Predictors of reoperation and noninfectious complications following craniotomy for cerebral abscess

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ABSTRACT

Objectives: There is a paucity of literature that examines predictors of reoperation and noninfectious complications following treatment of cerebral abscess with craniotomy. The goal of the present study is to identify predictors for each of these outcomes.

Patients and methods: The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database 2012–2016 file was the data source. Patients were identified using a combination of CPT and ICD-9/10 codes. Exclusions included missing age/gender, secondary surgery, and absent length of stay information. Univariate followed by multivariable analysis using logistic regression was used to identify significant predictors of reoperation and noninfectious postoperative complications ($p < 0.05$).

Results: 166 patients met the above criteria. Median age was 56 (IQR 44–65) and 68.1% of patients were men. The 30-day reoperation rate was 18.1% and increasing white blood cell count (WBC) was identified as a significant risk factor for reoperation (odds ratio [OR] 1.10, 95% CI 1.02–1.19, $p = 0.013$). Noninfectious complications occurred at a rate of 20.5% at 30 days. Significant predictors were ASA classification ≥ 4 (OR 4.13, 95% CI 1.74–9.81, $p = 0.001$), smoking (OR 3.04, 95% CI 1.18–7.78, $p = 0.020$), and increasing WBC count (OR 1.11, 95% CI 1.03–1.20, $p = 0.007$). Emergency case status, abscess location (supratentorial versus infratentorial), nor chronic steroid use demonstrated a significant relationship with the studied outcomes.

Conclusion: Increasing preoperative WBC count predicts both reoperation and noninfectious complications following craniotomy for cerebral abscess. Less modifiable predictors for noninfectious complications which may help anticipate operative risk are smoking and high ASA classification.

1. Introduction

Cerebral abscesses are walled-off, suppurative collections of cellular debris that usually arise from contiguous spread of an adjacent infection (e.g. otitis, osteomyelitis), hematogenous spread of a distant infection, or penetrating trauma [3,5,15,17]. Although outcomes have improved markedly over the past several decades [2,4,24], mortality rates in post-computed tomography (CT) cohorts can still be as high as 32% [13]. Clinical presentation is often ambiguous, as the classical symptoms of fever, headache, and focal neurological deficit are only apparent in approximately 10–20% of patients [4,20,22], making high clinical suspicion and timely diagnosis critical. In addition to intravenous antibiotics, open treatment via craniotomy is a viable treatment option [5]. Advances in microsurgical techniques for abscess drainage, including stereotactic guidance, have led to a paradigm shift in neurosurgical approaches to brain abscesses [5,9,10,15,17]. There are several clinical circumstances which call for open treatment of cerebral abscesses with craniotomy [3,5,9,10,15–17]. In addition, some neurosurgeons still favor craniotomy with lesion aspiration or excision as an initial approach for superficial abscesses in non-eloquent cortex [9,18].

Perhaps due to the overall low incidence of brain abscess [6] and the statistical power restriction this imposes, analysis of risk factors for adverse outcomes is difficult. Although several studies have described pretreatment neurological status as a strong predictor of overall outcomes [7,17,21,22], predictors of noninfectious morbidity and reoperation rates are sparse in the literature [3,14]. To our knowledge, such predictors have not been examined in post-craniotomy abscess patients, despite reports that recurrence rates and postsurgical morbidity are high [3,22,23]. We believe that identification of such indicators could help guide clinical management. Accordingly, the goals

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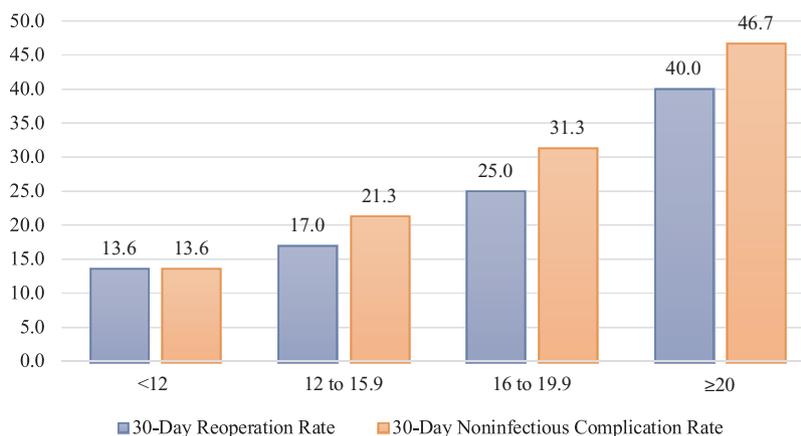## 30-Day Reoperation and Noninfectious Complication Rate by WBC Count

Fig. 1. 30-day reoperation and noninfectious complication rate by preoperative WBC count.

of the present study are to report the rates of noninfectious complications and reoperation following craniotomy for cerebral abscess and identify significant predictors for each of these outcomes.

