



## Emergency glioma resection but not hours of operation predicts perioperative complications: A single center study



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### ABSTRACT

**Objective:** Physical and mental status of neurosurgeons may vary with emergency status and hours of operation, which may impact the outcome of patients undergoing surgery. This study aims to clarify the influence of these parameters on outcome after surgery in glioma patients.

**Patients and methods:** A total of 477 nonemergency surgery (NES) and 30 emergency surgery (ES) were enrolled in this study. Using propensity score matching (PSM) analysis, 97 pairs of procedures from NES group were generated and then classified as group M (morning procedures, 8:00 a.m.–1:00 p.m.) or group A (afternoon or night procedures, 1:00 p.m.–8:00 p.m.). 30 emergency procedures were classified into group ESa (daytime emergency surgery, 8:00 a.m.–6:00 p.m.) and group ESb (nighttime surgery procedures, 6:00 p.m.–8:00 a.m. the next day). Differences in intraoperative risk factors and postoperative complications were analyzed.

**Results:** Postoperative complications, including death within 30 days ( $p = 0.004$ ), neurological function deficit ( $p = 0.012$ ), systemic infection ( $p < 0.001$ ) were significant higher in emergency procedures. Intraoperative risk factors including blood loss ( $p < 0.001$ ), blood transfusion ( $p = 0.036$ ) were also higher in emergency procedures than nonemergency procedures, although both procedures had comparable time duration ( $p = 0.337$ ). By PSM analysis, patients in group M and group A were well matched and no significant difference of intraoperative risk factors and postoperative complications (all  $p > 0.05$ ) were found. Furthermore, incidence of intraoperative risk factors and postoperative complications were similar in both groups ESa and ESb (all  $p > 0.05$ ).

**Conclusion:** Emergency glioma resection is a very important risk factors of perioperative mortality and morbidity for patients. However, hours of operation did not necessarily predict postoperative mortality or morbidity, either in emergency or nonemergency glioma resection.

### 1. Introduction

Medical errors reportedly cause between 48000 to 98,000 deaths each year in the USA [1]. Even if medical errors do not cause death, disability or performance impairment could also be traumatic events for patients, especially for those who undergo craniotomy. Understanding indicators of medical errors is critical for reducing perioperative complications in clinical trials.

Given the fact that surgery often requires careful preoperative planning, accurate intraoperative decision making and handling sophisticated instruments and tools, surgeons may have a higher probability to make medical errors when facing emergency surgery. A

retrospective study reported that delayed diagnosis or misdiagnosis was one of the leading cause for treatment error complained by the patients [2]. It may not reflect how surgeons work in reality, but it still provides us a glimpse of medical errors in emergency surgery. Some studies found that emergency surgical procedures were more likely to have higher rates of morbidity and mortality compared to elective procedures [3–6]. These findings are consistent with the notion that emergency surgery poses a level of risk to patients, however, it is still unknown if it is applicable to brain tumor surgeries.

When examining the underlying causes, it is widely accepted that fatigue and sleep deprivation could impair physical and cognition performance, including mood, movement, assessment of disease

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activity and treatment decision making, and contribute significantly to medical errors [7–9]. Increased complications in procedures performed by surgeons who had less than 6 hours of sleep, and increased morbidity in nighttime procedures compared to the daytime procedures has been demonstrated by several groups [9–13]. However, follow up studies did not replicate these findings [14–16]. Despite conflicting conclusion from different studies, it is still plausible that fatigue and sleep deprivation have certain influence on performance of surgeons and other surgical professions. Apart from acute sleep deprivation and obvious fatigue, neurosurgeons are more likely to get progressively fatigue and sleep loss due to continuous “high stakes” work.

These interesting findings prompted us to investigate the influence of emergency status and hours of operation on perioperative complications in glioma resection. Our objectives were to evaluate the relative ability of emergency status and operative start time to predict short time outcome in glioma patients, and to provide a recommendation about the optimal timing of tumor resection for patients with glioma.

## 2. Patients and methods

### 2.1. Patients cohorts

The medical records of patients diagnosed with glioma and received craniotomy at the First Affiliated Hospital of Xi'an Jiaotong University between June 2008–July 2014 were collected and retrospectively analyzed. The pathology diagnosis was determined by two senior neuropathologists according to the 2016 WHO classification of the central nervous system tumor. A total of 550 patients who had previously provided written consent for their medical records to be used in retrospective studies were retrieved. This study was approved by and conducted in accordance with the policies of the Scientific Ethics Committee of Xi'an Jiaotong University.

