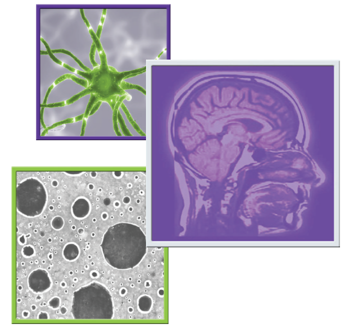
RESEARCH ARTICLE

CNS Oncology



Predictors of complications and readmission following spinal stereotactic radiosurgery

Daniel Lubelski[1], Joseph E Tanenbaum[2,3,4], Taylor E Purvis[1], Thomas T Bomberger[2,3,4], Courtney Rory Goodwin[1], Ilya Laufer[5] & Daniel M Sciubba*,[1]

Aim: to identify preoperative factors associated with morbidity/mortality, hospital length of stay (LOS), 30-day readmission and operation rates following spinal stereotactic radiosurgery (SRS) for spinal tumors. **Methods:** The American College of Surgeons National Quality Improvement Program was queried from 2012 to 2014 to identify patients undergoing SRS for spinal tumors. Logistic regression was performed to identify predictors. **Results:** 2714 patients were identified; 6.8% had major morbidity or mortality, 6.9% were readmitted within 30 days and 4.3% had a subsequent operation within 30 days. Age, BMI and American Society of Anesthesiologist (ASA) class were predictive of LOS. Major morbidity was predicted by age >80, BMI >35, high ASA, pretreatment functional dependence and baseline comorbidities. Predictors of operation within 30 days included preoperative steroid use, renal failure, BMI >35 and if the treatment was nonelective. **Discussion:** 4–7% of patients undergoing SRS for spinal tumors have morbidity following the procedure. Factors predictive of morbidity, LOS, and subsequent operation included age, BMI, baseline comorbidities and functional status. **Conclusion:** Identification of preoperative patient-specific factors that are predictive of post-treatment outcome will aid in patient selection and patient counseling leading to greater patient satisfaction and hospital efficiency.

First draft submitted: 16 December 2016; Accepted for publication: 7 March 2017; Published online: 18 July 2017

Symptomatic spinal metastases are found in more than 40% of cancer patients, many of whom suffer from neurological manifestations from epidural/intradural cord compression as well as axial back pain from structural compromise [1–3]. Systemic chemotherapies are enabling these patients to live longer, and stereotactic radiosurgery (SRS) has become an important adjuvant or primary treatment option. Current therapy is aimed to achieve local tumor control, palliate pain and maintain or improve neurological status.

The primary indications for SRS include stand-alone treatment for painful bony metastases, postoperatively following decompression separation surgery, as well as for progression or recurrence of local disease despite previous conventional external beam radiation therapy.

SRS has proven benefits over conventional external beam radiation therapy for radioresistant tumors as it enables increased tumoricidal dose delivery and spinal cord dose sparing. Surgery is still considered first-line therapy in patients with radioresistant tumors causing spinal cord compression,

KEYWORDS

• 30-day readmission • American College of Surgeons National Quality Improvement Program • major morbidity and mortality • predictors • spinal stereotactic radiosurgery • spinal tumors

[1]Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA
[2]Cleveland Clinic Center for Spine Health, Cleveland Clinic, Cleveland, OH 44195, USA
[3]Department of Neurological Surgery, Cleveland Clinic, Cleveland, OH 44195, USA
[4]Case Western Reserve University School of Medicine, Cleveland, OH 44106, USA
[5]Department of Neurosurgery, Memorial Sloan Kettering Hospital, New York, NY 10022, USA
*Author for correspondence: Tel.: +1 410 955 4424; Fax: +1 410 502 5768; Dsciubb1@jhmi.edu

Future Medicine part of fsg

due to the dose limitations to the spinal cord [4]. Risks of spinal radiosurgery include radiation myelopathy and post-treatment vertebral compression fractures [5,6].

There is a growing body of literature on the use of SRS for spinal lesions, and delineation of factors predictive of poor outcome will help guide treatment decisions. There is no doubt that patients with metastatic spinal lesions are often debilitated, physiologically deranged and have a decreased life expectancy. However, even within this population of patients, there are likely to be factors associated with increased morbidity and poorer outcomes. In the present study, we use a multicenter national database to investigate the association between baseline demographic patient-specific variables and post-treatment outcomes following SRS for spinal metastases. Identifying the predictors of increased length of stay (LOS), subsequent operation, readmission, morbidity and mortality may provide improved counseling to afflicted patients and their medical teams. Such information may allow for more appropriate options for family specific wishes and improvements in cost efficiency in our current resource-limited medical environment.

