An analysis of tumor-related potential spinal column instability (Spine Instability Neoplastic Scores 7–12) eventually requiring surgery with a 1-year follow-up

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OBJECTIVE Within the Spine Instability Neoplastic Score (SINS) classification, tumor-related potential spinal instability (SINS 7–12) may not have a clear treatment approach. The authors aimed to examine the proportion of patients in this indeterminate zone who later required surgical stabilization after initial nonoperative management. By studying this patient population, they sought to determine if a clear SINS cutoff existed whereby the spine is potentially unstable due to a lesion and would be more likely to require stabilization.

METHODS Records from patients treated at the University of California, San Francisco, for metastatic spine disease from 2005 to 2019 were retrospectively reviewed. Seventy-five patients with tumor-related potential spinal instability (SINS 7–12) who were initially treated nonoperatively were included. All patients had at least a 1-year follow-up with complete medical records. A univariate chi-square test and Student t-test were used to compare categorical and continuous outcomes, respectively, between patients who ultimately underwent surgery and those who did not. A backward likelihood multivariate binary logistic regression model was used to investigate the relationship between clinical characteristics and surgical intervention. Recursive partitioning analysis (RPA) and single-variable logistic regression were performed as a function of SINS.

RESULTS Seventy-five patients with a total of 292 spinal metastatic sites were included in this study; 26 (34.7%) patients underwent surgical intervention, and 49 (65.3%) did not. There was no difference in age, sex, comorbidities, or lesion location between the groups. However, there were more patients with a SINS of 12 in the surgery group (55.2%) than in the no surgery group (44.8%) ($p = 0.003$). On multivariate analysis, SINS > 11 (OR 8.09, CI 1.96–33.4, $p = 0.004$) and Karnofsky Performance Scale (KPS) score < 60 (OR 0.94, CI 0.89–0.98, $p = 0.008$) were associated with an increased risk of surgery. KPS score was not correlated with SINS ($p = 0.4$). RPA by each spinal lesion identified an optimal cutoff value of SINS > 10 , which were associated with an increased risk of surgical intervention. Patients with a surgical intervention had a higher incidence of complications on multivariable analysis (OR 2.96, CI 1.01–8.71, $p = 0.048$).

CONCLUSIONS Patients with a mean SINS of 11 or greater may be at increased risk of mechanical instability requiring surgery after initial nonoperative management. RPA showed that patients with a KPS score of 60 or lower and a SINS of greater than 10 had increased surgery rates.

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KEYWORDS Spine Instability Neoplastic Score; SINS; tumor

ALONG with the advent of the Patchell¹ criteria and NOMS² framework to guide indications for surgery in metastatic spine tumor patients, the Spine Instability Neoplastic Score (SINS) has also helped to determine the stability of the spine.^{2,3} SINS characterizes the stability of the spine with metastatic tumors.^{3,4} Scores

of 0–6 are considered to indicate spinal stability, those of 7–12 indicate potential instability, and those of 13–18 are defined as unstable. However, a paucity of literature exists regarding the optimal treatment of patients in the potentially unstable (scores 7–12) category.

SINS has been instrumental in assessing spinal stabil-

ABBREVIATIONS BED₃ = biologically effective dose; CCI = Charlson Comorbidity Index; KPS = Karnofsky Performance Scale; RPA = recursive partitioning analysis; SINS = Spine Instability Neoplastic Score.

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TABLE 1. Treatment, acute outcomes, and backward likelihood binary logistic regression for surgery in patients initially treated with radiation