Patient demographic characteristics, system diseases (hypertension, cardiovascular disease, lung disease, diabetes mellitus), tumor characteristics (pathology diagnose, tumor location and size), preoperative tumor stroke (defined as hemorrhagic or ischemic stroke within tumor area), pre- and postoperative blood laboratory tests (including blood routine test, blood coagulation function, and liver function), imaging (computer tomography, CT or magnetic resonance images, MRI) and neurosurgical intensive care unit (NICU) durations were recorded. The Karnofsky Performance Scale (KPS) score and perioperative complications were recorded. The operation associated intraoperative risk factors (operation route, starting and finishing time, intraoperative blood loss and blood transfusion), extent of resection (gross total resection, TR, 95–100% of enhancement; subtotal resection, STR, 80–95% of enhancement; and partial resection, PR, < 80% enhancement), American Society of Anesthesiologists (ASA) score were documented in operation and anesthesia records. The start of the procedure was defined as the start of skin incision. All the procedures were accomplished by senior neurosurgeons with more than 10 years of neurosurgical experience. Patients were randomly selected to morning surgery or afternoon surgery, those presented with declined consciousness, or newly found severe deteriorated symptoms (severe headache or declined consciousness) and consistently diagnosed tumor stroke or severe edema (brain midline shift > 5 mm) by CT or MRI when waiting for selective surgery were assigned to emergency surgery (ES).

Patients under 16 years, without complete medical records listed above, presented with uncontrolled systemic disease including abnormal blood pressure and blood glucose even with medication, and acute phase of cardiovascular disease and lung disease were also excluded, and 43 patients were excluded based on these exclusion criteria.

### 2.2. Study design

We grouped the all the procedures into nonemergency surgery group (NES group) and emergency surgery group (ES group) based on

emergency status. According to the operative start time, NES group was classified into group M (morning surgery, 8:00 a.m.–1:00 p.m.) and group A (afternoon or night surgery, 1:00 p.m.–8:00 p.m.), and ES group was subdivided into group ESa (daytime emergency surgery, 8:00 a.m.–6:00 p.m.) and group ESb (nighttime emergency, 6:00 p.m.–8:00 a.m. the next day).

Body mass index (BMI) was calculated from preoperative height and weight. Prognostic nutritional index (PNI) was calculated as follows:  $PNI = 10 \times \text{Serum albumin concentration (g/dl)} + 0.005 \times \text{lymphocyte count from peripheral blood}$ .

Intraoperative medical events (blood loss, blood transfusion, operation duration) and postoperative complications were considered as perioperative complications. Postoperative complications were subdivided into severe complications, central nerve system (CNS) complications and systemic complications. Severe complications were defined as death within 30 days, unplanned re-operation within 7 days after operation. CNS complications were defined as seizure, neurological deficit, intracranial infection and cerebrospinal fluid (CSF) leak. Systemic complications included deep venous thrombosis, electrolyte disturbance, systematic infections (pulmonary infection and urinary infection) and other medical conditions arising after surgery. For those recurrent patients, the newly diagnosed neurological deficits rather than presented after prior operation were considered as complications for the current operation.

### 2.3. PSM analysis

To eliminate selection bias and balance the baseline differences, we introduced propensity score matching (PSM) analysis into the present study and thereby simulated random group allocation [17]. Propensity score was calculated by patient characteristics including age, sex, BMI, primary disease, tobacco and alcohol use, KPS, tumor recurrent status, ASA score, blood routine tests, PNI, blood coagulation function, tumor size and location. PSM analysis with 2:1 matching was performed without replacement using a caliper with a width 0.2 of standard deviation.

### 2.4. Statistical analysis

Numerical data were expressed as mean  $\pm$  standard deviation and compared between two groups with Student's or *Mann-Whitney U* test. Categorical data was presented as percentages and compared with Chi-Squared test. Statistical analysis and propensity score matching analysis were carried out using SPSS 22.0 (Chicago, IL, USA). A *p* value < 0.05 was considered statistically significant.

## 3. Results

A total of 550 procedures performed on 481 patients were retrospectively reviewed. After exclusion of 43 procedures, 507 procedures were selected. Of these cohort of patients, 477 patients underwent nonemergency surgery (NES) and 30 patients underwent emergency surgery (ES). As shown in Table 1, there were significantly more patients in the group ES presented with either tumor hemorrhage stroke or ischemic stroke ( $p < 0.001$ ), worse preoperative physical status, KPS < 70 (30% vs 2.9%,  $p < 0.001$ ), high ASA score (mainly P4,  $p < 0.001$ ), lower BMI ( $21.8 \pm 1.9$  vs  $22.7 \pm 3.1$ ), higher white blood cell count ( $9.7 \pm 3.9$  vs  $6.8 \pm 2.7$ ,  $p = 0.006$ ) and longer APTT times ( $34.1 \pm 7.2$  vs  $33.5 \pm 4.6$ ,  $p = 0.014$ ). Interestingly, patients in ES group were more likely to be found with high grade glioma (grade 3 and grade 4,  $p = 0.057$ ), but there was no difference in tumor location ( $p = 0.627$ ). Notably, those patients in group ES lost more blood ( $1130.4 \pm 1772.1$  vs  $599.9 \pm 404.6$  ml,  $p < 0.001$ ), received more allogeneic blood transfusion ( $p = 0.036$ ) despite similar duration of surgery ( $4.82 \pm 1.68$  h vs  $4.05 \pm 1.27$  h,  $p = 0.337$ ). Additionally, consistent with previous studies [3–6], there were higher death

**Table 1**  
Baseline characteristics of patients underwent emergency surgery (ES Group) and nonemergency surgery (NES Group).