Methods

• Data source

We used data from the American College of Surgeons' (ACS) National Quality Improvement Program (NSQIP) database throughout the present study to quantify the association between patient demographics and comorbidities and 30-day post-treatment outcomes following SRS. We used data from 2012 to 2014 because readmission and reoperation data were added to the NSQIP registry beginning in 2012, and 2014 is the most recent year of available data.

NSQIP data are comprised of yearly submitted surgical case data from nearly 400 community and academic hospitals. NSQIP data are prospectively collected, audited for accuracy and reproducibility, validated by a trained surgical clinical nurse and are annually assessed to confirm that at least 95% of all patients are followed for 30 days postoperatively [7–9].

Data on patient demographics (age, sex, race, height and weight), surgical data (inpatient vs outpatient and elective vs nonelective), and comorbidities, including: diabetes, smoking status, dyspnea, functional status, ventilator dependency, history of ascites, bleeding disorders, chronic obstructive pulmonary disease (COPD), history of congestive heart failure (CHF), hypertension requiring medication, dialysis, disseminated cancer, renal failure, preoperative transfusion, evidence of wound infection, chronic steroid use, weight loss, sepsis and American Society of Anesthesiologist (ASA) Class.

NSQIP also includes data on superficial surgical site infection (SSI), deep SSI, organ space SSI, wound dehiscence, pneumonia, unplanned reintubation, renal insufficiency, acute renal failure, cerebrovascular accident, cardiac arrest, myocardial infarction, intra/postoperative transfusion, deep vein thrombosis, sepsis/septic shock and urinary tract infection. Furthermore, NSQIP includes data on all-cause readmission and reoperation within 30 days and hospital LOS. Importantly, variable definitions are standardized across NSQIP reporting sites. The ACS NSQIP Participant Use File lists these definitions [7]. Throughout NSQIP, Current Procedural Terminology codes are used to record the procedures that patients underwent.

Required NSQIP statement: "American College of Surgeons National Surgical Quality Improvement Program and the hospitals participating in the ACS NSQIP are the source of the data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors."

• Study population

All patients aged 18 years and older included in NSQIP from 2012 to 2014 that underwent SRS to the spine based on Current Procedural Terminology codes 61783, 63620 and 63621.

• Outcome definitions

The primary outcome of the present study was major morbidity and mortality (MMM), which was defined as all-cause patient mortality within 30 days following SRS or the occurrence of any of the following major morbidities (MM) recorded in NSQIP: deep SSI, organ space SSI, wound dehiscence, pneumonia, unplanned reintubation, renal insufficiency, acute renal failure, cerebrovascular accident, cardiac arrest, myocardial infarction, deep vein thrombosis and sepsis/septic shock. Presumably, in the SRS population, these outcomes were mainly the latter ones (e.g., renal failure, pneumonia and cardiac dysfunction) rather than the postoperative infectious complications.

We also analyzed secondary outcomes, which were (2) MM within 30 days, (3) hospital LOS (we dichotomized LOS to greater than or less than the 75th percentile of all LOS), (4) 30-day readmission for any reason to any hospital and (5) any 30-day subsequent operation that was related to the initial procedure.

• Missing data

We addressed missing data using multiple chained imputation based on a series of ten multivariable logistic regression equations. Using this technique, we were able to impute missing data based on available data. This method was chosen to prevent the potential misestimation of variance inherent to other methods of handling missing data [10].

• Multivariable analysis

For each outcome variable, we estimated a unique logistic regression model. We included each of the following covariates in each model because of their perceived clinical significance: age, sex, race, BMI (calculated based on patient height and weight and relative to BMI of ≥20 and ≤35), ASA class (relative to ASA class 1),

Table 1. Major morbidity or mortality.

Parameter	Estimate	95% CI	p-value
Age (years)			
40–59	0.85	0.71–1.03	0.09
60–79	0.99	0.83–1.18	0.91
80+	1.04	0.74–1.48	0.81
BMI (kg/m²)			
– <20	0.72	0.48–1.07	0.11
– >35	1.41	1.09–1.81	0.01
Nonelective operation	1.15	1.01–1.32	0.03
Female sex	0.88	0.79–0.97	0.01
Inpatient	1.24	0.69–2.22	0.47
Nonwhite race	1.11	0.96–1.29	0.16
ASA class			
(2) mild disturbance	0.89	0.65–1.22	0.47
(3) Severe disturbance	1.06	0.80–1.42	0.67
(4/5) Life-threatening/moribound	1.21	0.85–1.71	0.29
Comorbidities			
Bleeding disorders	0.97	0.71–1.34	0.87
Chronic obstructive pulmonary disorder	1.07	0.85–1.34	0.55
Congestive heart failure	1.31	0.83–2.07	0.25
Diabetes	0.95	0.81–1.10	0.47
Dialysis (current)	0.79	0.37–1.67	0.53
Disseminated cancer	0.99	0.86–1.13	0.85
Dyspnea	1.18	0.95–1.46	0.14
Functional dependence	1.19	0.97–1.46	0.09
Hypertension	1.05	0.94–1.18	0.36
Renal failure	2.48	1.32–4.66	0.00
Smoking	0.95	0.84–1.09	0.48
SIRS/sepsis/septic shock	0.94	0.72–1.22	0.63
Steroids (for chronic condition)	1.20	1.04–1.37	0.01
Transfusion (preoperative)	1.22	0.70–2.14	0.48
Ventilator dependent	0.99	0.63–1.56	0.98
Weight loss	1.09	0.77–1.53	0.64
Wound infection/open wound (preoperative)	1.32	0.90–1.95	0.16

