Clinical Neurology and Neurosurgery 172 (2018) 1–7

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Factors associated with post-operative sepsis following surgery for spinal tumors: An analysis of the ACS-NSQIP database

Azeem Tariq Malik, Nikhil Jain, Thomas J. Scharschmidt, Joel L. Mayerson, Safdar N. Khan*

Department of Orthopaedics, The Ohio State University Wexner Medical Center, United States

ARTICLE INFO

Keywords:
Spinal tumors
Sepsis
NSQIP
Predictors
Infection

ABSTRACT

Objectives: Sepsis is a rare but potentially devastating complication when it occurs after surgery for spinal tumors. Given the morbidity associated with sepsis, we sought to collate evidence using a large national surgical database to identify the incidence, pre-operative predictors and post-operative factors associated with sepsis following spinal tumor surgery.

Patients and Methods: The 2005–2014 ACS-NSQIP database was queried for patients undergoing surgery for spinal tumors using ICD-9 codes for primary (170.2, 170.6, 213.2, 213.6) or secondary (198.3, 198.4 and 198.5) spinal tumor. Data were then filtered to include patients who underwent a laminectomy, corpectomy and/or spinal fusion for the tumor. A total of 1468 patients were included in the final cohort. Pre-operative risk factors were assessed using univariate regression models while adjusting for the occurrence of missing variables. Post-operative infectious sources such as urinary tract infection (UTI), pneumonia and surgical site infection were assessed for any association with the occurrence of sepsis.

Results: A total of 44 patients (3.0%) had an episode of sepsis within 30 days after surgery. Independent pre-operative factors significantly associated with the occurrence of sepsis were history of prior systemic inflammatory response syndrome (SIRS) (OR 2.89 [95% CI 1.3–6.2]), presence of Insulin-dependent Diabetes Mellitus (IDDM) (OR 3.52 [95% CI 1.4–8.7] and a length of stay > 8 days (OR 2.5 [95% CI 1.0–6.2]). Independent infectious sources associated with occurrence of sepsis were surgical site infection (SSI) (OR 23.3 [95% CI 8.6–63.7]), pneumonia (OR 5.8 [95% CI 2.2–15.2]) and urinary tract infection (UTI) (OR 14.7 [95% CI 5.96–36.1]). Up to 52% of the cases of sepsis were associated with at least one source of infection (UTI, pneumonia or SSI) with UTI being the most common (29.5%) followed by pneumonia (22.7%) and SSI (18%).

Conclusion: Three percent of patients following surgery for spinal tumor experience an episode of sepsis within 30 days. The most likely sources of sepsis include UTI, pneumonia and SSI. Pre- and post-operative targeted interventions in these high risk patients will be most beneficial in reducing the incidence, morbidity and mortality from sepsis after surgery for spinal tumors.

1. Introduction

Spinal tumors are a major cause of morbidity and mortality, with an estimated incidence of 0.62 per 100,000 individuals in the United States [21]. Primary spinal tumors are rare, and majority of tumors of the spinal column are malignant metastases with estimates showing that at least 30%–70% of cancer patients will have malignant spread of primary cancer to the spinal column [2,10]. Common sources of metastases are from the lung, breast and prostate [25,33], with the thoracic spine being involved the most [10].

Tumors of the spinal column primarily cause symptoms secondary to spinal cord compression and/or pathological fracture of the vertebrae. The management of spinal tumors consists of a combination of surgical decompression/reconstruction, chemotherapy and/or radiation. Given the morbidity of treatments in addition to primary cancer itself, patients are prone to complications that are much worse when compared to other spine surgical procedures [12,13,17,19,20,30,34,35,39].

Sepsis is defined as the inherent systemic response of the human body to an infection. It can lead to multiple-organ dysfunction, which adds considerable risk of morbidity and mortality to the patient recovering from surgery [28]. Moreover, sepsis also poses a significant economic burden to the health-care system, with more than $20.3 billion US dollars spent on care associated with this complication [1,29].

Few studies have explored the relationship between sepsis and spine

* Corresponding author.
E-mail address: safdar.khan@osumc.edu (S.N. Khan).

https://doi.org/10.1016/j.clineuro.2018.06.019
Received 25 April 2018; Received in revised form 17 May 2018; Accepted 11 June 2018
Available online 18 June 2018

surgery, with the majority focusing on elective procedures [40]. Based on our thorough search of literature, no study has explored the incidence and risk factors associated with development of sepsis following surgery for spinal tumors. Considering the high morbidity posed by the presence of cancer as well as the economic burden of sepsis, we sought to use a national surgical database to identify the incidence, pre-operative and post-operative risk factors associated with developing sepsis. This will hopefully lead to interventions aimed at decreasing this devastating complication.

2. Materials and methods

2.1. Data collection

The ACS-NSQIP database collects surgical information from more than 500 hospitals across the United States. Data are recorded for more than 150 preoperative, intra-operative and post-operative variables up to 30 days following operation. The data are collated by trained surgical and clinical reviewers with audit reports showing an inter-reviewer disagreement rate of less than 2%.

The 2005–2014 ACS-NSQIP database was queried for patients undergoing surgery for spinal tumors using International Classification of Diseases 9th Edition (ICD-9) codes for primary (170.2, 170.6, 213.2, 213.6) or secondary (198.3, 198.4 and 198.5) spinal tumors. Data were then filtered to include patients who underwent a laminectomy, corpectomy and/or spinal fusion for the tumor. A total of 1468 patients were included in the final cohort.