	NES Group(n = 477)	ES Group (n = 30)	p value
Sex (male), n (%)	265(55.6)	13(43.3)	0.192
Age (years)	47 ± 13	46 ± 13	0.733
Body mass index (kg/m <sup>2</sup> )	22.7 ± 3.1	21.8 ± 1.9	0.041
Recurrent tumor, n (%)	88(10.4)	8(26.7)	0.265
Tumor stroke			< 0.001
Hemorrhagic stroke, n (%)	26(5.5)	16(53.3)	
Ischemic stroke, n (%)	0(0)	13(43.3)	
KPS (< 70), n (%)	14(2.9%)	9(30.0)	< 0.001
Hypertension, n (%)	69(14.5)	1(3.3)	<b>0.086</b>
Diabetes Mellitus, n (%)	18(3.8)	1(3.3)	0.902
Cardiovascular Disease, n (%)	8(1.7)	0(0)	0.475
Chronic Lung Disease, n (%)	8(1.7)	0(0)	0.475
Smoking, n (%)	78(16.4)	5(16.7)	0.964
Drinking, n (%)	60(12.6)	5(16.7)	0.516
White blood cells (10 <sup>9</sup> /L)	6.8 ± 2.7	9.7 ± 3.9	0.006
Platelet count (10 <sup>9</sup> /L)	186.9 ± 60.2	180.4 ± 67.9	0.550
Hemoglobin (g/L)	135.3 ± 17.2	137.8 ± 17.6	0.937
PT (s)	12.4 ± 0.9	12.6 ± 0.9	0.823
APTT (s)	33.5 ± 4.6	34.1 ± 7.2	0.014
Albumin (g/L)	40.6 ± 4.3	41.7 ± 5.4	0.335
PNI	40.6 ± 4.3	41.7 ± 5.4	0.335
ASA score, n (%)			< 0.001
P1	59(12.4)	1(3.3)	
P2	291(61.0)	3(10.0)	
P3	114(23.9)	5(16.7)	
P4	13(2.7)	21(70.0)	
Tumor Size (cm)	4.6 ± 1.6	5.0 ± 1.3	0.567
Tumor Location, n (%)			0.618
Frontal	155(32.5)	8(26.7)	
Temporal	88(18.4)	10(33.3)	
Parietal	39(8.2)	1(3.3)	
Occipital	20(4.2)	1(3.3)	
Thalamus	17(3.6)	1(3.3)	
Multiple location	137(28.8)	9(30.0)	
Infratentorial	21(4.4)	0(0)	
Tumor Grade, n (%)			0.057
WHO I	51(10.7)	0(0)	
WHO II	229(48.0)	12(40.0)	
WHO III	144(30.2)	11(36.7)	
WHO IV	53(11.1)	7(23.3)	

Group NES nonemergency surgery, group ES emergency surgery, PNI prognostic nutritional index.

incidence within 30 days (4.6% vs 16.7%,  $p = 0.004$ ), higher rate of neurological function deficit (15.7% vs 33.3%,  $p = 0.012$ ), higher incidence of systemic infection (8.2% vs 33.3%,  $p < 0.001$ ) in ES group (Table 2).

Within the NES group, 375 patients underwent glioma resection during morning hours, while 102 patients underwent afternoon or night surgery. There were more patients with infratentorial tumor ( $p = 0.015$ ) and lower prognostic nutrition index ( $40.4 \pm 4.5$  vs  $41.3 \pm 3.2$ ,  $p = 0.085$ ), while lacking statistical significance in the morning NES group (group M) (Table 3). In order to minimize the confounding bias, patients underwent elective procedures in group M and Group A were matched with the ratio of 2:1 by PSM analysis. Clinical variables including gender, age, BMI, history of hypertension, cardiovascular disease, diabetes mellitus, chronic lung disease, smoking and drinking, blood routine test, coagulation function, PNI, tumor size, location, recurrent status and ASA score were entered. A total of 291 patients (194:97) matched these criteria and all the baseline characteristics were comparable between both group ( $p > 0.05$ , Table 3). Not surprisingly, intraoperative risk factors and postoperative complications did not differ between morning, afternoon or night NES glioma resection (all  $P > 0.05$ ) based on PSM analysis (Table 4). Interestingly,