ASA: American Society of Anesthesiologist; SIRS: Systemic inflammatory response syndrome.

Table 2. Major morbidity.

Parameter	Estimate	95% CI	p-value
Age (years)			
40–59	0.84	0.72–0.97	0.02
60–79	1.07	0.93–1.24	0.33
80+	1.39	1.07–1.80	0.01
BMI (kg/m^2)			
– <20	0.80	0.59–1.08	0.14
– >35	1.33	1.09–1.62	0.00
Nonelective operation	1.12	1.01–1.25	0.03
Female sex	0.87	0.80–0.94	0.00
Inpatient	2.60	0.97–6.98	0.06
Nonwhite race	1.05	0.93–1.19	0.44
ASA class			
(2) Mild disturbance	0.70	0.53–0.93	0.01
(3) Severe disturbance	1.07	0.83–1.38	0.61
(4/5) Life-threatening/moribound	1.64	1.23–2.20	0.00
Comorbidities			
Bleeding disorders	1.15	0.92–1.43	0.22
Chronic obstructive pulmonary disorder	1.23	1.05–1.45	0.01
Congestive heart failure	1.03	0.67–1.57	0.91
Diabetes	0.97	0.86–1.09	0.62
Dialysis (current)	1.02	0.62–1.65	0.95
Disseminated cancer	0.96	0.86–1.07	0.45
Dyspnea	1.00	0.83–1.19	0.97
Functional dependence	1.30	1.11–1.51	0.00
Hypertension	1.00	0.92–1.10	0.92
Renal failure	2.37	1.29–4.35	0.01
Smoking	0.99	0.89–1.10	0.80
SIRS/sepsis/septic shock	1.44	1.22–1.71	<0.0001
Steroids (for chronic condition)	1.34	1.21–1.49	<0.0001
Transfusion (preoperative)	1.43	0.92–2.24	0.11
Ventilator dependent	1.79	1.35–2.38	<0.0001
Weight loss	1.25	0.98–1.60	0.08
Wound infection/open wound (preoperative)	1.87	1.42–2.48	<0.0001

ASA: American Society of Anesthesiologist; SIRS: Systemic inflammatory response syndrome.

history of diabetes, smoking, dyspnea, renal failure, functional status, ventilator dependency, history of COPD, history of CHF, hypertension requiring medication, dialysis, disseminated cancer, evidence of wound infection, chronic steroid use, weight loss, bleeding disorders, preoperative blood transfusion, sepsis and nonelective operation. We set our threshold for statistical significance at an α level of 0.05.

Results

A total of 2714 patients were identified who met inclusion criteria: 184 patients (6.8%) had 'MMM'; 193 (7.1%) had MM; 186 (6.9%) were readmitted within 30 days; and 116 (4.3%) had a subsequent operation within 30 days.

Of the included patients, 87% of patients were between 40 and 80 years old. About 91% of cases were done electively. About 36% of patients were ASA class 2 (mild comorbidity) and 57% of patinets were ASA class 3 (severe comorbidity). The most common comorbidities found in the patient population included hypertension (57%), diabetes (17%) and smoking history (20%).

Factors predictive of increased odds of MMM (Table 1) included BMI >35 (odds ratio [OR]: 1.5), ASA class 4/5 (OR: 2.8) and comorbidities including systemic inflammatory response syndrome (SIRS)/sepsis (OR: 1.9) and chronic steroid use (OR: 1.5). Factors protective of MMM included younger age (40–59; OR: 0.7) and low ASA class 2 (OR: 0.5).

Predictors of MM **(Table 2)** included BMI >35 (OR: 1.6). Low ASA class 2 was associated with decreased odds of MM (OR: 0.5) whereas ASA class 4/5 was associated with increased odds (OR: 2.5). A number of comorbidities were associated with increased risk of post-treatment morbidity, including SIRS/sepsis (OR: 1.9), chronic steroid use (OR: 1.6) or pretreatment wound infection (OR: 2.1).

