 months after the surgical procedure

Table 3 Neurological state at 3 months stratified by score-treatment agreement

Contingency Tables

Treatment Score Agreement		**Value**	**p**
Yes	χ^2	53.4	< 0.001
	N	78	
No	χ^2	NaN	NaN
	N	22	
Total	χ^2	45.5	< 0.001
	N	100	

			Neurological State at 3 months			
Treatment Score Agreement	**Neurological Deficit**		**Worsened**	**Stable**	**Improved**	**Total**
Yes	No	Observed	0	44	0	44
		% within row	0.0%	100.0%	0.0%	100.0%
	Yes	Observed	1	7	26	34
		% within row	2.9%	20.6%	76.5%	100.0%
	Total	Observed	1	51	26	78
		% within row	1.3%	65.4%	33.3%	100.0%
No	No	Observed	2	5	0	7
		% within row	28.6%	71.4%	0.0%	100.0%
	Yes	Observed	6	9	0	15
		% within row	40.0%	60.0%	0.0%	100.0%
	Total	Observed	8	14	0	22
		% within row	36.4%	63.6%	0.0%	100.0%
Total	No	Observed	2	49	0	51
		% within row	3.9%	96.1%	0.0%	100.0%
	Yes	Observed	7	16	26	49
		% within row	14.3%	32.7%	53.1%	100.0%
	Total	Observed	9	65	26	100
		% within row	9.0%	65.0%	26.0%	100.0%

suffered from impairment only at lower limbs (27/34, 79%) and improved from mean MRC values < 4 to 4–5 (84% of them), then indicating a concrete clinical motor advantage after treatment. At 6-months follow-up 16 patients were lost because were dead (AG/NAG 7/9).

Analyzing data regarding axial and/or mechanical pain, a statistically significant association was observed both at 3 months ($p < 0.001$) and 6 months follow up ($p < 0.001$) in the AG, while no statistically significant associations resulted in NAG; Tables 5 and 6 reported the specific results regarding different categories for pain assessment. Specifically, the majority of patients in the AG complaining axial and/or radicular pain before treatment reported better percentage of improvement when compared with patients belonging to the NAG (62.7% improved in AG vs. 72.2% worsened in NAG) (Table 5).

Comparable results were observed at 6-months follow up, since 72.1% of patients with pre-operative pain improved and no patients without pre-operative pain reported worsening in the AG. In the NAG, on the other hand, 72.7% of patients with pre-operative pain continued to feel pain despite opioids use (Table 6). Differently from the previous work, statistical analysis of the score grey zone was not conducted because of the small number of patients with grey NSE score.

Finally, statistical analysis was performed focusing on patients over 75 years old. A statistically significant association was found both for neurological status and axial/radicular pain in the AG, while no differences resulted among patients belonging to NAG confirming results of the global study population (Fig. 3; Table 7).

Specifically, as reported in Tables 7 and 100% of patients without pre-operative deficit remained stable and 37.5% of

Table 4 Neurological state at 6 months stratified by score-treatment agreement

Contingency Tables

Treatment Score Agreement		**Value**	***p***
Yes	χ^2	36.4	< 0.001
	N	61	
No	χ^2	NaN	NaN
	N	12	
Total	χ^2	37.5	< 0.001
	N	73	

			Neurological State at 6 months			
Treatment Score Agreement	**Neurological Deficit**		**Worsened**	**Stable**	**Improved**	**Total**
Yes	No	Observed	2	39	0	41
		% within row	4.9%	95.1%	0.0%	100.0%
	Yes	Observed	2	5	13	20
		% within row	10.0%	25.0%	65.0%	100.0%
	Total	Observed	4	44	13	61
		% within row	6.6%	72.1%	21.3%	100.0%
No	No	Observed	3	4	0	7
		% within row	42.9%	57.1%	0.0%	100.0%
	Yes	Observed	4	1	0	5
		% within row	80.0%	20.0%	0.0%	100.0%
	Total	Observed	7	5	0	12
		% within row	58.3%	41.7%	0.0%	100.0%
Total	No	Observed	5	43	0	48
		% within row	10.4%	89.6%	0.0%	100.0%
	Yes	Observed	6	6	13	25
		% within row	24.0%	24.0%	52.0%	100.0%
	Total	Observed	11	49	13	73
		% within row	15.1%	67.1%	17.8%	100.0%