**Table 2**  
Comparison of perioperative complications between ES Group and NES Group.

	NES Group (n = 477)	ES Group (n = 30)	p value
Operation Duration (h)	4.8 ± 1.7	4.1 ± 1.3	0.337
Blood-loss (ml)	599.9 ± 404.6	1130.4 ± 1772.1	< 0.001
Blood transfusion (ml)	306.9 ± 447.1	596.7 ± 609.4	0.036
Extent of resection, n (%)			0.807
GTR	388(81.3)	24(80.0)	
STR	69(14.5)	4(13.3)	
PR	20(4.2)	2(6.7)	
NICU duration(days)	3 ± 5	4 ± 4	0.152
Death within 30 days	22(4.6)	5(16.7)	0.004
Re-operation, n (%)	22(4.6)	2(6.7)	0.607
Hemorrhage, n (%)	26(5.5)	2(6.7)	0.777
Severe edema, n (%)	23(4.8)	2(6.7)	0.651
Hydrocephalus, n (%)	5(1.0)	0(0)	0.573
Neurological deficit, n (%)	75(15.7)	10(33.3)	0.012
Intracranial infection, n (%)	60(12.6)	5(6.7)	0.516
Seizure, n (%)	36(7.5)	1(3.3)	0.389
Systemic infection, n (%)			< 0.001
Pulmonary infection, n (%)	34(7.1)	7(23.3)	
Urinary infection, n (%)	5(1.0)	3(10.0)	
Venous thrombosis, n (%)	0(0)	0(0)	
CSF leak, n (%)	54(11.3)	2(6.7)	0.430
Porencephalia, n (%)	9(1.9)	1(3.3)	0.580
Severe complication, n (%)	44(9.2)	3(10.0)	0.887
CNS complication, n (%)	187(39.2)	14(46.7)	0.418
Systemic complication, n (%)	39(8.2)	10(33.3)	< 0.001
Total complication, n (%)	227(47.6)	19(63.3)	<b>0.094</b>

Group NES nonemergency surgery, group ES emergency surgery, GTR gross total resection, STR subtotal resection, PR partial resection, NICU neurosurgical intensive care unit, CSF cerebrospinal fluid, CNS central nerve system.

the patients received afternoon or night glioma resection stayed longer in NICU ( $4 \pm 9$  vs  $2 \pm 1$  days,  $p < 0.001$ ) (Table 4).

Since operative workload differed between emergency and non-emergency glioma resection, and performance of neurosurgeons differed between daytime and nighttime shifts, we further compared difference of perioperative complications between daytime and nighttime emergency surgery. We found similar rate of postoperative complications, including all severe complications, neurological complications, regional complications and systemic complications (all  $p > 0.05$ ) between both group. However, we observed more intraoperative blood loss ( $654.99 \pm 304.49$  ml vs  $1493.95 \pm 2301.74$  ml,  $p = 0.061$ ) and more blood transfusion in group ESb ( $635.29 \pm 762.35$  vs  $546.15 \pm 343.06$ ,  $p = 0.072$ ) even though this parameter failed to reach statistical significance (Table 5).

#### 4. Discussion

Reducing perioperative complications is always the primary goal of neurosurgeons in particular and all the surgeons in general. With advances in surgical techniques and perioperative management of glioma, complications have declined during recent times [18–20]. However, complications might be also caused by “non-technical” factors other than instrumentation or management, such as general mood, health, and well-being of the primary surgeon.

The association of emergency surgery and increased postoperative morbidity and mortality is well documented in general surgery, vascular surgery and colorectal surgery by large population based studies [3,6,12,21–24]. In neurosurgical profession, one report showed that emergency cerebrovascular surgery was associated with higher rates of mortality than nonemergency procedures [5]. In the present study, we confirmed the significantly higher incidence of postoperative morbidity and mortality in emergency procedures involving neurosurgery.