Factors predicting prolonged LOS **(Table 3)** were ASA class 4/5 (OR: 2.6) and comorbidities such as CHF, disseminated cancer, renal failure, pretreatment transfusions and weight loss. Younger age was associated with decreased odds of prolonged LOS.

Only a few factors were predictive of readmission within 30 days **(Table 4)**. Age greater than 80 had 2.1-times the odds of needing readmission. Patients with COPD (OR: 1.35) and functional dependence (OR: 1.4) had significantly greater odds, while those with a low ASA class (OR: 0.56) had lower odds of requiring readmission. Last, subsequent operation within 30 days

Table 3. Prolonged length of stay (>6 days, >75th percentile).

Parameter	Estimate	95% CI	p-value
Age (years)			
40–59	0.76	0.68–0.84	<0.0001
60–79	0.96	0.86–1.06	0.42
80+	1.54	1.26–1.88	<0.0001
BMI (kg/m^2)			
– < 20	0.93	0.76–1.14	0.50
– > 35	1.00	0.87–1.14	0.94
Nonelective operation	2.55	2.38–2.74	<0.0001
Female sex	0.99	0.93–1.04	0.61
Inpatient	2.11	1.36–3.29	<0.0001
Nonwhite race	1.19	1.09–1.31	<0.0001
ASA class			
(2) Mild disturbance	0.78	0.64–0.95	0.01
(3) Severe disturbance	1.19	0.99–1.43	0.07
(4/5) Life-threatening/moribound	2.12	1.70–2.63	<0.0001
Comorbidities			
Bleeding disorders	1.04	0.86–1.26	0.68
Chronic obstructive pulmonary disorder	1.01	0.88–1.15	0.94
Congestive heart failure	1.76	1.24–2.50	<0.0001
Diabetes	1.15	1.06–1.26	<0.0001
Dialysis (current)	1.28	0.80–2.06	0.31
Disseminated cancer	0.99	0.92–1.07	0.84
Dyspnea	1.09	0.95–1.24	0.23
Functional dependence	1.35	1.18–1.53	<0.0001
Hypertension	1.05	0.98–1.12	0.18
Renal failure	2.82	1.25–6.35	0.01
Smoking	1.09	1.01–1.17	0.02
SIRS/sepsis/septic shock	1.12	0.96–1.30	0.16
Steroids (for chronic condition)	0.98	0.90–1.07	0.60
Transfusion (preoperative)	1.99	1.14–3.46	0.02
Ventilator dependent	1.24	0.91–1.69	0.16
Weight loss	1.26	1.01–1.56	0.04
Wound infection/open wound (preoperative)	1.24	0.93–1.65	0.04

ASA: American Society of Anesthesiologist; SIRS: Systemic inflammatory response syndrome.

Table 4. Readmission within 30 days.

Parameter	Estimate	95% CI	p-value
Age (years)			
40–59	0.83	0.72–0.96	0.01
60–79	0.93	0.81–1.06	0.27
80+	1.21	0.94–1.55	0.14
BMI (kg/m²)			
– <20	0.92	0.70–1.21	0.56
– >35	1.06	0.88–1.27	0.53
Nonelective operation	1.00	0.91–1.11	0.96
Female sex	0.95	0.88–1.03	0.19
Inpatient	1.71	0.96–3.05	0.07
Nonwhite race	1.11	0.99–1.25	0.08
ASA class			
(2) Mild disturbance	0.85	0.66–1.09	0.20
(3) Severe disturbance	1.26	1.00–1.60	0.05
(4/5) Life-threatening/moribound	1.18	0.89–1.57	0.25
Comorbidities			
Bleeding disorders	1.07	0.85–1.35	0.58
Chronic obstructive pulmonary disorder	1.12	0.95–1.32	0.18
Congestive heart failure	1.12	0.74–1.71	0.58
Diabetes	1.02	0.91–1.14	0.76
Dialysis (current)	0.99	0.57–1.69	0.96
Disseminated cancer	1.11	1.00–1.23	0.05
Dyspnea	0.97	0.82–1.16	0.78
Functional dependence	1.09	0.92–1.29	0.31
Hypertension	1.08	0.99–1.18	0.07
Renal failure	1.25	0.58–2.70	0.57
Smoking	0.98	0.89–1.08	0.69
SIRS/sepsis/septic shock	1.01	0.82–1.24	0.90
Steroids (for chronic condition)	1.25	1.13–1.38	<0.0001
Transfusion (preoperative)	0.89	0.48–1.64	0.70
Ventilator dependent	0.89	0.58–1.38	0.61
Weight loss	1.13	0.88–1.47	0.34
Wound infection/open wound (preoperative)	1.33	0.97–1.82	0.08

ASA: American Society of Anesthesiologist; SIRS: Systemic inflammatory response syndrome.

