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Original Article

Perioperative Clinical Course Variables Associated with Length of Hospital Stay after Primary Intracranial Meningioma Resection

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The relationship between perioperative clinical course variables and postoperative length of hospital stay (LOS) in patients undergoing primary intracranial meningioma resection has not been fully elucidated. We therefore aimed to identify the perioperative clinical course variables that predict postoperative LOS in such patients. We retrospectively collected data concerning demographics, tumor characteristics, and perioperative clinical course variables in 76 patients who underwent primary intracranial meningioma resection between January 2010 and December 2019, and tested for associations with postoperative LOS. Univariate analyses showed that younger age, fewer days to postoperative initiation of standing/walking, preoperative independence in activities of daily living (ADL), and ADL independence one week after surgery were associated with shorter postoperative LOS. Multiple regression analyses with these factors identified that days to stand/walk initiation and ADL independence one week after surgery were associated with postoperative LOS. Based on these results, we conclude that rehabilitation programs that promote early mobilization and the early acquisition of independence may reduce postoperative LOS in patients who undergo primary intracranial meningioma resection.

Key words: early mobilization, functional independence, perioperative clinical course, length of hospital stay, meningioma

Meningioma is the most common type of benign brain neoplasm, occurring in approximately 300,000 people annually in the United States [1]. Craniotomy is necessary if tumor growth or peripheral edema causes neurological abnormalities; however, patients with intracranial meningioma often have a good postoperative functional prognosis, and do not require radiation therapy or chemotherapy. Therefore, among all patients undergoing intracranial tumor resection, those with primary meningioma are generally expected to have the earliest discharge dates. However, in practice, patients who have undergone primary meningioma resection often have a prolonged postoperative length of stay (LOS) in the hospital.

In patients who undergo brain tumor resection, older age [2-4], preoperative frailty [5], preoperative hyperglycemia [2,6], race, poor preoperative physical function, and preoperative hypoalbuminemia [2] have been reported as risk factors for longer postoperative LOS. In addition, older age may be a risk factor for longer postoperative LOS in patients who undergo intracranial meningioma resection specifically [7,8]. However, most studies have only examined the relationship between preoperative and tumor characteristics and postoperative LOS, and not that between the

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perioperative clinical course and postoperative LOS. If the perioperative clinical course variables associated with longer postoperative LOS could be clarified, clinicians might be able to identify improvements to the clinical course to shorten postoperative LOS.

Therefore, we aimed to identify perioperative clinical course variables that are associated with postoperative LOS in patients who undergo primary meningioma resection, and to determine the preoperative and tumor characteristics related to longer postoperative LOS.

Materials and Methods

Ethical committee approval. All procedures involving human participants were performed in accordance with the ethical standards of the institutional research committee and the 1964 Helsinki Declaration (including later amendments). This study was approved by the Ethics Committee of the Kagawa University Faculty of Medicine (approval no. 2019-199).

Subjects. We retrospectively analyzed data from 112 adults with single primary intracranial meningiomas who underwent tumor resection surgeries at Kagawa University Hospital between January 2010 and December 2019. We excluded patients who had a complication or physical condition that clearly affected activities of daily living (ADLs) before surgery, including intellectual disability ($n=1$), paralysis or ataxia due to brain infarction ($n=5$), Parkinson's disease ($n=1$), chronic heart failure ($n=1$), upper limb amputation ($n=1$), and pregnancy ($n=1$). Moreover, we excluded those who had a postoperative complication that required treatment or care for >1 week, with the observed complications including subcutaneous hematoma or epidural hematoma ($n=3$), paralysis ($n=2$), worsened low back pain ($n=2$), low cerebrospinal fluid pressure ($n=2$), worsened sciatica ($n=1$), deterioration of homonymous hemianopia ($n=1$), exacerbation of heart failure ($n=1$), intraoperative brain hemorrhage ($n=1$), delirium ($n=1$), and external decompression to reduce cerebral edema ($n=1$). Finally, we excluded patients who underwent treatments other than tumor resection during their hospital stay ($n=5$), and those who were transferred to other medical facilities ($n=6$). The remaining 76 patients were included in our analyses.