2. Materials and methods

2.1. Data source and study design

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database (2012–2016) was utilized for the present study. NSQIP collects perioperative parameters from almost 700 participating institutions, achieves a high rate of inter-observer reliability, and is regularly audited. [1,11,19] Being that the NSQIP database collects information prospectively, this is a retrospective review of prospectively-collected data. The present study is exempt from the institutional review board due to the de-identified nature of the information.

2.2. Inclusions and exclusions

Inclusion in the current study required an assigned Current Procedural Terminology (CPT) code for craniotomy for abscess evacuation (61320, 61321, 61514, 61522) and a corresponding ICD-9/10 code for cerebral abscess (324.0, G06.0). Exclusions included 1) missing age or gender information, 2) missing reoperation information, or 3) missing length of stay information. 166 total patients remained that met these criteria. All patients were ≥ 18 years of age and admitted between 2012 and 2016.

2.3. Missing data

No more than 5 patient records contained missing data regarding any of the analyzed covariates. If data was found to be missing, these values were controlled for during multivariable logistic regression.

2.4. Analyzed covariates

Age, body mass index (BMI), time from admission to surgery, total length of stay, operative time, preoperative white blood cells (WBC), and preoperative hematocrit were analyzed as continuous covariates. Gender, smoking, diabetes, chronic obstructive pulmonary disease (COPD), hypertension, chronic steroid use, emergency case, American Society of Anesthesiologists (ASA) classification (≥4, < 4), and location (supratentorial, infratentorial) were analyzed as dichotomous covariates.

2.5. Outcomes of interest

The primary outcomes of interest which formed the dependent variables during our analysis were 30-day reoperation (all unplanned) and 30-day noninfectious complications. Noninfectious complications were recorded in the affirmative if a patient experienced reintubation, requirement for mechanical ventilation greater than 48 h, venous thromboembolism, progressive renal insufficiency, acute renal failure, coma, stroke, cardiac arrest, or myocardial infarction within 30 days of surgery. Reintubation and mechanical ventilation greater than 48 h were not recorded as noninfectious complications if the patient required reoperation to avoid potential confounding. Neurological outcomes were not collected due to incomplete data in the analyzed sample.

2.6. Statistical analysis

General characteristics of the cohort are reported as frequencies/percentages for dichotomous covariates and medians/interquartile ranges for continuous covariates. First, univariate tests using Fischer's exact and Wilcoxon-Mann-Whitney tests were performed for categorical and continuous parameters, respectively, to identify potential predictors of reoperation and noninfectious complications. Parameters with probability values less than 0.20 were included in multivariate logistic regression models controlled for age and gender. To ensure appropriate model calibration, Hosmer-Lemeshow goodness-of-fit statistics were utilized; probability values greater than 0.05 indicated satisfactory calibration [12]. Probability values less than 0.05 in multivariable analysis were considered statistically significant. Stata IC 15.1 software (StataCorp, College Station, Texas) was used throughout the analysis. Microsoft Excel was used to construct Fig. 1.

3. Results

3.1. Cohort characteristics

The baseline information, comorbidities, laboratory values, and intraoperative characteristics of the cohort can be found in Table 1. Median age and BMI were 56.0 years and 26.8 kg/m^2. The cohort was predominantly male (68.1%) and most patients were admitted from home (56.0%). The most common comorbidities were hypertension (56.6%), diabetes (22.9%), and smoking (27.7%). Less than half the cases were classified as emergent (40.4%), yet the median time from admission to surgery was 1 day (IQR 0–2). A significant portion of patients carried ASA classifications ≥4 (30.7%). Expectantly, abscess

Table 1
Baseline preoperative and intraoperative characteristics of the cohort.