**Table 3**  
Baseline characteristics of patients underwent nonemergency surgery based on PSM analysis.

	After matching			Before matching		
	Group M(n = 194)	Group A(n = 97)	p value	Group M(n = 375)	Group A(n = 102)	p value
Sex (male), n (%)	104(53.6)	51(52.6)	0.868	211(56.3)	54(52.9)	0.549
Age (years)	48 ± 12	48 ± 12	0.883	46 ± 13	49 ± 12	0.835
Body mass index (kg/m <sup>2</sup> )	22.9 ± 3.3	22.9 ± 2.9	0.168	22.8 ± 3.1	23.0 ± 3.0	<b>0.249</b>
Recurrent tumor, n (%)	41(21.1)	19(19.6)	0.759	71(18.5)	25(20.3)	0.651
Tumor stroke			0.574			0.829
Hemorrhagic stroke, n (%)	9(4.6)	6(6.2)		20(5.3)	6(5.9)	
Ischemic stroke, n (%)	0(0)	0(0)		0(0)	0(0)	
KPS (< 70), n (%)	3(1.5)	3(3.1)	0.382	11(2.9)	3(2.9)	0.997
Hypertension, n (%)	18(9.3)	9(9.3)	1.000	59(15.7)	10(9.8)	0.131
Diabetes Mellitus, n (%)	3(1.5)	1(1.0)	0.722	17(4.5)	1(1.0)	0.095
Cardiovascular Disease, n (%)	4(2.1)	2(2.1)	1.000	6(1.6)	2(2.0)	0.801
Chronic Lung Disease, n (%)	1(0.5)	1(1.0)	0.616	7(1.9)	1(1.0)	0.537
Smoking, n (%)	41(21.1)	19(19.6)	0.759	58(15.5)	20(19.8)	0.316
Drinking, n (%)	30(15.5)	16(16.5)	0.820	43(11.5)	17(16.7)	0.160
White blood cells (10 <sup>9</sup> /L)	6.61 ± 2.59	6.85 ± 2.95	0.214	6.7 ± 2.7	6.8 ± 2.9	0.415
Platelet count (10 <sup>9</sup> /L)	188.2 ± 53.4	190.9 ± 66.9	0.106	185.6 ± 58.5	191.8 ± 66.1	0.300
Hemoglobin (g/L)	135.3 ± 16.9	136.6 ± 19.6	0.106	134.9 ± 16.7	136.6 ± 19.2	0.132
PT (s)	12.4 ± 0.8	12.4 ± 0.9	0.710	12.4 ± 0.9	12.5 ± 0.9	0.792
APTT (s)	33.6 ± 4.62	33.5 ± 4.6	0.713	33.4 ± 4.7	33.8 ± 4.7	0.586
Albumin (g/L)	40.7 ± 3.9	41.4 ± 3.3	0.710	40.4 ± 4.5	41.3 ± 3.2	<b>0.086</b>
PNI	40.67 ± 3.9	41.4 ± 3.3	0.710	40.4 ± 4.5	41.3 ± 3.2	<b>0.085</b>
ASA score, n (%)			0.438			0.173
P1	22(11.3)	13(13.4)		46(12.3)	13(12.7)	
P2	121(62.4)	56(57.7)		232(61.9)	59(57.3)	
P3	46(23.7)	22(22.7)		90(24.0)	24(23.5)	
P4	5(2.6)	6(6.2)		7(1.9)	6(5.9)	
Tumor Size (cm)	4.6 ± 1.5	4.5 ± 1.7	0.187	4.7 ± 1.5	4.5 ± 1.7	0.205
Tumor Location, n (%)			0.786			<b>0.073</b>
Frontal	73(37.6)	38(39.2)		116(30.9)	39(38.2)	
Temporal	40(20.6)	18(18.6)	0.826	68(18.3)	20(19.6)	
Parietal	18(9.3)	11(11.3)		27(7.2)	12(11.8)	
Occipital	8(4.1)	5(5.2)		15(4.0)	5(4.9)	
Thalamus	12(6.2)	4(4.1)		12(3.2)	5(4.9)	
Multiple location	43(22.2)	21(21.6)		110(29.3)	20(19.6)	
Infratentorial	0(0)	0(0)		21(5.6)	0(0)	
Tumor Grade, n (%)						0.358
WHO I	17(8.8)	7(7.2)		44(11.7)	7(6.9)	
WHO II	99(51.0)	50(51.5)		178(47.5)	51(50.0)	
WHO III	57(29.4)	32(33.0)		109(29.1)	35(34.3)	
WHO IV	21(10.8)	8(8.2)	0.382	44(11.7)	9(8.8)	
WHO IV	191(98.5)	94(96.9)				

PSM propensity score matching, Group M morning surgery, Group A afternoon and night surgery, PNI prognostic nutritional index.

Although baseline characteristics were similar amongst the group, patients with a high grade tumor had highly vascularized regions with micro- or massive necrotic area [25,26] and therefore were more likely to develop tumor stroke. Once developed, hemorrhage or ischemic stroke immediately initiates pathological chain reaction of regional hypoxia, increased vascular permeability and brain edema, local and systemic inflammation storm, then causes worse physical status and worse outcome [5,27–29].