(Table 5) was the rarest of the adverse outcomes following SRS and the only significant predictor was if the SRS was performed in an urgent/nonelective fashion (OR: 1.9). In contrast, younger age was associated with a 34% decreased odds of requiring subsequent operation within 30 days (OR: 0.66).

Discussion

Metastatic spinal disease is a significant source of morbidity and mortality among cancer patients. While SRS is well established for treatment of patients with intracranial pathology, there is less evidence among patients with spinal disease. The growing body of evidence has led to increasing use of SRS for spinal tumors as it has shown good short- and long-term results with improved back pain and quality of life.

One of the largest series to date, by Gerszten *et al.*, found that 86% of their patients experienced long-term improvement in pain control [11]. Hsu *et al.* found that 43–97% of patients have improvement in back pain following SRS [12]. Moreover, while survival is low in this patient population (median 8 months), SRS leads to local control in 80–100% of patients [12].

For many patients, SRS is used to improve pain symptoms and overall quality of life during the final months of their lives. Many of these patients have comorbidities that preclude surgical intervention. These patients, however, may still benefit from stand-alone SRS treatment. As the goal of SRS is to improve quality of life, a close understanding of the factors that predispose to complications and adverse outcomes is needed. To date, there are no large-scale studies investigating the predictors of poor outcomes. Additionally, since most of the patients have substantial comorbidities, it is important to understand the relative contribution of each of these, to quantify the patients' individual risk profiles.

Our analysis revealed that specific patient demographics and comorbidities were associated with higher rates of morbidity and mortality, LOS, readmission and subsequent operation following SRS for spinal tumors. For most of the outcomes, predictors of worse outcome included elevated BMI greater than 35, nonelective procedure and pretreatment baseline comorbidities including high ASA class, COPD, renal failure, functional dependence and chronic steroid use. Many of the patients, who undergo SRS, cannot tolerate surgery due to baseline comorbidities. Accordingly, while the aim of identifying

Table 5. Reoperation within 30 days.

Parameter	Estimate	95% CI	p-value
Age (years)			
40–59	0.85	0.71–1.03	0.09
60–79	0.99	0.83–1.18	0.91
80+	1.04	0.74–1.48	0.81
BMI (kg/m²)			
– <20	0.72	0.48–1.07	0.11
– >35	1.41	1.09–1.81	0.01
Nonelective operation	1.15	1.01–1.32	0.03
Female sex	0.88	0.79–0.97	0.01
Inpatient	1.24	0.69–2.22	0.47
Nonwhite Race	1.11	0.96–1.29	0.16
ASA class			
(2) Mild disturbance	0.89	0.65–1.22	0.47
(3) Severe disturbance	1.06	0.80–1.42	0.67
(4/5) Life-threatening/moribound	1.21	0.85–1.71	0.29
Comorbidities			
Bleeding disorders	0.97	0.71–1.34	0.87
Chronic obstructive pulmonary disorder	1.07	0.85–1.34	0.55
Congestive heart failure	1.31	0.83–2.07	0.25
Diabetes	0.95	0.81–1.10	0.47
Dialysis (current)	0.79	0.37–1.67	0.53
Disseminated cancer	0.99	0.86–1.13	0.85
Dyspnea	1.18	0.95–1.46	0.14
Functional dependence	1.19	0.97–1.46	0.09
Hypertension	1.05	0.94–1.18	0.36
Renal failure	2.48	1.32–4.66	0.00
Smoking	0.95	0.84–1.09	0.48
SIRS/sepsis/septic shock	0.94	0.72–1.22	0.63
Steroids (for chronic condition)	1.20	1.04–1.37	0.01
Transfusion (preoperative)	1.22	0.70–2.14	0.48
Ventilator dependent	0.99	0.63–1.56	0.98
Weight loss	1.09	0.77–1.53	0.64
Wound infection/open wound (preoperative)	1.32	0.90–1.95	0.16

ASA: American Society of Anesthesiologist; SIRS: Systemic inflammatory response syndrome.

baseline risk factors predictive of poor outcomes is for improved patient selection, in this instance, it can also serve as an aid for improved patient counseling and pretreatment preparation.