Parameter (n = 166 patients)	n
Median age (IQR)	56 (44-65)
Median body mass index kg/m^2 (IQR)	26.8 (22.5-31.9)
Transfer status (%)	
From home	93 (56.0)
Not transferred from home	73 (44.0)
Gender (%)	
Male	113 (68.1)
Female	53 (31.9)
Diabetes (%)	
Not diabetic	128 (77.1)
Diabetic	38 (22.9)
Smoking history (%)	
Nonsmoker	120 (72.3)
Smoker	46 (27.7)
Hypertension (%)	
Not hypertensive	94 (56.6)
Hypertension	72 (43.4)
Functional status (%)	
Independent	150 (90.4)
Dependent (Partial or Total)	16 (9.6)
COPD (%)	
No COPD	157 (94.6)
COPD	9 (9.6)
Steroid use (%)	
No steroid use	150 (90.4)
Chronic steroid use	16 (9.6)
ASA Classification (%)	
< 4	115 (69.3)
≥4	51 (30.7)
Emergency status (%)	
Non-emergent	99 (59.6)
Emergent	67 (40.4)
Abscess location (%)	
Supratentorial	150 (90.4)
Infratentorial	16 (9.6)
Median WBC x10^9/L (IQR)	11.6 (8.4-15.3)
Median Hematocrit (IQR)	37.2 (33.8-41.2)
Median days from admission to surgery (IQR)	1 (0-2)
Median operative time in minutes (IQR)	107 (67-161)
Postoperative outcomes at 30 days (%)	
Reoperation	30 (18.1)
Noninfectious complication	34 (20.5)
Mortality	7 (4.2)

location was most often supratentorial (90.4%) versus infratentorial (9.6%). Patients had a marginal leukocytosis, as the median WBC was 11.6 (IQR 8.4–15.3) and were borderline anemic with a median hematocrit of 37.2% (IQR 33.8–41.2). Most cases were less than two hours in duration; the median operative time was 107 min (IQR 67–161).

Reoperation occurred in 18.1% of cases within 30 days of surgery (n = 30). The principal CPT codes corresponding to the procedures are outlined in Supplementary Table 1. The most common procedure was repeat craniotomy, which was performed in 9.0% of cases overall. Noninfectious complications following surgery occurred at a rate of 20.5% (n = 34). Supplementary Table 2 outlines the frequency of each of these complications. The 30-day mortality rate was 4.2%.

3.2. Predictors of reoperation

Univariate analysis for reoperation following craniotomy for cerebral abscess is reported in Table 2 (columns 2–4). Covariates that met the threshold for inclusion in multivariable analysis were admission from home (p = 0.16), preoperative WBC (p = 0.04) and operative time (p = 0.04). As stated above, age and gender were included in the model to minimize confounding. Multivariate logistic regression identified an increasing preoperative WBC as the sole independent predictor of unplanned return to the operating room (odds ratio [OR] 1.10, 95% CI 1.02–1.19, p = 0.013). The model was appropriately calibrated as

evidenced by Hosmer-Lemeshow p = 0.12.

3.3. Predictors of noninfectious complications

Table 2 (columns 5–7) also displays results from univariate analysis for postoperative noninfectious complications. Several parameters achieved the desired threshold for inclusion in multivariable analysis: age (p = 0.05), smoking (p = 0.13), ASA classification ≥4 (p < 0.001), increasing preoperative WBC (p = 0.001), chronic steroid use (p = 0.10), and operative time (p = 0.15). Ultimately, three independent predictors of noninfectious postoperative complications were identified: smoking (OR 3.04, 95% CI 1.18–7.78, p = 0.020), ASA classification ≥4 (OR 4.13, 95% CI 1.74–9.81, p = 0.001), and increasing preoperative WBC (OR 1.11, 95% CI 1.02–1.20, p < 0.001). Increasing age was borderline significant (OR 1.03, 95% CI 1.00–1.06, p = 0.063) (Table 3).

3.4. Association of WBC count with outcomes

Fig. 1 shows the rate of reoperation and noninfectious complications in patients with WBC counts < 12, 12–15.9, 16–19.9, and ≥20 cells x10^9/L, demonstrating that rising WBC was associated with adverse outcomes. The groups were comprised of 88, 47, 16, and 15 patients, respectively. Unsurprisingly, the rate of reoperation and complications was lowest in the < 12 cells x10^9/L group (both 13.6%) and highest in the ≥20 cells x10^9/L group (40.0 and 46.7%).

