Brain Neurorehabil. 2023 Jul;16(2):e11
https://doi.org/10.12786/bn.2023.16.e11
pISSN 1976-8753·eISSN 2383-9910

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Brain & NeuroRehabilitation

Original Article

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Relation between Lower Urinary Tract Dysfunction and Functional Outcome in Patients After Brain Tumor Resection

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Received: Mar 3, 2023
Revised: Mar 28, 2023
Accepted: Apr 7, 2023
Published online: May 10, 2023

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HIGHLIGHTS

- Rehabilitation is effective for patients with brain tumor.
- Early functional status is associated with initial urinary retention
- Initial urinary retention is related to poor functional status after rehabilitation

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Funding
None.

Conflict of Interest
The authors have no potential conflicts of interest to disclose.

ABSTRACT

This study aimed to compare functional outcomes after rehabilitation with initial degree of urinary retention (UR) in patients operated on for brain tumors. Medical records of 61 patients transferred to the Department of Rehabilitation Medicine of single center, from January 2011 to December 2021, were reviewed retrospectively. Patient data included post-void residual (PVR) urine, tumor characteristics, and functional status. Functional status was evaluated on the Mini-Mental Status Examination (MMSE), Modified Barthel Index (MBI), Functional Ambulation Category (FAC), Modified Rankin Scale (mRS), Motricity Index (MI)-lower limb, and Berg Balance Scale (BBS). MMSE, FAC, mRS, and MI-lower limb were re-evaluated 3 weeks after standard inpatient rehabilitation. Twenty-four patients were in the UR group and 37 in the non-UR group. Initial MMSE, MBI, BBS, FAC, and mRS were significantly worse in the UR group, and both groups showed significant functional improvement after rehabilitation. After rehabilitation, MMSE, FAC, MRS, MI-lower were still worse in the UR group, but the degree of improvement between the groups was not significantly different. Rehabilitation was shown to be effective for brain tumor patients regardless of UR. Initial UR after brain tumor surgery is significantly associated with poor functional status in both the early stages of rehabilitation and after rehabilitation.

Keywords: Urinary Retention; Brain Tumor; Rehabilitation

INTRODUCTION

Brain tumors are one of the major causes of disability [1-3]. Not only the effect of the tumor itself but also various treatments such as chemotherapy, radiation therapy, and surgery can cause disabilities [3]. With the recent development of treatment technology for tumors, the survival rate is improving, and the interest in disability and quality-of-life effects is also increasing [4]. There is a steady growth in attention to rehabilitation after brain tumor surgery, and the effectiveness of rehabilitation in the population has been proven in previous studies [3,5,6].

The functional impairments that can result from brain tumors include a range of disabilities, such as impaired urinary function [7,8]. Several studies have shown that poor urinary function in patients with stroke can be indicative of poor functional outcomes [9,10]. However, few is known about this relationship in patients with brain tumors.

Among the various brain diseases that can cause urinary dysfunction, brain tumors as well as strokes belong to the group of diseases that can be best localized [11-13]. Urinary function is controlled by various structures in the brain, including the prefrontal cortex and pons [14,15]. If brain tumors involve the neuroanatomy related to urinary function, clinical dysfunction of the bladder may occur. These symptoms can significantly impact a patient's overall functional status, including their ability to perform activities of daily living, ambulate, and communicate effectively. Moreover, the central nervous structure that controls urinary function is also associated with other domains of function, such as motor and cognition, through various complex pathways [16-19]. Therefore, it can be hypothesized that the impairments of urinary function in brain tumor patients may be neuroanatomically related to other functional impairments. Nonetheless, there is a dearth of research exploring the degree of correlation between urinary dysfunction and other domains of functional impairments in brain tumor patients, as well as the response of such association to rehabilitation therapy.

While previous studies have investigated the impact of urinary function on functional outcomes in stroke patients [9,10], there is limited research on the relationship between urinary retention (UR) and functional outcomes in brain tumor patients. Given the potential impact of brain tumors on urinary function and the potential implications for overall functional status, investigating this relationship may provide valuable insights into the rehabilitation needs of brain tumor patients. Therefore, we aim to investigate whether UR is related to other functional outcomes in brain tumor patients. Additionally, we will evaluate the effectiveness of rehabilitation in improving functional outcomes in this population.