Variable	All Patients (n = 75)	No Surgery (n = 49)	Surgery (n = 26)	p Value
Chemotherapy	15 (20.0%)	3 (6.1%)	12 (46.2%)	<0.001
Mean BED ₃ radiation dosing (SD)	56.1 (30.1)	53.1 (30.3)	63.12 (30.5)	0.181
Kyphoplasty	3 (4.0%)	0 (0.0%)	3 (11.5%)	0.015
Vertebroplasty	3 (4.0%)	0 (0.0%)	3 (11.5%)	0.015
Any peri-admission complication	20 (26.7%)	9 (18.4%)	11 (42.3%)	0.026
30-day readmission	5 (6.7%)	1 (2.0%)	4 (15.4%)	0.046
90-day readmission	7 (9.3%)	1 (2.0%)	6 (23.1%)	0.006
30-day reoperation	4 (5.3%)	0 (0.0%)	4 (15.4%)	0.012
90-day reoperation	4 (5.3%)	0 (0.0%)	4 (15.4%)	0.012
Variable	OR	95% CI		p Value
SINS 11	3.86	0.81–18.4		0.090
SINS 12	8.09	1.96–33.4		0.004
KPS score	0.94	0.89–0.98		0.008

Values represent the number of patients (%) unless stated otherwise.

ity as a validated metric^{5–7} with high inter-rater reliability among different medical specialties;^{8–12} it also has been seminal for assessing spinal stability in the setting of spinal metastases. The utility of SINS has been applied to other aspects of spine oncology care as well, such as predicting vertebral body fracture after radiotherapy,^{13,14} predicting mechanical pain/instability in patients with metastatic disease,^{15,16} and correlating SINS with prognosis.^{17,18} However, questions remain in the potentially unstable spine category, which includes patients with SINS of 7–12. Versteeg et al. stated, “Within the SINS potentially unstable group, distinct clinical profiles were observed in patients treated with surgery or radiotherapy alone.”⁶ Although a general consensus exists for the treatment of lesions falling into the stable and unstable SINS categories, the potentially unstable category encompasses a wide range of lesions and patients, with variation in treatment strategies. We evaluated patients with SINS of 7–12 and studied which patients ultimately underwent surgical stabilization. We attempted to identify a threshold score for surgical stabilization within this category of tumor-related potential spinal instability.

Methods

Patient Population

Adult patients who were diagnosed with metastatic spine disease from June 2005 to November 2019 at the University of California, San Francisco, were retrospectively studied. Inclusion criteria were potential spinal column instability (SINS 7–12), initial nonoperative management (i.e., radiotherapy or chemotherapy), and a minimum 1-year follow-up. Exclusion criteria included incomplete medical records, patients who were initially treated with surgery followed by adjuvant therapy, lack of a minimum 1-year follow-up, and lack of proper imaging to calculate SINS.

Data Collection

Data were collected by four independent observers. Demographic variables included age and sex. Clinical variables included date of initial evaluation, date of pre-operative chemotherapy, SINS score (location, pain, bone lesion, radiographic spinal alignment, vertebral body collapse, posterior spinal element involvement), primary tumor histology, and date of latest follow-up. Treatment variables included the date of initial radiation treatment, total radiation dose (in Gy), radiation dose per fraction, biologically effective dose (BED₃) to normal tissue, surgery date, and surgical procedure. Patients who required stabilization via kyphoplasty or vertebroplasty were included in the group requiring surgery. Physical status variables included the Charlson Comorbidity Index (CCI) score, Karnofsky Performance Scale (KPS) score, and the American Society of Anesthesiologists class. Complications, readmission rates, and revision surgeries were recorded for all patients (Table 1).

Statistical Analysis

The univariate chi-square test and Student t-test were used to compare categorical and continuous outcomes, respectively, between patients treated with surgery and without. A backward likelihood multivariate binary logistic regression model involving all variables with a p value < 0.20 on univariate analysis was used to investigate the relationship between clinical characteristics and surgical intervention. KPS scores and SINS were initially included in the model. A similar model was utilized to assess the relationship between a perioperative complication and patient clinical characteristics. Variables initially incorporated into the model included patient age, BED₃, and whether the patient had surgical intervention. A logistic regression model as a function of SINS was utilized to determine if there existed a SINS cutoff at which surgical intervention

FIG. 1. RPA per patient (A) and per lesion (B).

was more probable than not. Recursive partitioning analysis (RPA) was also utilized to identify risk factors for surgical intervention and clinically relevant cutoffs. RPA was performed using per-patient (Fig. 1A) and per-lesion (Fig. 1B) data; $p < 0.05$ was used as the threshold of statistical significance. All statistical analysis was performed using IBM SPSS Statistics (version 26; IBM Corp.).