patients with neurological impairment improved after surgery among the AG at 6-months follow up. Conversely, a significant percentage of patients of the NAG with or without pre-existing neurological deficits worsened. Comparable results were observed analyzing neurological status at 3-month follow up and axial and/or radicular pain both at 3 and 6-month follow up (Table 8). Globally, in the AG group ECOG values were < 3 in the majority of patients at follow-up (88%/69% at 3/6 months in the group over 65 years old, 84%/68% at 3/6 months in the group over 75 years old).

Discussion

Elderly patients represent a unique challenge in oncological surgery. Old age has always been associated with a condition of frailty, in order to describe declining functional and nutritional status, physiologic reserves and comorbidities. The increasing number of older patients as well as the improvement of life expectancy in neoplastic disease have then remarked the necessity to revise and redirect many paradigms of treatment and decisional management to face this quantitative and qualitative issue.

Surgical literature about management of metastases in elderly patients has moved in the last decades from few expert recommendations (3) to more structured and focused – although limited – studies [5, 19]. One of the most important considered aspects has been the rejection of the assumed equation between age and frailty, together with the growing interest of functional status as a main starting point and target in spinal metastatic care.

In 2017 a study by Amelot et al. investigated whether age significantly influences quality of life and survival in surgical interventions for spinal metastases [19]. They analyzed data

Table 5 Pain assessment at 3 months stratified by score-treatment agreement

Contingency Tables

Treatment Score Agreement		Value	p
Yes	χ^2	43.5	< 0.001
	N	77	
No	χ^2	5.25	0.072
	N	21	
Total	χ^2	50.1	< 0.001
	N	98	

			Axial/Radicular pain at 3 months			
Treatment Score Agreement	**Axial or Radicular Pain**		**Improved**	**Worsened**	**Stable**	**Total**
Yes	Yes	Observed	37	13	9	59
		% within row	62.7%	22.0%	15.3%	100.0%
	No	Observed	0	0	18	18
		% within row	0.0%	0.0%	100.0%	100.0%
	Total	Observed	37	13	27	77
		% within row	48.1%	16.9%	35.1%	100.0%
No	Yes	Observed	3	13	2	18
		% within row	16.7%	72.2%	11.1%	100.0%
	No	Observed	0	1	2	3
		% within row	0.0%	33.3%	66.7%	100.0%
	Total	Observed	3	14	4	21
		% within row	14.3%	66.7%	19.0%	100.0%
Total	Yes	Observed	40	26	11	77
		% within row	51.9%	33.8%	14.3%	100.0%
	No	Observed	0	1	20	21
		% within row	0.0%	4.8%	95.2%	100.0%
	Total	Observed	40	27	31	98
		% within row	40.8%	27.6%	31.6%	100.0%

from a multicentric prospective study by the Global Spine Study Group (GSTSG) involving 1266 patients admitted at 22 spinal centers from different countries followed up for 2 years after surgery. Three different age groups were considered (< 70, 70–80, and > 80 years). Interestingly, findings showed a higher chance for patients > 80 years to undergo emergency surgery and palliative procedures if compared to younger patients, despite no statistical difference in ASA score, Frankel neurologic score and Karnofsky performance status at presentation. Although complications were more common in the oldest age group and survival expectancy was significantly longer in patients < 70 years old, as well as less probable a neurological recovery in patients > 80 years, authors argued that age itself should not be considered a contraindication for surgery: the rate of emergency or palliative procedures despite good performance status clearly showed that surgeons were probably biased against surgery in elderly patients. In a considerable population of 78 octogenarians' patients Hussain et al. showed that although the increased complication rate, the percentage of fatal events was acceptable (7%) [5].