MATERIALS AND METHODS

Study design and subjects

The medical records of patients who had received brain tumor surgery at the Neurosurgery Department of single center, who had been transferred to the Department of Rehabilitation Medicine after surgery, and discharged between January 2011 and December 2021, were reviewed retrospectively. Institutional Review Board of Asan Medical Center approved this study (IRB No. 2022-0655) and waived the need to obtain informed consent because of its retrospective nature. This study was conducted in accordance with the Declaration of Helsinki and our institutional guidelines.

The inclusion criteria were as follows: received standard inpatient rehabilitation for at least three weeks; confirmed primary or metastatic brain tumors through pathological examination of biopsy specimens; age > 18 years; transferred within 4 months after surgery; voiding sheet written after indwelling bladder catheter removal; no pre-existent or co-existent urologic disease; and a level of consciousness better than a minimally conscious state at the time of transfer. Patients whose brain tumor was located at pons were also excluded, as it could directly affect urine function [14,15]. Finally, patients with other co-existent neurological diseases such as stroke and neurodegenerative disorders were excluded from the study.

https://doi.org/10.12786/bn.2023.16.e11

Urinary function measurement

We evaluated the post-void residual (PVR) urine volumes in bladders within 30 minutes after urination. To date, there is no consensus in the literature about cutoff values for defining UR. As PVR volumes of more than 150 mL require interventions such as catheterizations [20], we used the value as a cutoff for PVR. The PVR urine volumes of the patients included in this study were measured using a bladder scanner BioCon-900 (Mcube Technology Co. Ltd., Seoul, Korea). BioCon-900 shares the same hardware and software as its predecessor model, BioCon-700, and has the same level of accuracy. The accuracy of BioCon-700 has been validated in previous literature for measuring PVR in adults [21]. A 3-day average of PVR was collected, and if not all PVR were measured, at least one documented PVR volume after indwelling catheter removal was collected. If PVR was less than 150 mL, the patient was categorized as not having UR (non-UR group). A measurement of 150 mL or more was categorized as UR (UR group). For additional evaluation of urinary functions, we reviewed the dates of indwelling catheter removal and self-voiding, as well as the occurrence of urinary tract infections (UTIs) during rehabilitation, and the administration of urologic medications such as alpha-blockers and cholinergics.

Clinical data

All patients' demographic data including sex and age at the time of surgery were reviewed. The characteristics of each brain tumor, such as location, size, treatment modality, resection extent, resection date, and malignancy were reviewed retrospectively. According to the World Health Organization (WHO) 2016 classification, brain tumors that fell into WHO I and II categories were classified as benign, and those in WHO III and IV categories were classified as malignant [22].

Functional evaluation

Mini-Mental Status Examination (MMSE), Modified Barthel Index (MBI), Functional Ambulation Category (FAC), Modified Rankin Scale (mRS), Motricity Index (MI)-lower limb, and Berg Balance Scale (BBS) were evaluated at the time of transfer to department of rehabilitation medicine, and MMSE, FAC, mRS and MI-lower limb were evaluated at discharge after 3 weeks of standard rehabilitation. The rehabilitation mainly consisted of neurodevelopmental therapy provided in various domains according to the specific functional impairments of the patients. Along with lower limb strength and range of motion exercises, appropriate gait training or mobilization was conducted based on the initial FAC scale, and upper limb activities of daily living training was also provided. Additionally, if there were impairments in language, speech, or cognition domains, language therapy, speech therapy, and cognitive rehabilitation were carried out accordingly. MMSE is a widely used tool for assessing cognitive function, which yields a score ranging from 0 to 30. It specifically evaluates memory, language orientation, attention, and visuospatial skills. MBI was used to evaluate independency in activities in daily living (ADL). It consists of 10 areas of functioning, with each item composed of 5-levels and scored from 0 (total dependence) to 100 (independence). FAC divides ambulatory function into 6 stages according to the presence and degree of assistance required. It is graded on a scale from 0 (walking is impossible) to 5 (walking independently). The mRS is used to evaluate the degree of disability or dependence in daily activities, with the score quantified on a scale of 0 to 6, ranging from 0 when no symptoms are present to 6 in the case of death. As the score increases, more severe dysfunction is indicated. MI is one of the tools used to evaluate motor strength, and it is composed of upper and lower extremities scales. In this study, only the MI for lower extremity examination was evaluated due to the limitation of medical records. The minimum value of evaluation is 0 and the maximum value is 100. BBS is an objective measure of balance function and is recognized as a highly specific and reliable balance function evaluation tool. This test consists of a total of 14 items, and each item can be scored from 0 to 4 points. Higher scores indicate better balance function.