4. Discussion

4.1. Predictors of reoperation and complications

The management of cerebral abscess is highly complex, requiring an interdisciplinary team of neurosurgeons, radiologists, and infectious disease specialists. Lu et al. proposes that the approach to brain abscess management is guided by, "anatomic location, number/size of abscess (es), stage of formation, age of patient, and neurological status." [15] Although CT-guided aspiration is often the preferred surgical intervention [5,9,10,15,17], several clinical circumstances call for a craniotomy with aspiration or excision. Patients with rapidly deteriorating neurological function or with signs of significant mass effect require urgent decompression [8,17]. In addition, abscesses that are singular and multiloculate, secondary to penetrating trauma, located in the posterior fossa, or carry the possibility of fungus or atypical bacteria (such as *Nocardia* or *Actinomyces species*) should be addressed with craniotomy/craniectomy [5,8,10,15–17,23]. Further, abscesses refractory to stereotactic aspiration may require decompression with craniotomy to adequately resect the infectious nidus [17]. Although the role for craniotomy in the treatment of cerebral abscess is reduced today from what it once was, it remains necessary for a sizable portion of patients. Given our study population's reoperation rate (18.1%) and noninfectious complication rate (20.5%), data which aids clinicians in identifying those at high risk is critical for optimal patient care.

Predictors of overall outcomes in post-treatment abscess patients are, overall, sparsely reported. Tattevin et al. identified pretreatment Glasgow Coma Score (GCS) ≤9 to be significantly associated with in-hospital mortality (p = 0.006) [21]. This finding was echoed by Xiao et al. whom determined that achievement of favorable outcomes (partial dependence or better) was more likely in patients with a higher initial GCS (p < 0.001) or immunocompetent status (p = 0.004) [22]. Similarly, Çavuşoglu et al. determined that pretreatment neurological status was strongly predictive of outcomes (p < 0.001) [7] and this finding was later corroborated by Muzumdar et al. [17] Other predictors of poor outcomes reported in a recent review by Brook include a delay in diagnosis, > 1 abscess, deep abscesses, and intraventricular abscess rupture [3].

The present study is the first to identify predictors of reoperation

Table 2

Univariate analysis of reoperation and noninfectious postoperative complications.

Parameter	No reoperation	Reoperation	p-value	No noninfectious complication	Noninfectious complication	p-value
Median age (IQR)	56 (44-66)	52 (36-64)	0.23[*]	54 (44-63)	59 (41-69)	0.05[‡]
Median BMI (IQR)	26.6 (22.8-32.1)	27.4 (21.2-31.0)	0.76	26.8 (22.7-32.1)	26.9 (21.9-31.1)	0.52
Transfer from home (%)	80 (58.9)	13 (43.3)	0.16[*]	75 (59.1)	18 (46.2)	0.25
Male (%)	90 (66.2)	23 (76.7)	0.29[*]	88 (69.3)	25 (64.1)	0.41[‡]
Diabetic (%)	32 (23.5)	6 (20.0)	0.81	28 (22.1)	10 (25.6)	1.00
Smoking (%)	39 (28.7)	7 (23.3)	0.66	31 (24.4)	15 (38.5)	0.13[‡]
Hypertension (%)	61 (44.9)	11 (36.7)	0.52	52 (40.9)	20 (51.3)	0.25
Functional dependence (%)	14 (10.3)	2 (6.7)	0.74	14 (11.0)	2 (5.1)	0.20
COPD (%)	4 (4.4)	3 (10.0)	0.21	6 (4.7)	3 (7.7)	1.00
Chronic steroid use (%)	14 (10.3)	2 (6.7)	0.74	10 (7.8)	6 (15.4)	0.10[‡]
ASA Classification ≥4 (%)	41 (30.2)	10 (33.3)	0.83	28 (22.1)	23 (59.0)	< 0.001[‡]
Emergent case (%)	52 (38.2)	15 (50.0)	0.30	49 (38.6)	18 (46.2)	0.44
Supratentorial abscess (%)	121 (89.0)	29 (96.7)	0.31	113 (89.0)	37 (94.9)	0.53
Median WBC x 10^9/L (IQR)	11.3 (8.1-14.9)	13.0 (8.9-17.1)	0.04[*]	10.5 (7.9-13.6)	14.2 (11.6-17.8)	0.001[‡]
Median Hematocrit (IQR)	37.0 (33.7-41.0)	37.6 (34.0-41.4)	0.65	38.0 (33.9-41.7)	35.2 (33.1-39.8)	0.20
Median days from admission to surgery (IQR)	1 (0-3)	1 (0-2)	0.24	1 (0-2)	1 (0-3)	0.80
Median operative time (IQR)	101 (66-140)	123 (84 -189)	0.04[*]	97 (63-154)	122 (90-189)	0.15[‡]

[*] indicates inclusion in multivariate model for reoperation; [‡] indicates inclusion in multivariate model for noninfectious complications.