De La Garza Ramos et al. developed a preoperative metastatic frailty index (MSTFI) in order to help in the prediction of morbidity, mortality and length of stay [20]. 9 independent parameters were identified: anemia, chronic lung disease, coagulopathy, electrolyte abnormalities, pulmonary circulation disorders, renal failure, malnutrition, emergent/urgent admission, and anterior/combined surgical approach. Later, Massaad et al. conducted a performance assessment of the MSTFI demonstrating poor discrimination for predicting complications and in-hospital mortality [21]. Machine learning approaches showed greater advantages over the model used to develop the index, and the random forest model resulted to have the highest positive

Table 6 Pain assessment at 6 months stratified by score-treatment agreement

Contingency Tables

Treatment Score Agreement		**Value**	***p***
Yes	χ^2	41.5	< 0.001
	N	58	
No	χ^2	4.76	0.093
	N	14	
Total	χ^2	46.4	< 0.001
	N	72	

			Axial/Radicular pain at 3 months			
Treatment Score Agreement	**Axial or Radicular Pain**		**Improved**	**Worsened**	**Stable**	**Total**
Yes	Yes	Observed	31	8	4	43
		% within row	72.1%	18.6%	9.3%	100.0%
	No	Observed	0	0	15	15
		% within row	0.0%	0.0%	100.0%	100.0%
	Total	Observed	31	8	19	58
		% within row	53.4%	13.8%	32.8%	100.0%
No	Yes	Observed	2	8	1	11
		% within row	18.2%	72.7%	9.1%	100.0%
	No	Observed	0	1	2	3
		% within row	0.0%	33.3%	66.7%	100.0%
	Total	Observed	2	9	3	14
		% within row	14.3%	64.3%	21.4%	100.0%
Total	Yes	Observed	33	16	5	54
		% within row	61.1%	29.6%	9.3%	100.0%
	No	Observed	0	1	17	18
		% within row	0.0%	5.6%	94.4%	100.0%
	Total	Observed	33	17	22	72
		% within row	45.8%	23.6%	30.6%	100.0%

predictive value (0.53, 95% CI 0.43–0.64) and the highest negative predictive value (0.77, 95% CI 0.72–0.81), with chronic lung disease, coagulopathy, anemia, and malnutrition which were identified as the most important predictors of postoperative complications. Given this, this study confirmed how challenging could be the definition and evaluation of frailty. Recently, the AO Spine Knowledge Forum Tumor conducted an international cross-sectional survey of the AO Spine community to better understand how members of the international community usually conceptualize, define and assess frailty in spinal metastatic disease. The results showed that frailty constitutes a major concern, but also that more than existing frailty tools surgeons base their decisions on general clinical impressions, mostly according to existing systemic conditions, while expected outcomes were neurological recovery, change in performance status and major complications [22].

Actually, evidence about spine surgery of elderly patients has always suffered from controversial results because - mainly - of too heterogeneous considerations about the objectification of frail condition. Li et al. [23] described a 12.17% complication rate and a 0.17% mortality rate for lumbar decompression in a normal population, while these rates increased up to an 18.9% complication rate, and 1.4% mortality rate, in patients older than 85 years old depending on co-morbidities. Raffo and Lauerman [24] described a total rate of major complications of 35% in patients older than 80 years old after spine fusion and Deyo et al. [25] shared similar findings in patients older than 75 years old undergoing lumbar surgery. Other authors did not report significative difference: Reindl et al. [26] found no significative difference in the comparison between lumbar surgery and hip arthroplasty in the elderly population; Balabaud et al. [27] in their series about lumbar spine surgery, described