Limited evidence exists on the outcomes and complications following SRS for spine tumors [13]. Moreover, there are no published risk factors for SRS therapy for spinal tumors. The preoperative risk factors identified in the present study have been demonstrated in the spine surgery literature with regard to other surgical interventions. Obesity, for example, is a well-supported risk factor for post-treatment complications [14,15]. In the present study, obesity was a major risk factor (53% greater odds) for MMM after SRS for spinal metastases. Age was a predictor as well. Patients older than 80 years had two-times greater odds of requiring readmission within 30 days and trended toward significantly increased odds (51% greater odds) of MMM. Patients of advanced age are more at risk for venous thromboembolism, due to poor nutritional status, poor mobility and greater baseline comorbidities [16,17]. Among SRS patients, vertebral compression fracture is a well-known postoperative complication that has been associated with age greater than 55 years [18]. In another NSQIP study, Cote *et al.* [19] found that among 98,000 neurosurgical patients, older age and dependent functional status predicted postoperative respiratory failure. In the present analysis, we found that functional dependence prior to SRS was predictive of readmission within 30 days (42% greater odds) and of prolonged LOS (40% greater odds). Functional dependence prior to surgery has also been identified as a major risk factor for postoperative complications following various neurosurgical operations including adult spinal deformity, as well as following vascular and urologic surgery [20–22]. Those patients with a reduced ability to engage in daily tasks may have a more sedentary postoperative state and thus increased complication rates and frailty [15,20,21].

Other risk factors for prolonged LOS included CHF, disseminated cancer and renal failure. These risk factors for complications have been identified in other studies on spine surgery patients [23–28]. CHF has been implicated in poor patient outcomes, particularly due to its association with an increased risk of venous thromboembolism [29–31].

Although most of the significant predictive risk factors cannot be changed prior to SRS, there were some variables identified that could be modified to improve outcomes. A significant predictor of MMM was chronic steroid use (which increased the odds of the complication by 52%). Chronic steroid use is associated with infections, overall increases in mortality, and cardiac, renal and respiratory complications [32]. Local radiotherapy, such as SRS, can lead to a systemic inflammatory response, and with the increased inflammatory milieu and immunogenic response, the risk of these systemic complications appears to be heightened [33]. Our results reveal that the patients undergoing SRS for metastatic disease already have many comorbidities and are at high risk for post-treatment complications. Most of the predictive factors cannot be modified, but clinicians may consider trying to modify the ones that can be to reduce odds of complications. This could thereby improve the chance of improved quality of life following SRS treatment. Stopping or reducing steroids prior to treatment may be one avenue that can be considered. Future prospective and well-controlled studies are needed to further validate these findings.

There are limitations in the present study that should be considered. First, the NSQIP database only captures in-hospital and 30-day outcomes and cannot account for more long-term complications. Complications that can potentially develop outside of this 30-day postoperative window among SRS patients include radiation-induced myelopathy, which would not be captured in this database, but is a known complication associated with SRS for metastatic spine tumors [13,34–37]. Second, the NSQIP database did not separate metastatic tumors by location with regard to the spinal cord (extradural intramedullary or intradural extramedullary). Studies have suggested that location can differentially affect complication rates and symptom improvement associated with SRS treatment [36,38–40]. Future studies, designed to look at this, would be helpful to better understand these differential post-treatment courses. More generally, the design of the present study is observational, and accordingly we are only able to make associations rather than causal relationships. It is also important to note that the relatively high rate of adverse outcomes likely relates to the fact that many of those undergoing stand-alone SRS for spinal metastases have worse disease at baseline or greater comorbidities and may not be surgical candidates. The results herein, however, are helpful for risk stratification, patient counseling, and understanding cost and benefit of undergoing SRS. Despite the limitations, the present study is the first multi-institutional large-scale study looking at predictive factors for complications following SRS for metastatic spine tumors. The large national sample size enables generalization of the data.

Conclusion

The present study utilized a multicenter national database to evaluate the baseline factors associated with poor outcomes following SRS for spinal tumors. We found that increased age, greater BMI, and comorbidities such as renal failure, functional dependence, COPD, chronic steroid use and greater ASA class were associated with MM, 30-day readmission/operation and prolonged LOS. These data enable the clinician to provide better pretreatment patient counseling to prepare patients for likelihood of post-treatment complications and poor outcomes. Furthermore, with the transition to value-based medicine, hospital identification of risk factors will enable pathways for these patient populations that may ultimately improve cost efficiency and minimizing poor patient outcomes.

Financial & competing interests disclosure

CR Goodwin is a UNCF Merck Postdoctoral Fellow and has received an award from the Burroughs Wellcome Fund and the Johns Hopkins Neurosurgery Pain Research Institute. I Laufer has consulting relationships with Globus, DePuy/Synthes and SpineWave. DM Sciubba has consulting relationships with Medtronic, Globus, DePuy and Stryker. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

SUMMARY POINTS

- Symptomatic spinal metastases are found in greater than 40% of cancer patients.
- Stereotactic radiosurgery (SRS) is used as stand-alone treatment or as adjuvant following separation surgery.
- Risk of SRS includes radiation myelopathy and vertebral fractures.
- Identifying predictors of complications and readmission can allow for more appropriate counseling for patients and may improve cost efficiency.
- Following SRS, 7.1% of patients develop a major morbidity (MM), 6.9% are readmitted within 30 days, 4.3% have a subsequent operation within 30 days.
- Greater BMI, older age and chronic steroid use are predictive of MM following SRS.
- SRS performed in an urgent fashion is predictive of requiring a subsequent operation.
- Chronic steroid use is associated with 52% greater odds of MM following SRS.
- Most predictive factors are nonmodifiable; however potentially stopping steroids may lead to superior outcomes.