Results

SINS Scores and Primary Cancer Pathologies

A total of 75 patients with 292 metastatic lesions were included in this study. SINSs of the patients were as follows: 3 (4.0%) with SINS of 7, 7 (9.3%) with SINS 8, 7 (9.3%) with SINS 9, 12 (16.0%) with SINS 10, 17 (22.7%) with SINS 11, and 29 (38.7%) with SINS 12 (Fig. 2). Patient and lesion SINSs can be found in Table 2. A number of different primary cancers were represented (Table 2), with breast cancer being the most common per patient (20, 26.7%) and per lesion (82, 28.1%).

Predictors of Surgical Intervention

A comparison of clinical characteristics and demographics between patients with and without surgical intervention is shown in Table 3. Of the 75 patients, 26 (34.7%) underwent surgical intervention and 49 (65.3%) did not. The average age was 59.1 years with no difference between patients with surgical intervention and those without (61.8 years vs 57.6 years, $p = 0.204$). Similarly, there were no differences in patient sex, BED₃, or CCI score between patients who underwent upfront surgery and those not requiring immediate stabilization. However, patients with a SINS of 12 were more likely to undergo surgical intervention than those who did not (55.2% vs 44.8%, $p = 0.004$, Table 1). Patients who underwent surgical intervention also had a lower median KPS score than those without surgical intervention (60 vs 70, $p = 0.001$). Specific SINS components that were significantly different between those requiring stabilization and those that did not included lesion type (lytic, mixed, or blastic) ($p = 0.015$) and extent of posterior element involvement (bilat-

FIG. 2. Histogram of the percentages of patients who underwent surgery in the SINS 7–12 category.

TABLE 2. SINS and primary cancer pathologies

	No. of Patients (%) (n = 75)	No. of Lesions (%) (n = 292)
SINS		
7	3 (4.0)	18 (6.2)
8	7 (9.3)	25 (8.6)
9	7 (9.3)	32 (11.0)
10	12 (16.0)	82 (28.1)
11	17 (22.7)	83 (28.4)
12	29 (38.7)	52 (17.8)
Pathology		
Salivary	2 (2.6)	9 (3.1)
Kidney	3 (4.0)	8 (2.7)
Breast	20 (26.7)	82 (28.1)
Colorectal	1 (1.3)	5 (1.7)
Lung	10 (13.3)	36 (12.3)
Prostate	17 (22.7)	66 (22.6)
Gastroesophageal	1 (1.3)	4 (1.4)
Unknown GI	1 (1.3)	7 (2.4)
Lymphoma	1 (1.3)	4 (1.4)
Myeloma	3 (4.0)	17 (5.8)
Melanoma	3 (4.0)	8 (2.7)
Liver	2 (2.7)	4 (1.4)
Pancreatic	3 (4.0)	15 (5.1)
Chordoma	3 (4.0)	7 (2.4)
Neuroblastoma	2 (2.7)	6 (2.1)
Sarcoma	1 (1.3)	6 (2.1)

GI = gastrointestinal.