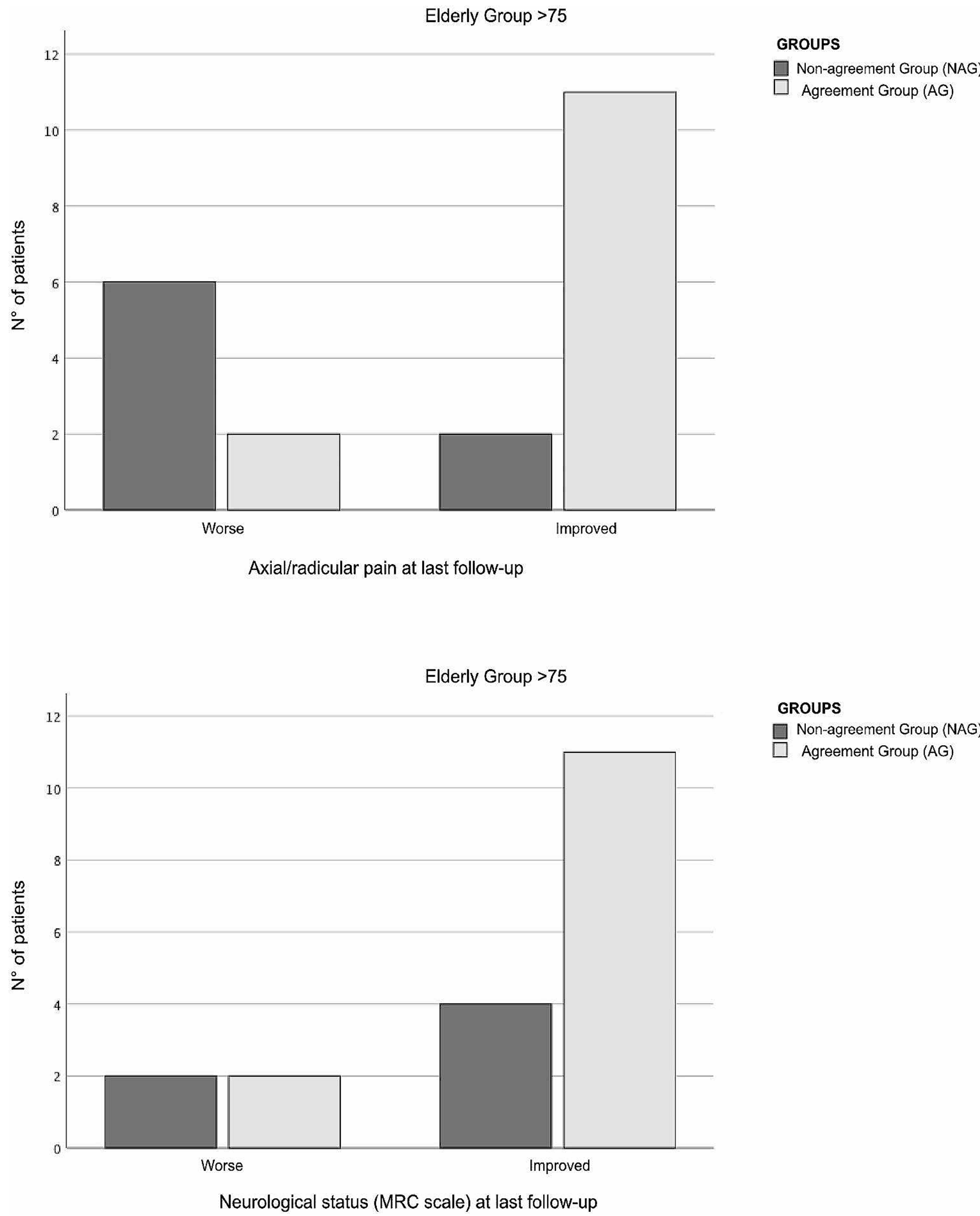

Fig. 3 A statistically significant association was found both for neurological status and axial/radicular pain in the AG considering the older group (> 75) as shown in graph bar chart

an acceptable profile of complications rates in octogenarian patients.

The ghost of post-surgical complications usually has a strong impact on decision-making process: the frailer the patient, the greater the risk of an irreversible negative evolution of disease condition. The issue is - today - to overcome the concept according to which the weight of age could overshadow any considerations about performance status, as well as its key role in decision making strategies. Any consideration about the age of a single patient requiring treatment should not neglect, primarily, a reliable systemic assessment. In brain surgery It is well known that KPS is one of the most important factors predicting outcomes and old paradigms considering age as an independent limit have been progressively reviewed, replaced by functional evaluations and then increasing the number of elderly patients undergoing surgery and post-surgical treatments with radiotherapy and conventional systemic protocols [28, 29]. Many other studies for other neoplastic entities have shown how functional status could represent a reliable prognostic factor, more than age [30, 31]. Apart from that, the importance of anesthesiologic risk should be also highlighted as well: although not as objectifiable as functional status, the ASA score represents a handy tool to identify frail patients in a more comprehensive way, taking into account previous or current pathologies which could negatively affect a delicate balance. Unsurprisingly, the use of both performance status and ASA evaluation has already showed to be a reliable prognostic factor in previous studies about spinal cord compression [32]. Actually, previous - and already mentioned