References

1 Bilsky MH, Lis E, Raizer J, Lee H, Boland P. The diagnosis and treatment of metastatic spinal tumor. *Oncologist* 4(6), 459–469 (1999).

2 Roodman GD. Mechanisms of bone metastasis. *N. Engl. J. Med.* 350(16), 1655–1664 (2004).

3 Turner S, Marosszeky B, Timms I, Boyages J. Malignant spinal cord compression: a prospective evaluation. *Int. J. Radiat. Oncol. Biol. Phys.* 26(1), 141–146 (1993).

4 Gibbs IC, Kamnerdsupaphon P, Ryu MR *et al.* Image-guided robotic radiosurgery for spinal metastases. *Radiother. Oncol.* 82(2), 185–190 (2007).

5 Rose PS, Laufer I, Boland PJ *et al.* Risk of fracture after single fraction image-guided intensity-modulated radiation therapy to spinal metastases. *J. Clin. Oncol.* 27(30), 5075–5079 (2009).

6 Sahgal A, Whyne CM, Ma L, Larson DA, Fehlings MG. Vertebral compression fracture after stereotactic body radiotherapy for spinal metastases. *Lancet Oncol.* 14(8), e310–e320 (2013).

7 American College of Surgeons National Surgical Quality Improvement Program. User Guide for the 2015 ACS NSQIP Participant Use Data File (PUF) (2015). https://www.facs.org

8 Shiloach M, Frencher SK Jr, Steeger JE *et al.* Toward robust information: data quality and inter-rater reliability in the American College of Surgeons National Surgical Quality Improvement Program. *J. Am. Coll. Surg.* 210(1), 6–16 (2010).

9 Khuri SF, Henderson WG, Daley J *et al.* Successful implementation of the Department of Veterans Affairs' National Surgical Quality Improvement Program in the private sector: the Patient Safety in Surgery study. *Ann. Surg.* 248(2), 329–336 (2008).

10 Chan KK, Xie F, Willan AR, Pullenayegum E. Underestimation of variance of predicted health utilities derived from multiattribute utility instruments: the use of multiple imputation as a potential solution. *Med. Descis. Making* 37(3), 262–272 (2016).

11 Gerszten PC, Burton SA, Ozhasoglu C, Welch WC. Radiosurgery for spinal metastases: clinical experience in 500 cases from a single institution. *Spine* 32(2), 193–199 (2007).

12 Hsu W, Nguyen T, Kleinberg L *et al.* Stereotactic radiosurgery for spine tumors: review of current literature. *Stereotact. Funct. Neurosurg.* 88(5), 315–321 (2010).

13 Veeravagu A, Lieberson RE, Mener A *et al.* CyberKnife stereotactic radiosurgery for the treatment of intramedullary spinal cord metastases. *J. Clin. Neurosci.* 19(9), 1273–1277 (2012).

14 Tayton ER, Frampton C, Hooper GJ, Young SW. The impact of patient and surgical factors on the rate of infection after primary total knee arthroplasty: an analysis of 64,566 joints from the New Zealand Joint Registry. *Bone Joint J.* 98-B(3), 334–340 (2016).

15 Sing DC, Yue JK, Metz LN *et al.* Obesity is an independent risk factor of early complications after revision spine surgery. *Spine* 41(10), E632–E640 (2016).

16 Guo F, Shashikiran T, Chen X, Yang L, Liu X, Song L. Clinical features and risk factor analysis for lower extremity deep venous thrombosis in Chinese neurosurgical patients. *J. Neurosci. Rural Pract.* 6(4), 471–476 (2015).

17 Deyo RA, Cherkin DC, Loeser JD, Bigos SJ, Ciol MA. Morbidity and mortality in association with operations on the lumbar spine. The influence of age, diagnosis, and procedure. *J. Bone Joint Surg. Am.* 74(4), 536–543 (1992).

18 Papanastassiou ID, Aghayev K, Saleh E, Gerochristou M, Vrionis FD. The actual management of tumor and vertebral compression fractures. *J. Neurosurg. Sci.* 56(2), 77–85 (2012).

19 Cote DJ, Karhade AV, Burke WT, Larsen AM, Smith TR. Risk factors for post-operative respiratory failure among 94,621 neurosurgical patients from 2006 to 2013: a NSQIP analysis. *Acta Neurochir. (Wien)* 158(9), 1639–1645 (2016).