2.2. Baseline demographics and pre-operative clinical characteristics

Patient demographics that were extracted from the database included age, gender, race, body mass index (BMI; kg/m^2), comorbidities (diabetes, ischemic heart disease, chronic kidney disease, hypertension, chronic lung disease, etc.,), surgery location (cervical, thoracic, lumbar, thoracolumbar, sacral), type of cancer (malignant/benign and source of primary), American Society of Anesthesiologists (ASA) class, type of anesthesia, discharge disposition, yearly quarter of admission, total operative time and length of stay (LOS). Additionally, relevant pre-operative labs such as serum levels of sodium (Na), albumin (Alb), creatinine (Cr), hematocrit (Hct), WBC (white blood cell count), and PTT (partial thromboplastin time) were retrieved. The variables were dichotomized as "normal" or "abnormal" to allow for adjustment during logistic regression. Hyponatremia was defined as serum sodium < 135mEq/L; increased creatinine was defined as ≥ 1.1 mg/dL; a low WBC was defined as $< 4{,}500/\mu$L, low hematocrit was defined as $< 36\%$, increased PTT was defined as ≥ 25 s, and hypoalbuminemia was defined as serum Alb < 3.5 g/dL.

2.3. Assessment of post-operative sepsis and other post-operative complications

The NSQIP defines an occurrence of sepsis as meeting both of the following diagnostic criteria: 1) Clinical or laboratory evidence of an infectious source and (2) Presence of a systematic inflammatory response. Criteria 1 is further defined as the presence of at least one of the following: "positive blood culture"; "positive culture or purulence from any site thought to be the cause of the sepsis"; "bowel infarction leading to surgery"; or "suspected infection leading to surgical intervention." The presence of a systemic inflammatory response is defined as the presence of at least two of the following: tachycardia > 90 beats per minute, tachypnea > 20 breaths per minute, temperature $> 38\,^{\circ}$C or $< 36\,^{\circ}$C, leukocytosis $> 12{,}000$ cells/mm^3 or leukopenia < 4000 cells/mm^3 or bandemia of $> 10\%$ of total leukocyte count, or an anion-gap acidosis > 12. In order to classify a patient as having sepsis, at least one condition from criteria 1 and at least two conditions from criteria 2 are to be met.

In addition to assessing sepsis, we also included the following variables as potential sources of sepsis- urinary tract infection (UTI), pneumonia and surgical site infection (SSI). SSI was defined as the presence of either a superficial, deep or organ/space infection at the surgical site. To establish a causal relationship between infection sources and occurrence of sepsis, only those complications recorded before or on the day of diagnosis of sepsis were included in the "complication" cohort. All complications occurring after the diagnosis of sepsis were not deemed to be directly causing sepsis and were thus included in the "no complication" cohort.

2.4. Statistical analysis

Baseline demographics of the study population were reported using frequency and percentage for categorical data and mean with standard deviation for continuous data. The study cohort was defined into two populations: 1) Those who developed post-operative sepsis within 30 days following the index procedure and 2) Those who did not develop any post-operative sepsis within 30 days following index procedure. Since data were missing for several variables, the missing indicator variable method was used to adjust for the presence of missing data [8,9]. This method has previously been used in studies, as data absent in the NSQIP has been reported to be not missing at random [15]. Each variable was entered separately into a logistic regression model (univariate logistic regression). All variables from the univariate analysis were then entered into a backward elimination multivariate regression model while controlling for baseline clinical characteristics.

Two separate logistic regression models were created, one for assessing pre-operative and procedural risk factors, and the other to assess post-operative infectious sources associated with occurrence of sepsis. All statistical analysis was carried out using SPSSv23 (IBM, Armonk, NY). For all analytical purposes, a p-value of less than 0.05 was considered significant.

3. Results

A total of 1468 patients met the inclusion criteria. Table 1 shows the baseline demographics of the study population. The majority of the patients fell in the age group of 61–70 years (31.4%) and were male (61.3%). A total of 51.2% of the surgeries were done for thoracic location of tumors, followed by lumbar (19.8%) and cervical (15.1%). The most common type of spinal tumor was malignant metastases (77.3%). A plurality of the patients stayed for more than 8 days (42.4%), with the surgeries being distributed more or less equally throughout the different quarters of the year.

3.1. Incidence, pre-operative and procedural risk factors for sepsis

Forty-four patients (3.0%) patients developed sepsis within 30 days of the index procedure. Univariate regression analysis showed that presence of Insulin Dependent Diabetes Mellitus (IDDM), pre-operative ventilator dependency, Systemic Inflammatory Response syndrome (SIRS), ASA Class $\geq$ III, transfer from acute-care inpatient hospital, a length of stay > 8 days, pre-operative Hct $< 36\%$, hypoalbuminemia (< 3.5 g/dL) and hyponatremia (< 135eq/mL) were significantly associated with increased occurrence of sepsis (Table 2). Following multivariate backward elimination regression, only a history of prior SIRS (OR 2.89 [95% CI 1.3–6.2]), presence of IDDM (OR 3.52 [95% CI 1.4–8.7] and a length of stay > 8 days (OR 2.5 [95% CI 1.0–6.2]) were associated with an increased occurrence of post-operative sepsis (Table 3).

3.2. Post-operative sources of infection leading to sepsis

Out of 44 patients, 29 (65.9%) patients had at least one infection source such as UTI, SSI or pneumonia (Table 4). The most common