TABLE 3. Comparison of patients with and patients without stabilization surgery

Variable	All Patients (n = 75)	No Surgery (n = 49)	Surgery (n = 26)	p Value
Mean age, yrs	59.1 (13.5)	57.6 (14.2)	61.8 (12.1)	0.204
Sex				0.637
Female	29 (38.7%)	18 (62.1%)	11 (37.9%)	
Male	46 (61.3%)	31 (67.4%)	15 (32.6%)	
Median KPS score	70	70	60	0.001
Mean CCI score	8.7 (2.3)	8.5 (1.9)	9.3 (2.9)	0.211
SINS				
7	3 (4.0%)	3 (100.0%)	0 (0.0%)	0.547
8	7 (9.3%)	6 (85.7%)	1 (14.3%)	0.410
9	7 (9.3%)	6 (85.7%)	1 (14.3%)	0.410
10	12 (16.0%)	10 (83.3%)	2 (16.7%)	0.198
11	17 (22.7%)	11 (64.7%)	6 (35.3%)	0.951
12	29 (38.7%)	13 (44.8%)	16 (55.2%)	0.003
Location				0.655
Junctional	41 (54.7%)	27 (65.9%)	14 (34.1%)	
Mobile	13 (17.3%)	9 (69.2%)	4 (30.8%)	
Semirigid	19 (25.3%)	11 (57.9%)	8 (42.1%)	
Rigid	2 (2.7%)	2 (100.0%)	0 (0.0%)	
Pain				0.088
Mechanical	65 (86.7%)	40 (61.5%)	25 (38.5%)	
Oncological	2 (2.7%)	1 (50.0%)	1 (50.0%)	
None	8 (10.7%)	8 (100.0%)	0 (0.0%)	
Lesion type				0.015
Lytic	19 (25.3%)	8 (42.1%)	11 (57.9%)	
Mixed	35 (46.7%)	23 (65.7%)	12 (34.3%)	
Blastic	21 (28.0%)	18 (85.7%)	3 (14.3%)	
Alignment				0.711
Subluxation	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Kyphosis	9 (12.0%)	5 (55.6%)	4 (44.4%)	
None	66 (88.0%)	44 (66.7%)	22 (33.3%)	
Vertebral body involvement				0.033
>50% collapse	19 (25.3%)	14 (73.7%)	5 (26.3%)	
<50% collapse	25 (33.3%)	14 (56.0%)	11 (44.0%)	
>50% involvement	17 (22.7%)	8 (47.1%)	9 (52.9%)	
None	14 (18.7%)	13 (92.9%)	1 (7.1%)	
Posterior involvement				0.929
Bilateral	66 (88.0%)	43 (65.2%)	23 (34.8%)	
Unilateral	9 (12.0%)	6 (66.7%)	3 (33.0%)	
None	0 (0.0%)	0 (0.0%)	0 (0.0%)	

Values represent the number of patients (%) or mean (SD) unless stated otherwise.

eral, unilateral, or none) ($p = 0.033$). Patients who initially underwent radiation therapy but subsequently converted to surgery underwent intervention for 1) spinal cord compression, 2) severe intractable pain, or 3) tumor growth despite radiation and chemotherapy with impending cord compression. The mean time from radiation to conversion to surgical treatment was 17.77 ± 25.16 months. Indications for surgery, types of surgery, and time to surgery are summarized in Table 4 for both patients who were initially

treated with radiation and those initially treated with surgery.

A subsequent multivariate backward likelihood binary regression analysis revealed SINS > 11 (OR 8.09, CI 1.96–33.4, $p = 0.004$) was independently associated with an increased risk of surgical intervention. The model also revealed that an increased KPS score (OR 0.94, CI 0.89–0.98, $p = 0.008$) was associated with a reduced risk of surgical intervention. However, KPS score was not sig-

TABLE 4. Indications for surgery in patients with SINS 7–12 initially undergoing radiation therapy versus upfront surgery

Variable	Value
Indication for surgery following initial RT (n = 26)	
Spinal cord compression	9 (34.62%)
Severe intractable pain	7 (26.92%)
Treatment-resistant tumor growth w/ impending cord compression	10 (38.46%)
Surgical treatment	
Vertebroplasty	2 (7.69%)
Tumor debulking	6 (23.07%)
Fixation	18 (69.23%)
Mean time from initial RT to surgery (mos)	17.77 (25.16)
Indication for upfront surgery (n = 98)	
Spinal cord compression	43 (43.87%)
Severe intractable pain	37 (37.76%)
Tumor growth w/ impending cord compression	18 (18.37%)
Surgical treatment	
Vertebroplasty	3 (3.06%)
Tumor debulking	38 (38.78%)
Fixation	57 (58.16%)

RT = radiation therapy.