Table 3

Predictors of noninfectious complications following craniectomy/craniotomy for cerebral abscess.

Parameter	Odds Ratio	95% Confidence Interval	p-value
Smoking	3.04	1.19-7.78	0.020
ASA Classification ≥4	4.13	1.74-9.81	0.001
WBC x10^9/L	1.11	1.03-1.20	0.007
Age[*]	1.03	1.00-1.06	0.063

[*]age was marginally significant with p-value between 0.05 and 0.10.
Hosmer-Lemeshow goodness-of-fit p = 0.16.

and noninfectious complications following craniotomy for cerebral abscess. Although several prior studies determined that preoperative WBC did not correlate with outcomes [7,22], our data contrasts this notion, as we found WBC to be predictive of both reoperation and noninfectious complications. Specifically, a 1 unit increase in preoperative WBC (e.g. 11–12 × 10^9 cells/L) was associated with an approximate 10% increase in odds of reoperation and noninfectious postoperative complications. This disparity between previous studies and our own may well be a product of endpoints examined, as our primary outcomes were reoperation and noninfectious morbidity, whereas prior studies analyzed preoperative WBC's relationship with mortality and neurological function. Additionally, ASA classification ≥ 4 and smoking were associated with 4.13 and 3.04 times increased odds of noninfectious complications. Although high ASA classification and smoking are largely unmodifiable in the context of cerebral abscesses due to the acuity the disease process, our findings emphasize the importance of timely initiation of antibiotics to attenuate the systemic inflammation, as this may reduce returns to the operating room and overall morbidity.

Ultimately, it appears that pre-treatment neurological status is the strongest predictor of recovery based on previous literature, irrespective of management strategy. And as shown by our median time from admission to surgery (1 day [IQR 0–2]), an emphasis is rightfully placed on prompt diagnosis and timely intervention. We believe that the predictors identified from the present study can help improve patient outcomes and may be helpful in stratifying operative risk.

4.2. Strengths & limitations

The strengths of this study include a large patient sample, use of a prospectively-collected database with high inter-observer reliability, and application of controlled multivariate analyses to identify significant predictors of outcomes. The present study is one of the largest

to date to address cerebral abscess, and to our knowledge the largest study which has examined decompressive management specifically in a contemporary cohort.

However, our study also has several unavoidable limitations. Perhaps the most significant is the fact that we are unable to assess pretreatment neurological status or whether these patients failed nonoperative management prior to surgical treatment due to constraints of the NSQIP database. Additionally, while we know all patients underwent craniotomy, we are unable to discern whether the lesion was aspirated or excised, which could affect reoperation and morbidity rates. [9,23] Regarding reoperation data, we also do not have access to the full list of assigned CPT codes to each patient and therefore cannot fully describe the procedures each patient underwent. Notwithstanding, we can say with certainty that each reoperation was unplanned as this is recorded by the NSQIP database. Other limitations include a lack of access to radiographic images and microbiological information.

4.3. Future directions

Brain abscess management is highly complex and numerous treatment modalities are available to clinicians. To validate our findings and perhaps discover other significant predictors of outcomes, we believe further study of reoperation and postsurgical complications of cerebral abscess is needed. Much of the data used to guide management of this difficult entity is derived from case series and retrospective comparisons. As such, prospective studies are needed to formulate evidence-based guidelines regarding management. Potential obstacles to this include the acuity of cases, surgeon preference for certain procedures, institutional limitations, and the relatively low incidence of abscesses overall.

5. Conclusion

Increasing preoperative WBC count is predictive of both reoperation and noninfectious complications following craniotomy for abscess evacuation, emphasizing importance of swift initiation of antimicrobial therapy prior to surgery. Predictors of noninfectious complications include smoking and ASA classification ≥ 4. Further study is needed to validate our results in post-craniotomy cerebral abscess patients.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.clineuro.2019.02.020.

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