Table 7 Analysis of patients over 75 years old. Neurological status at 6-month follow-up in the AG and NAG

Contingency Tables

Treatment Score Agreement		**Value**	***p***
Yes	χ^2	20.5	< 0.001
	N	35	
No	χ^2	NaN	NaN
	N	10	
Total	χ^2	14.0	< 0.001
	N	45	

			Neurological State at 3 months			
Treatment Score Agreement	**Neurological Deficit**		**Worsened**	**Stable**	**Improved**	**Total**
Yes	No	Observed	0	22	0	22
		% within row	0.0%	100.0%	0.0%	100.0%
	Yes	Observed	1	4	8	13
		% within row	7.7%	30.8%	61.5%	100.0%
	Total	Observed	1	26	8	35
		% within row	2.9%	74.3%	22.9%	100.0%
No	No	Observed	1	1	0	2
		% within row	50.0%	50.0%	0.0%	100.0%
	Yes	Observed	2	6	0	8
		% within row	25.0%	75.0%	0.0%	100.0%
	Total	Observed	3	7	0	10
		% within row	30.0%	70.0%	0.0%	100.0%
Total	No	Observed	1	23	0	24
		% within row	4.2%	95.8%	0.0%	100.0%
	Yes	Observed	3	10	8	21
		% within row	14.3%	47.6%	38.1%	100.0%
	Total	Observed	4	33	8	45
		% within row	8.9%	73.3%	17.8%	100.0%

Table 8 Analysis of patients over 75 years old. Neurological status at 3-month follow-up, Pain assessment both at in the AG and NAG at 3 and 6-month follow-up

Agreement Group (AG)	Improved	Stable	Worsened	*p* value
Neurological status at 3 months*(patients with deficit)*	8 (61.5%)	4 (30.8%)	1 (7.7%)	**< 0.01**
Axial or radicular pain at 3 months*(patient with pain)*	14 (60.4%)	3 (13%)	6 (25%)	**0.015**
Axial or radicular pain at 6 months*(patient with pain)*	11 (69.3%)	1 (6.3%)	4 (25.1%)	**0.03**
Non Agreement Group (NAG)				
	Improved	**Stable**	**Worsened**	**p value**
Neurological status at 3 months*(patients with deficit)*	0 (0%)	6 (75%)	2 (25%)	> 0.05
Axial or radicular pain at 3 months*(patient with pain)*	0 (0%)	0 (0%)	7 (100%)	> 0.05
Axial or radicular pain at 6 months*(patient with pain)*	0 (0%)	0 (0%)	3 (100%)	> 0.05

- studies reflecting attempts to objectify frailty index, or witnessing surgeons' clinical impressions in decision making, focused on systemic major conditions and highlighted the importance of a proper performance status [19–21]. Gao et al. [33] enrolled 55 consecutive patients aged 75 years or older treated for metastatic spinal cord compression. Their results clearly showed how surgery should be encouraged for elderly patients with a neurological compromised status, few comorbidities and low ECOG scores.

This is why both ECOG and ASA scores were used to characterize patients suitable for surgery in the first validation of the score and - most important - to verify with this study if the same considerations could identify elderly patients able to take advantage from surgery when needed or not. This analysis showed how the use of easy functional and anesthesiologic evaluation of the patient was able to confirm the reliability of the score also in this selected and debated population: the group of agreement was statistically associated with restoration or preservation of neurological status and/or reduction of mechanical pain. The same analysis, on the subgroup of patients older than 75 years old, confirmed the results strengthening how limited could be the pure role of age if compared to a systemic assessment. As for the validation of the score in the general adult population, the ASA and ECOG assessments has been made basing on the condition before the occurrence of symptoms related to spinal metastases (neurological impairment or axial pain) which are supposed to improve after treatment. This could be a potential source of bias, although usually surgeons and radiation oncologists give a major role to clinical history and its timing to plan and justify the need for treatment. In this study the grey zone analysis was not feasible because of small number: this could be due to the retrospective evaluation mainly involving, as per the study of Amelot et al. [17], patients undergoing emergency procedures or - on the other hand - low NSE score patients performing non-surgical treatments.