All patients resumed oral nutritional intake the day after meningioma resection. Registered dietitians routinely supported patients in improving their oral intake. Mild dysphagia was observed in several patients, but was dealt with by modifying food texture through such means as chopping up food. In accordance with the clinical pathway, the attending physicians allowed most of the patients to initiate standing or walking on postoperative day 2 if they had no particular problems. In addition, rehabilitation (*e.g.*, physical therapy, occupational therapy, and speech therapy) was initiated upon request from the patient's attending physician. Rehabilitation programs consisted of neuromuscular facilitation techniques, resistance training, aerobic exercises, balance training, articulation exercises, swallowing training, training for other higher cerebral functions, and ADL training.

Data collection. We collected data concerning the following preoperative characteristics from subjects' medical records: basic clinical data, such as age, sex, height, weight, and body mass index (BMI); and data on tumor characteristics, such as lesion laterality, lesion location (*i.e.*, supratentorial or infratentorial), tumor size (*i.e.*, longest diameter), and tumor grade according to the 2016 World Health Organization (WHO) classification of central nervous system tumors (*i.e.*, WHO grade) [9]. Additionally, we collected data concerning perioperative clinical course variables, such as operative duration, intraoperative blood loss, number of days to postoperative initiation of standing/walking (stand/walk initiation), and postoperative LOS.

We calculated the total energy expenditure (TEE) for each patient with the Harris-Benedict equation [10]. The formulae were as follows: TEE (men) = $[66.47 + (13.75 \times \mathrm{weight}) + (5 \times \mathrm{height}) - (6.78 \times \mathrm{age})] \times 1.2$ (active factor) $\times 1.0$ (stress factor); and TEE (women) = $[655.1 + (9.56 \times \mathrm{weight}) + (1.85 \times \mathrm{height}) - (4.68 \times \mathrm{age})] \times 1.2$ (active factor) $\times 1.0$ (stress factor). We also divided each patient's actual energy intake by his or her TEE to calculate the energy adequacy rates before and one week after surgery. Finally, we obtained each patient's preoperative and one-week postoperative Eastern Cooperative Oncology Group performance status (ECOG-PS), and classified each as being either independent (*i.e.*, having an ECOG-PS of 0-2) or dependent (*i.e.*, having an ECOG-PS of 3-4) at the preoperative and one-week postoperative timepoints.

Statistical analyses. To identify the variables associated with postoperative LOS, we used Spearman rank correlation coefficients for quantitative variables and the Mann–Whitney *U* test for qualitative variables

(except for lesion laterality, for which we used the Kruskal-Wallis test). We then conducted a multiple regression analysis using the factors that were associated with postoperative LOS in the univariate analyses. All p values were two-sided, and we defined statistical significance as $p<0.05$. All analyses were conducted using SPSS version 24.0 for Microsoft Windows (IBM, Armonk, NY, USA).

Results

Subjects. The median age of subjects was 65.0 years (range, 31.0-85.0 years). There were 46 women (60.5%) and 30 men (39.5%). The median postoperative LOS was 14.0 days (range, 9.0-26.0 days). Table 1 lists the demographic and tumor characteristics of subjects, and Table 2 presents the perioperative clinical course data.

Associations with postoperative LOS. The associations between quantitative variables and postoperative LOS in univariate analyses are shown in Table 3. The quantitative variables associated with shorter postoperative LOS were younger age ($r=0.23$, $p=0.04$) and fewer days to stand/walk initiation ($r=0.37$, $p<0.01$). However, we found no associations between postoperative LOS and height, weight, BMI, tumor size, preoperative energy adequacy rate, energy adequacy rate one week after surgery, surgery duration, or intraoperative blood loss levels. Table 4 shows the associations between qualitative variables and postoperative LOS in univariate analyses. The qualitative variables that exhibited associations with shorter postoperative LOS

Table 1 Preoperative clinical and cancer characteristics of subjects (n=76)

Variable	Median [range] or count (percentage)
Age, years	65.0 [31.0–85.0]
Sex	
Women	46 (60.5%)
Men	30 (39.5%)
Height, cm	158.0 [136.2–178.8]
Weight, kg	58.7 [41.5–95.6]
BMI, kg/m^2	23.9 [17.9–31.3]
Lesion laterality	
Right	32 (42.1%)
Left	35 (46.1%)
Both	9 (11.8%)
Lesion location	
Supratentorial	70 (92.1%)
Infratentorial	6 (7.9%)
Tumor size, mm	33.6 [13.4–86.9]
WHO grade	
I	54 (71.1%)
II	22 (28.9%)

BMI, body mass index; WHO, World Health Organization.