20 Suskind AM, Walter LC, Jin C *et al.* Impact of frailty on complications in patients undergoing common urological procedures: a study from the American College of Surgeons National Surgical Quality Improvement database. *BJU Int.* 117(5), 836–842 (2016).

21 Partridge JS, Fuller M, Harari D, Taylor PR, Martin FC, Dhesi JK. Frailty and poor functional status are common in arterial vascular surgical patients and affect postoperative outcomes. *Int. J. Surg.* 18, 57–63 (2015).

22 Di Capua J, Somani S, Kim JS *et al.* Hospital acquired conditions (HACs) in adult spinal deformity surgery: predictors for HACs and other 30 day postoperative outcomes. *Spine* 42(8), 595–602 (2016).

23 Simpson JM, Silveri CP, Balderston RA, Simeone FA, An HS. The results of operations on the lumbar spine in patients who have diabetes mellitus. *J. Bone Joint Surg. Am.* 75(12), 1823–1829 (1993).

24 Phan K, Kim JS, Lee N, Kothari P, Cho SK. Impact of insulin dependence on perioperative outcomes following anterior cervical discectomy and fusion (ACDF). *Spine* 42(7), 456–464 (2016).

25 Koutsoumbelis S, Hughes AP, Girardi FP *et al.* Risk factors for postoperative infection following posterior lumbar instrumented arthrodesis. *J. Bone Joint Surg. Am.* 93(17), 1627–1633 (2011).

26 Guzman JZ, Iatridis JC, Skovrlj B *et al.* Outcomes and complications of diabetes mellitus on patients undergoing degenerative lumbar spine surgery. *Spine* 39(19), 1596–1604 (2014).

27 Fang A, Hu SS, Endres N, Bradford DS. Risk factors for infection after spinal surgery. *Spine* 30(12), 1460–1465 (2005).

28 Browne JA, Cook C, Pietrobon R, Bethel MA, Richardson WJ. Diabetes and early postoperative outcomes following lumbar fusion. *Spine* 32(20), 2214–2219 (2007).

29 Howell MD, Geraci JM, Knowlton AA. Congestive heart failure and outpatient risk of venous thromboembolism: a retrospective, case–control study. *J. Clin. Epidemiol.* 54(8), 810–816 (2001).

30 Haskins IN, Amdur R, Sarani B, Vaziri K. Congestive heart failure is a risk factor for venous thromboembolism in bariatric surgery. *Surg. Obes. Relat. Dis.* 11(5), 1140–1145 (2015).

31 Dean SM, Abraham W. Venous thromboembolic disease in congestive heart failure. *Congest. Heart Fail.* 16(4), 164–169 (2010).

32 Ismael H, Horst M, Farooq M, Jordon J, Patton JH, Rubinfeld IS. Adverse effects of preoperative steroid use on surgical outcomes. *Am. J. Surg.* 201(3), 305–309 (2011).

33 Formenti SC, Demaria S. Systemic effects of local radiotherapy. *Lancet Oncol.* 10(7), 718–726 (2009).

34 Dodd RL, Ryu MR, Kamnerdsupaphon P, Gibbs IC, Chang SD Jr, Adler JR Jr. CyberKnife radiosurgery for benign intradural extramedullary spinal tumors. *Neurosurgery* 58(4), 674–685 (2006).

35 Gerszten PC, Burton SA, Ozhasoglu C, McCue KJ, Quinn AE. Radiosurgery for benign intradural spinal tumors. *Neurosurgery* 62(4), 887–896 (2008).

36 Gibbs IC, Patil C, Gerszten PC, Adler JR Jr, Burton SA. Delayed radiation-induced myelopathy after spinal radiosurgery. *Neurosurgery* 64(2 Suppl.), A67–A72 (2009).

37 Marchetti M, De Martin E, Milanesi I, Fariselli L. Intradural extramedullary benign spinal lesions radiosurgery. Medium- to long-term results from a single institution experience. *Acta Neurochir. (Wien)* 155(7), 1215–1222 (2013).

38 Santacroce A, Kamp MA, Budach W, Hanggi D. Radiobiology of radiosurgery for the central nervous system. *Biomed. Res. Int.* 2013, 362761 (2013).

39 Saraceni C, Ashman JB, Harrop JS. Extracranial radiosurgery – applications in the management of benign intradural spinal neoplasms. *Neurosurg. Rev.* 32(2), 133–141 (2009).

40 Shin DA, Huh R, Chung SS, Rock J, Ryu S. Stereotactic spine radiosurgery for intradural and intramedullary metastasis. *Neurosurg. Focus* 27(6), E10 (2009).