Values represent the number of patients (%) unless stated otherwise. Mean values are presented as the mean (SD).

nificantly correlated with SINS (coefficient = -0.08 , $p = 0.40$). Solving the logistic regression model, $P = e^{-8+0.678X} / (1 + e^{-8+0.678X})$, as a function of SINS for a probability of 50% provided a SINS cutoff of 11.8. Patients with SINS < 11 required surgery 17.1% of the time compared with 50.6% in patients with SINS ≥ 11 ($p = 0.001$).

RPA was then utilized to further evaluate prognosticators of surgical intervention and clinically relevant cutoffs. In a patient-specific analysis, RPA identified a SINS cutoff of > 10 as having a 47.8% incidence of surgical intervention and SINS ≤ 10 as having a 13.8% incidence of surgical intervention (Fig. 1A). Similarly, a per-lesion RPA identified a cutoff of SINS 10. On the per-lesion analysis, lesions with SINS ≤ 10 had a 24.2% incidence of surgical intervention, but SINS > 10 had a 50.4% incidence of surgical intervention (Fig. 1B). RPA per-patient subanalysis identified clinical KPS score cutoffs as well. The first de-

cision node identified in the RPA was a KPS cutoff of 60. Patients with a KPS score > 60 had a 17.6% incidence of surgical intervention as compared with 70.8% in patients with a KPS score ≤ 60 . In patients with a KPS score > 60 , patients with SINS > 10 had a 32.1% incidence of surgical intervention, relative to a 0.0% incidence in patients with SINS ≤ 10 (Fig. 3). RPA analysis did not identify a SINS cutoff among patients with a KPS score < 60 .

Treatment, Perioperative, 30-Day, and 90-Day Outcomes

A comparison of treatment, perioperative, 30-day, and 90-day outcomes between patients with and those without surgical intervention is shown in Table 1. An MR image of a spine lesion with potential instability is shown in Fig. 4. Patients with a surgical intervention were more likely to have undergone chemotherapy (46.2% vs 6.1%, $p < 0.001$), kyphoplasty (11.5% vs 0.0%, $p = 0.015$), and vertebroplasty (11.5% vs 0.0%, $p = 0.015$). Similarly, patients with surgical intervention had a higher incidence of perioperative complications (42.3% vs 18.4%, $p = 0.026$), 30-day readmission (15.4% vs 2.0%, $p = 0.046$), and 90-day readmission (23.1% vs 2.0%, $p = 0.006$). The 30- and 90-day reoperation rates for patients who underwent stabilization surgery were both 15.4%. A multivariate backward likelihood binary regression analysis revealed surgical intervention to be independently associated with development of a perioperative complication (OR 2.96, CI 1.01–8.71, $p = 0.048$).

Discussion

Although the SINS classification by Fisher et al.³ has defined stable and unstable spinal metastatic lesions, there is no clear consensus within the potentially unstable category (SINS 7–12). Our study is the largest to date. We focused only on patients with potentially unstable SINS who were initially managed nonoperatively, quantified the proportion of patients who required eventual surgical stabilization, and attempted to determine if there exists an optimal cutoff above which a potentially unstable lesion would be more likely to require stabilization. Previous studies have suggested that a SINS of 10 or greater may represent a more appropriate score for stabilization as opposed to a SINS of 13 or greater.¹⁹ The impetus to further define a score necessitating stabilization arises from the need to treat pain as well as prevent adverse spinal events which could result in catastrophic neurological complications. Studies have correlated metastatic disease causing

FIG. 3. KPS score recursive partition subanalysis.

FIG. 4. Sagittal T1-weighted (A) and T2-weighted (B) MR images of a potentially unstable spine.

spinal instability with adverse spinal events as well as SINS ability to predict those events.^{20–23} Lam et al. reported that $SINS \geq 11$ resulted in more than 2.5 times the risk of adverse spinal events following stereotactic body radiotherapy compared with patients with $SINS \leq 10$.²² Versteeg et al. performed a multicenter study of 1509 patients and compared SINS of operative and nonoperative patients.²⁴ They identified a mean SINS of 7.2 in the nonoperative group and 10.7 in the operative group. These results are consistent with our findings as well as those of Pennington et al.¹⁹