Table 2 Perioperative clinical course variables of subjects (n=76)

Variable	Median [range] or count (percentage)
Preoperative data	
Energy adequacy rate (n=55)	113.0% [9.2–151.2%]
Preoperative independence	
Independent (ECOG-PS of 0–2)	66 (86.8%)
Dependent (ECOG-PS of 3–4)	10 (13.2%)
Operative features data	
Surgery duration, min	426 [211–817]
Intraoperative blood loss (n=71), ml	280 [15–1600]
Postoperative data	
Stand/walk initiation, days	2 [2–8]
Energy adequacy rate one week after surgery	99.4% [24.7–150.8%]
One-week postoperative independence	
Independent (ECOG-PS of 0–2)	51 (67.1%)
Dependent (ECOG-PS of 3–4)	25 (32.9%)
Postoperative LOS, days	14.0 [9.0–26.0]

"Stand/walk initiation" refers to the number of days to the postoperative initiation of standing/walking. "Preoperative independence" and "one-week postoperative independence" refer to independence in activities of daily living independence at preoperative and one-week postoperative time points, respectively.

ECOG-PS, Eastern Cooperative Oncology Group performance status; LOS, length of hospital stay.

were preoperative independence ($p=0.02$) and one-week postoperative independence ($p<0.01$). No significant associations with postoperative LOS were found for sex, lesion laterality, lesion location (*i.e.*, supratentorial or infratentorial), or WHO grade.

Table 3 Associations between quantitative variables and postoperative LOS

Variable	*r*	*P*-value
Preoperative characteristics		
Age	0.23	0.04
Height	−0.13	0.25
Weight	−0.17	0.14
BMI	−0.08	0.47
Tumor size	0.19	0.09
Perioperative clinical courses		
Preoperative energy adequacy rate	0.32	0.82
Surgery duration	0.07	0.53
Intraoperative blood loss	0.09	0.46
Stand/walk initiation	0.37	<0.01
Energy adequacy rate one week after surgery	−0.18	0.12

"Stand/walk initiation" refers to the number of days to the postoperative initiation of standing/walking.
BMI, body mass index; LOS, length of hospital stay.

Based on these results, we conducted a multiple regression analysis with age, days to stand/walk initiation, preoperative independence, and one-week postoperative independence as independent variables, and postoperative LOS as the dependent variable. The resulting analysis identified fewer days to stand/walk initiation $p=0.02$) and one-week postoperative independence ($p<0.01$) as exhibiting associations with shorter postoperative LOS (Table 5).

Discussion

We conducted this study to identify perioperative clinical course variables that exhibit associations with postoperative LOS in patients who undergo primary meningioma resection. Moreover, we also aimed to identify preoperative clinical and tumor characteristic variables that exhibit associations with postoperative LOS in such patients. We found that fewer days to stand/walk initiation and one-week postoperative independence were both associated with shorter postoperative LOS.

We chose postoperative LOS as the main outcome of

Table 4 Associations between qualitative variables and postoperative LOS

Variable	Median postoperative LOS [range], days	*P*-value
Preoperative characteristics		
Sex		0.13
Women	15.0 [9.0–26.0]	
Men	12.0 [9.0–21.0]	
Lesion laterality		0.41
Right	13.5 [9.0–24.0]	
Left	15.0 [9.0–23.0]	
Both	12.0 [9.0–26.0]	
Lesion location		0.39
Supratentorial	14.0 [9.0–26.0]	
Infratentorial	16.0 [12.0–19.0]	
WHO grade		0.80
I	14.0 [9.0–24.0]	
II	14.0 [9.0–26.0]	
Perioperative clinical courses		
Preoperative independence		0.02
Independent (ECOG-PS of 0–2)	13.0 [9.0–26.0]	
Dependent (ECOG-PS of 3–4)	16.5 [12.0–22.0]	
One-week postoperative independence		<0.01
Independent (ECOG-PS of 0–2)	12.0 [9.0–20.0]	
Dependent (ECOG-PS of 3–4)	17.0 [11.0–26.0]	

"Preoperative independence" and "one-week postoperative independence" refer to independence in activities of daily living independence at preoperative and one-week postoperative time points, respectively.
ECOG-PS, Eastern Cooperative Oncology Group performance status; LOS, length of hospital stay; WHO, World Health Organization.