Intuitively, progressive fatigue and sleep loss of the neurosurgeon while “common”, can be easily neglected thus causing complications in patient welfare. We have demonstrated that operative start time did not predict postoperative complications in patients that underwent either emergency surgery or nonemergency surgery. Notably, we also found significant difference of NICU duration in nonemergency procedures after PSM analysis (Table 4). One explanation for these finding is that the influence of mood, movement and cognition impairment on complications could be somehow compensated by the experience and highly sophisticated techniques of neurosurgeon [30,31]. The other explanation is that experienced attending physicians at our center could have benefit from assistance directly through chief residents or experienced residents capable of handling complex surgical procedures, including craniotomy, drainage placement and skull closure, while the experienced physicians solely performed surgical resection of tumor and less direct hands on procedures. However, these reasoning may not

be applicable to junior residents or neurosurgeons [32,33].

While the physical and mental status of the neurosurgeon may be a cause of concern in emergency procedures, perioperative complications were less likely in elective glioma resection. Furthermore, while we did not observe a direct correlation of start time of the surgical procedures to higher blood loss and blood transfusion in emergency glioma resection, this observation must be validated in a larger cohort of patients. Given the closed environment of emergency patients, assessing physical/cognitive performance of surgeons and analyzing work flow in emergency room is complicated. Furthermore, simple classification of daytime and nighttime emergency glioma resection was unavailable to predict risk factors for emergency surgery. Further studies are required to study the combined influence of patient physical status, time point of each treatment and physical and mental performance of surgeon on perioperative complications in those with emergency glioma resection.

There are several limitations in this study. Retrospective methodology is the major limitation as outlined in previous sections. Considering it is hard to capture all the potential confounding factors, we include PSM analysis based on as many as 23 clinical variables for patient matching to minimize selection bias. Given the nature of single center study, small sample size is another limitation. As mentioned before, simple classification of daytime and nighttime emergency surgery is not enough to evaluate the physical and mental performance. Also, further studies are needed in other type of craniotomy when

**Table 4**  
Comparison of perioperative complications between morning and afternoon procedures based on PSM analysis.

	After matching			Before matching		
	Group M(n = 194)	Group A(n = 97)	p value	Group M(n = 375)	Group A(n = 102)	p value
Operation Duration (h)	4.8 ± 1.6	4.4 ± 1.6	0.719	4.9 ± 1.7	4.4 ± 1.6	0.749
Blood-loss (ml)	595.2 ± 419.4	535.3 ± 339.6	0.810	615.57 ± 420.08	542.5 ± 337.3	0.990
Blood transfusion (ml)	302.1 ± 470.6	241.2 ± 330.3	0.524	324.3 ± 472.6	243.1 ± 331.3	0.478
Extent of resection, n (%)			0.653			0.916
GTR	162(83.5)	78(80.4)		306(81.6)	82(80.4)	
STR	26(13.4)	14(14.4)		54(14.4)	15(14.7)	
PR	6(3.1)	5(5.2)		15(4.0)	5(4.9)	
NICU duration(days)	2 ± 1	4 ± 9	< 0.001	3 ± 3	4 ± 9	< 0.001
Death within 30 days	10(5.2)	5(5.2)	1.000	17(4.5)	5(4.9)	0.875
Re-operation, n (%)	10(5.2)	5(5.2)	1.000	17(4.5)	5(4.9)	0.875
Hemorrhage, n (%)	11(5.7)	3(3.1)	0.333	23(6.1)	3(2.9)	0.208
Severe edema, n (%)	14(7.2)	3(3.1)	0.157	20(5.3)	3(2.9)	0.317
Hydrocephalus, n (%)	1(0.5)	2(2.1)	0.218	3(0.8)	2(2.0)	0.307
Neurological deficit, n (%)	28(14.4)	21(21.6)	0.121	53(14.1)	22(21.6)	<b>0.067</b>
Intracranial infection, n (%)	22(11.3)	10(10.3)	0.791	49(13.1)	11(10.8)	0.538
Seizure, n (%)	15(7.7)	4(4.1)	0.240	31(8.3)	5(4.9)	0.254
Systemic infection, n (%)			0.163			0.077
Pulmonary infection, n (%)	14(7.2)	9(9.3)		25(6.7)	9(8.8)	
Urinary infection, n (%)	1(0.5)	3(3.1)		2(0.5)	3(2.9)	
Venous thrombosis, n (%)	0(0)	0(0)		0(0)	0(0)	
CSF leak, n (%)	22(11.3)	13(13.4)	0.610	40(10.7)	14(13.7)	0.387
Porencephalia, n (%)	3(1.5)	4(4.1)	0.176	5(1.3)	4(3.9)	<b>0.088</b>
Severe complication, n (%)	21(10.8)	8(8.2)	0.489	36(9.6)	8(7.8)	0.587
CNS complication, n (%)	71(36.6)	41(42.3)	0.349	143(38.1)	44(43.1)	0.359
Systemic complication, n (%)	15(7.7)	12(12.4)	0.198	27(7.2)	12(11.8)	0.136
Total complication, n (%)	87(44.8)	51(52.6)	0.213	173(46.1)	54(52.9)	0.222

PSM propensity score matching, Group M morning surgery, Group A afternoon and night surgery, GTR gross total resection, STR subtotal resection, PR partial resection, NICU neurosurgical intensive care unit, CSF cerebrospinal fluid, CNS central nerve system.