Finally, besides the reliability of the identification of frail patients with ECOG and ASA scores, this study also confirmed that a proper clinical and radiological assessment made with the combined evaluation of neurology, spine stability and spinal cord compression was associated to significant better outcomes. Being the restoration or the preservation of a proper functional status the goal of spinal metastases treatment, one should never underestimate the evaluation of spinal stability and neurological integrity in the decision-making process. Although elderly patients could be considered at risk of a frailer condition, it is true as well that the impact of neurological deficits and pain on them could contribute more to general and irreversible worsening than in younger patients. Neurological deficits caused by spinal cord compression are associated with reduced life expectancy and health-related quality of life (HRQoL) and should be properly addressed [18, 34]. Spinal instability usually results in mechanical axial/radicular pain and increased risk of neurological deficits, and the SINS score proved to be a practical and reliable tool to identify the loss of stability, being also progressively related to disability [15]. The assessment of epidural compression with the Bilsky scale [16] is able to identify the risk or the reason of neurological deficits, being also useful to evaluate the need for separation surgery or the feasibility of radiosurgery. How disability and bed rest could be a source of fatal complication in elderly patients [35] could not be underestimated: this is probably why the identification of a proper treatment targeting functional goals resulted in better outcomes in the agreement group, once identified patients suitable for surgery.

Limitations and further studies

Principal limitations of this study derive from its retrospective nature, although prospective validation hampers ethical issues. Furthermore, the multicentric data source carries probably different treatment methods through the years and in different involved hospitals according to general practice. Given the nature of this study and, mainly, its goal, this potential limitation could effectively empower the reliability of the analysis because of the functional evaluation needed for its validation: the evaluation of the agreement or non-agreement to the score is able to nullify this potential source of bias while providing significant numbers for the analysis.

The use of ASA and ECOG scores can give a comprehensive systemic assessment of the patient according to the purpose of the NSE score, but no data are provided to single risk factors for worst outcomes. As for the first evaluation of this score, no indications are provided on the type of treatment needed, because the goal of this study was to verify if this tool could be reliable establishing the need for surgery in elderly and not its modality. Finally, care should be taken in decision making of patients with a complete cord damage: although the score encourages surgery in patients with a < 72 h deficit, it is authors' belief and recommendation that these cases should be analyzed individually. The limit of 72 h was chosen according to the discrepancy and uncertainty of evidence about cord damage recoverability timing after traumatic injury. Then, although any chance of neurological recovery should be always pursued, one should consider that elderly patients could share a low favorable profile of biological recovery and clinical rehabilitation after treatment [18] and the small number of patients belonging to this subgroup do not allow to draw significant conclusions about that.

Conclusion

Far from the need or the aim to build dogmatic algorithms, the goal of preserving a proper performance status plays a key role in a modern oncological management: functional outcomes of the multicentric study group showed that the NSE score represents a reliable tool to establish the need for surgery also for elderly patients. The comprehensive inclusion of ECOG and ASA score resulted able to identify patients suitable for surgery when needed, also in the subgroup of patients over 75 years old. Agreement between the score and the performed treatments resulted in better clinical outcomes, when compared with patients without agreement. Further studies are needed to identify single risk factors for surgical outcomes.

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Declarations

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Conflict of interest We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome. We wish to draw the attention of the Editor to the following facts which may be considered as potential conflicts of interest and to significant financial contributions to this work.

Informed consent Informed consent was obtained from all individual participants included in the study. No patients under the Age 18 were included. Any potentially identifiable images or data included in this article The patient has consented to the submission of this review article to the journal. Written consent for publication was obtained from all patients.
We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.
We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.
We further confirm that any aspect of the work covered in this manuscript that has involved either experimental animals or human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.
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