Table 5 Results of the multiple regression analysis for postoperative LOS

Variable	*B*	95% confidence interval	*P*-value
Age			0.84
Stand/walk initiation	0.88	0.26 to 1.61	0.02
Preoperative independence			0.78
One-week postoperative independence	−4.26	−6.03 to −2.48	<0.01

$R^2 = 0.38$

"Stand/walk initiation" refers to the number of days to the postoperative initiation of standing/walking. "Preoperative independence" and "one-week postoperative independence" refer to independence in activities of daily living independence at preoperative and one-week postoperative time points, respectively.

LOS, length of hospital stay.

the present study because shortening LOS will lead to earlier reintegration of patients into society and reduce medical costs. LOS has been found to be a major factor in the total cost of various neurosurgical procedures [11-13], and it is increasingly used as an indicator of the quality of neurosurgical care [14]. We therefore believe that it is crucial to shorten LOS even for patients with benign tumors such as meningiomas.

The fact that time to stand/walk initiation was associated with postoperative LOS in patients who underwent primary meningioma resection suggests that early postoperative mobilization may contribute to shorter hospital stays. Prolonged bed rest causes skeletal muscle atrophy (particularly in older patients) [15], with muscle weakness of 9-15% occurring after only one week of bed rest [16]. The resulting muscle weakness can contribute to postoperative functional decline. Therefore, in recent years, the usefulness of perioperative management, including early postoperative mobilization, for patients undergoing various surgical invasions has attracted attention. Wang *et al.* [17], who studied outcomes after brain tumor resection, further reported that a protocol for enhanced postoperative recovery that included early postoperative mobilization led to shortened LOS compared to usual management.

In the present study, the reasons for delayed stand/walk initiation included headache, fatigue, quickness to anger, and symptoms of low cerebrospinal fluid pressure. Furthermore, in 80.3% of cases, rehabilitation was not prescribed because meningiomas are usually benign, and clinicians expected a good postoperative functional prognosis. If rehabilitation had been initiated earlier in the postoperative period, mobilization may also have started earlier. This in turn could have shortened LOS. Based on this hypothesis, we are currently planning to establish a system in which physical therapists can start rehabilitation for patients before surgery. If patients do not have any problems, such as severe motor paralysis after surgery, physical therapists could then start standing or gait training on the second day after surgery.

The other variable associated with shorter LOS in our multiple regression analysis was one-week postoperative independence. In general, patient independence is a major factor in determining the timing of discharge. Among patients with meningioma, those whose physical function at discharge is equal to or better than their preoperative physical function have shorter postoperative LOS [18]. Rehabilitation is one of the most effective treatments for patients after various surgical treatments, including meningioma resection, and it can be expected to restore physical and cognitive functions and improve ADL abilities. Therefore, if more proactive rehabilitation could be provided, it might improve the level of postoperative independence and reduce LOS after meningioma resection.

Several studies have shown that older age is associated with prolonged postoperative LOS in patients who undergo meningioma resection [7,8]; however, we did not observe an association in our multiple regression analysis. It is crucial to note, however, that a few other studies have obtained negative results after testing for such an association [19,20]. We can thus say that there is not yet a consensus on whether age is associated with postoperative LOS in patients who undergo meningioma resection. In the future, it will be necessary to conduct large-scale global studies to further clarify the relationship between age and LOS after meningioma resection.

The present study had several limitations. It was a

single-center, small-sample study, and large-scale, multicenter studies are warranted. Furthermore, this was a retrospective observational study, and interventional studies are needed to determine whether early mobilization and early independence acquisition can shorten LOS after primary meningioma resection. Another limitation is the possibility that some tumors were located in sites that affected the ability to stand or walk. Future studies should therefore examine the site of tumor development in more detail. In addition, the post-discharge living environment, including the presence or absence of family members with caregiving ability, may have also affected LOS. It may be desirable for future studies to consider this factor.

In conclusion, one-week postoperative independence and shorter times to stand/walk initiation were associated with shorter postoperative LOS in patients who underwent primary meningioma resection. This suggests that proactively providing rehabilitation aimed at early mobilization and early acquisition of independence after surgery can shorten postoperative LOS for patients who undergo primary meningioma resection.

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