**Table 5**  
Comparison of perioperative complication between daytime emergency surgery and nighttime emergency surgery.

	Group ESa (n = 13)	Group ESb (n = 17)	p value
Operation Duration (h)	3.8 ± 1.0	4.3 ± 1.4	0.352
Blood-loss (ml)	655.0 ± 304.5	1494.0 ± 2301.7	<b>0.061</b>
Blood transfusion (ml)	546.2 ± 343.1	635.3 ± 762.4	<b>0.072</b>
Extent of resection, n (%)			0.934
GTR	10(76.9)	14(82.4)	
STR	2(15.4)	2(11.8)	
PR	1(7.7)	1(5.9)	
NICU duration(days)	4 ± 4	4 ± 4	0.931
Death within 30 days	2(15.4)	3(17.6)	0.869
Re-operation, n (%)	0(0)	2(11.8)	0.201
Hemorrhage, n (%)	0(0)	2(11.8)	0.201
Severe edema, n (%)	1(7.7)	1(5.9)	0.844
Hydrocephalus, n (%)	0(0)	0(0)	
Neurological deficit, n (%)	5(38.5)	5(29.4)	0.602
Intracranial infection, n (%)	3(23.1)	2(11.8)	0.410
Seizure, n (%)	1(7.7)	0(0)	0.245
Systemic infection, n (%)			0.575
Pulmonary infection, n (%)	2(15.4)	5(29.4)	
Urinary infection, n (%)	1(7.7)	2(11.8)	
Venous thrombosis, n (%)	0(0)	0(0)	
CSF leak, n (%)	1(7.7)	1(5.9)	0.844
Porencephalia, n (%)	0(0)	1(5.9)	0.374
Severe complication, n (%)	1(7.7)	2(11.8)	0.713
CNS complication, n (%)	8(61.5)	6(35.3)	0.153
Systemic complication, n (%)	3(23.1)	7(41.2)	0.297
Total complication, n (%)	9(69.2)	(10)58.8	0.558

Group ESa daytime emergency surgery, group ESb nighttime emergency surgery, GTR gross total resection, STR subtotal resection, PR partial resection, NICU neurosurgical intensive care unit, CSF cerebrospinal fluid, CNS central nerve system.

expanding our finding to other neurosurgical professions since we do not include other types of brain procedure.

## 5. Conclusion

Emergency glioma resection is one of the important risk factors of perioperative mortality and morbidity for patients with glioma. However, operation start time does not necessarily predict post-operative mortality and morbidity, irrespective of in emergency or nonemergency glioma resection.

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## References

- [1] Institute of medicine committee on quality of health care in, a, in: L.T. Kohn, J.M. Corrigan, M.S. Donaldson (Eds.), To Err Is Human: Building a Safer Health System, National Academies Press (US), Washington (DC), 2000Copyright 2000 by the National Academy of Sciences. All rights reserved.
- [2] Y.H. Hu, et al., Analysis of the causes of surgery-related medical disputes in Taiwan: need for acute care surgeons to improve quality of care, J. Chin. Med. Assoc. 79 (11) (2016) 609–613.
- [3] M.G. Mullen, et al., Risk associated with complications and mortality after urgent surgery vs elective and emergency surgery: implications for defining "Quality" and reporting outcomes for urgent surgery, JAMA Surg. 152 (8) (2017) 768–774.
- [4] S.E. Regenbogen, et al., Patterns of technical error among surgical malpractice claims: an analysis of strategies to prevent injury to surgical patients, Ann. Surg.