In a retrospective review, Pennington et al.¹⁹ analyzed 38 patients with SINS indicating potential instability and suggested that lesions with a $SINS < 10$ may not require stabilization. In their study, patients who underwent fusion had a higher mean SINS (11 vs 8), higher proportion of lytic lesions, higher mean KPS score, and more extensive epidural involvement. The authors reported an optimal SINS cutoff of 10, with patients with $SINS \geq 10$ having > 50% odds of undergoing stabilization surgery. This supports the optimal SINS cutoff of 10, above which surgical stabilization may be appropriate, that was also identified in our study. In contrast to Pennington et al., however, we found that patients who underwent stabilization surgery had lower rather than higher KPS scores, and reduced KPS score was associated with increased risk of surgical intervention on multivariable analysis. This could potentially be reflective of increased spine instability and pain contributing to lower KPS scores, translating to a need for surgical intervention. The association of higher KPS score and increased risk of undergoing stabilization surgery observed by Pennington et al. may be reflective of selection bias as patients with higher KPS scores may be offered surgery more readily due to their higher functioning status and ability to tolerate an operation.

Because mechanical instability represents a main indication for surgery in spinal oncology patients, clarifying the role of surgical intervention in the potentially unstable SINS category can be helpful. Studies have reported up to 75% of patients appear in the potentially unstable category, further underscoring the need for additional analysis of this population.¹⁹ Dosani et al. found that patients with SINS of 7–12 were more likely to undergo surgical consultation for consideration of stabilization.²⁵ Our findings of higher rates of surgical intervention correlating with higher SINS in the potentially unstable group is consistent with the lit-

erature, as is the finding of a suggested threshold of SINS of 10. Surgeons may be more likely to offer these patients stabilization given the possible instability and possible impending collapse of the spine. In patients who were initially chosen to undergo radiation only, the main reasons were 1) the patients did not meet the Patchell criteria for surgery, 2) there was no gross instability of the spine based on radiographic imaging, or 3) the patients were simply too ill to undergo surgery. In our study, some patients with SINS 7–12 who initially received radiation therapy were subsequently converted to surgery. Progressive, incapacitating pain was a driver for surgery. Spinal cord compression with resultant neurological changes would have been another impetus for surgery. Asymptomatic patients were converted to surgery if there was radiographic follow-up showing spinal canal stenosis, continued tumor growth despite chemotherapy or radiation, or impending spinal cord compression.

Study Limitations

There are limitations to this study. First, it is a retrospective, single-institution review, and larger, multiinstitutional studies would be useful to validate our findings. There may be selection bias in this study in that patients with lower KPS scores may be in more pain and may have been more likely to undergo surgery. This may have been independent of SINS score, but it certainly may also have been correlated with the SINS and pain from the spine. There are other factors which should be considered when interpreting the data. The overall patient context is important. Patients with a $SINS \geq 12$ may not undergo surgical stabilization if their prognosis is poor. Alternatively, patients with stable lesions may undergo surgery for spinal cord compression issues, not for stability issues. In order to help minimize these confounders, we performed per-patient and per-lesion analyses.

It is also important to acknowledge the significantly higher rate of complications and readmissions observed in the surgical subgroup, as this could potentially be due to baseline differences. For example, it is plausible that the higher rate of chemotherapy in patients undergoing surgery could lead to related complications such as fever, neutropenia, and anemia. Of the 26 patients requiring surgical treatment, 30.7% of the patients developed a complication or required readmission for medical causes not directly related to the surgery (e.g., pneumonia, arrhythmia, and anemia). The rest of the patients developed at least one complication directly related to their surgery (e.g., hematoma evacuation, surgical site infection, or wound dehiscence). These data support the notion that most of the complications and readmissions were a sequelae of surgery.

Conclusions

In patients with potentially unstable SINS, lesions with scores ≥ 10 may be at increased risk for mechanical instability requiring stabilizing surgery. KPS score was not associated with SINS. RPA found a significant SINS cutoff of 10 for patients with KPS scores > 60; however, no similar cutoff was observed in patients with KPS scores ≤ 60 .

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Disclosures

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