- 246 (5) (2007) 705–711.
- [5] S.M. Michalak, J.D. Rolston, M.T. Lawton, Incidence and predictors of complications and mortality in cerebrovascular surgery: national trends from 2007 to 2012, *Neurosurgery* 79 (2) (2016) 182–193.
- [6] A.M. Ingraham, et al., Comparison of hospital performance in nonemergency versus emergency colorectal operations at 142 hospitals, *J. Am. Coll. Surg.* 210 (2) (2010) 155–165.
- [7] E.J. Olson, L.A. Drage, R.R. Auger, Sleep deprivation, physician performance, and patient safety, *Chest* 136 (5) (2009) 1389–1396.
- [8] B.J. Wilhelm, et al., Objective and quantitative analysis of daytime sleepiness in physicians after night duties, *Int. J. Psychophysiol.* 72 (3) (2009) 307–313.
- [9] J.M. Rothschild, et al., Risks of complications by attending physicians after performing nighttime procedures, *JAMA* 302 (14) (2009) 1565–1572.
- [10] G. Fechner, et al., Kidney's nightshift, kidney's nightmare? Comparison of daylight and nighttime kidney transplantation: impact on complications and graft survival, *Transplant. Proc.* 40 (5) (2008) 1341–1344.
- [11] W.M. Ricci, et al., Is after-hours orthopaedic surgery associated with adverse outcomes? A prospective comparative study, *J. Bone Joint Surg. Am.* 91 (9) (2009) 2067–2072.
- [12] R.R. Kelz, et al., Time-of-day effects on surgical outcomes in the private sector: a retrospective cohort study, *J. Am. Coll. Surg.* 209 (4) (2009) 434–445 e2.
- [13] Y. Beduk, et al., Comparison of clinical and urodynamic outcome in orthotopic ileocaecal and ileal neobladder, *Eur. Urol.* 43 (3) (2003) 258–262.
- [14] A. Govindarajan, et al., Outcomes of daytime procedures performed by attending surgeons after night work, *N. Engl. J. Med.* 373 (9) (2015) 845–853.
- [15] P.I. Ellman, et al., Acute sleep deprivation in the thoracic surgical resident does not affect operative outcomes, *Ann. Thorac. Surg.* 80 (1) (2005) 60–64 discussion 64–65.
- [16] B.E. Lonze, et al., Operative start times and complications after liver transplantation, *Am. J. Transplant.* 10 (8) (2010) 1842–1849.
- [17] C.G. Patil, et al., Prognosis of patients with multifocal glioblastoma: a case-control study, *J. Neurosurg.* 117 (4) (2012) 705–711.
- [18] S.M. Chang, et al., Perioperative complications and neurological outcomes of first and second craniotomies among patients enrolled in the glioma outcome project, *J. Neurosurg.* 98 (6) (2003) 1175–1181.
- [19] R.S. D'Amico, et al., The safety of surgery in elderly patients with primary and recurrent glioblastoma, *World Neurosurg.* 84 (4) (2015) 913–919.
- [20] N.B. Riblet, et al., Improving the quality of care for patients diagnosed with glioma during the perioperative period, *J. Oncol. Pract.* 10 (6) (2014) 365–370.
- [21] J.D. Bohnen, et al., Perioperative risk factors impact outcomes in emergency versus nonemergency surgery differently: time to separate our national risk-adjustment models? *J. Trauma Acute Care Surg.* 81 (1) (2016) 122–130.
- [22] S. Casillas-Berumen, et al., Morbidity and mortality after emergency lower extremity embolectomy, *J. Vasc. Surg.* 65 (3) (2017) 754–759.
- [23] J. Pettersson, et al., Aortic graft infections after emergency and non-emergency reconstruction: incidence, treatment, and long-term outcome, *Surg. Infect (Larchmt)* 18 (3) (2017) 303–310.
- [24] S.P. Sharp, et al., Impact of interhospital transfer on outcomes in non-emergency colorectal surgery, *World J. Surg.* 42 (5) (2018) 1542–1550.
- [25] P. Mao, et al., Mesenchymal glioma stem cells are maintained by activated glycolytic metabolism involving aldehyde dehydrogenase 1A3, *Proc. Natl. Acad. Sci. U. S. A.* 110 (21) (2013) 8644–8649.
- [26] S. Bao, et al., Glioma stem cells promote radioresistance by preferential activation of the DNA damage response, *Nature* 444 (7120) (2006) 756–760.
- [27] S. Ronsin, et al., Pseudotumoral presentation of cerebral amyloid angiopathy-related inflammation, *Neurology* 86 (10) (2016) 912–919.
- [28] C. Sanchez-Moreno, et al., Decreased levels of plasma vitamin C and increased concentrations of inflammatory and oxidative stress markers after stroke, *Stroke* 35 (1) (2004) 163–168.
- [29] B. von Sarnowski, et al., Long-term health-related quality of life after decompressive hemicraniectomy in stroke patients with life-threatening space-occupying brain edema, *Clin. Neurol. Neurosurg.* 114 (6) (2012) 627–633.
- [30] A.A. Cohen-Gadol, Microvascular decompression surgery for trigeminal neuralgia and hemifacial spasm: nuances of the technique based on experiences with 100 patients and review of the literature, *Clin. Neurol. Neurosurg.* 113 (10) (2011) 844–853.
- [31] W.Z. Ray, et al., Developing an anterior cervical discectomy and fusion simulator for neurosurgical resident training, *Neurosurgery* 73 (Suppl. 1) (2013) 100–106.
- [32] P.D. Patterson, D.M. Yealy, Resident fatigue, distress, and medical errors, *Jama* 303 (4) (2010) 329 author reply 330.
- [33] C.P. West, et al., Association of resident fatigue and distress with perceived medical errors, *JAMA* 302 (12) (2009) 1294–1300.