Statistical analysis

Computational statistics were processed using the R version 4.0.5 program (R Foundation for Statistical Computing, Vienna, Austria), and the detailed method was as follows. The statistical significance level was set to $p < 0.05$. To test whether variables were normally distributed, the Shapiro-Wilks test was used. For categorical variables, the χ^2 test was used, and for continuous variables, the t-test and Mann-Whitney U test were used.

RESULTS

Patient characteristics

Three hundred and ninety-seven out of 458 discharged patients during the period were excluded for various reasons (unable to check voiding sheet, early discharge after transfer, combined stroke), and a total of 61 patients were included in the study (**Fig. 1**). A total of 24 patients were categorized to UR group as their PVR was measured over 150 mL at the time of transfer, and 37 patients categorized as non-UR group. Baseline demographics and clinical characteristics between the 2 groups were shown in **Table 1**. There were no statistically significant differences in parameters including age, sex, tumor side, tumor malignancy, and occurrence of UTI between the 2 groups. In the UR group, urological medications were administrated more frequently.

Functional outcomes

Table 2 compares functional status before and after rehabilitation in the 2 groups, which is visualized in **Fig. 2**. MMSE, MBI, BBS, FAC, and mRS at the time of transfer were significantly worse in UR group. All functional parameters, except for MI-lower in the non-UR group, showed significant improvements after rehabilitation in both groups. MMSE and FAC after rehabilitation were still significantly worse in UR group. MI-lower and mRS were also worse in UR group after rehabilitation, but this was not statistically significant. **Table 3** compares the degree of functional improvement in the two groups. In the UR group, FAC showed slightly less improvement than in the non-UR group ($p = 0.54$), whereas MMSE, mRS, and MI-lower showed slightly more improvement than in the non-UR group ($p = 0.75$, $p = 0.21$,

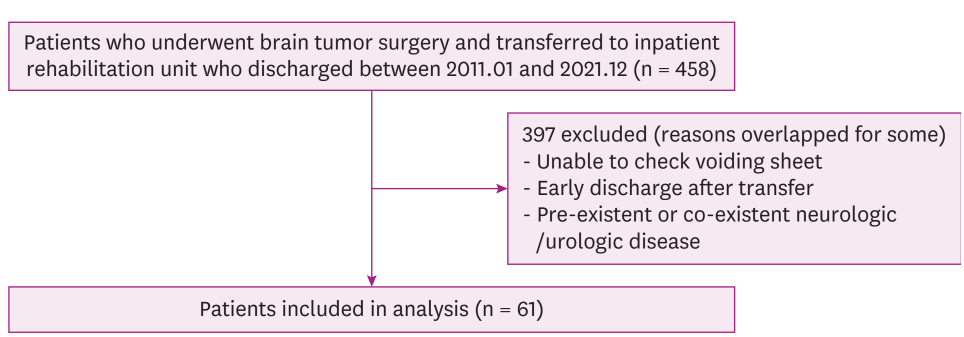

Fig. 1. Flow chart of the patient selection process.
In some patients, multiple reasons overlapped and led to exclusion from the study.

https://doi.org/10.12786/bn.2023.16.e11

Table 1. Participant baseline characteristics

Variable	Non-UR (n = 37)	UR (n = 24)	p value
Age (yr)	55.5 ± 13.3	59.1 ± 11.9	0.28
Sex			0.96
Male	20 (54.1)	12 (50.0)	
Female	17 (45.9)	12 (50.0)	
Days from operation to transfer	8.86 ± 5.67	12.75 ± 9.65	0.08
Tumor side			0.62
Right	17 (45.9)	14 (58.3)	
Left	15 (40.5)	7 (29.2)	
Bilateral	5 (13.5)	3 (12.5)	
Tumor malignancy			1.00
Benign	14 (37.8)	9 (37.5)	
Malignant	23 (62.2)	15 (62.5)	
Alpha-antagonist use	2 (5.4)	18 (75.0)	< 0.05*
Cholinergic use	1 (2.7)	13 (54.2)	< 0.05*
UTI	2 (5.4)	2 (8.3)	0.08

Values are shown as mean ± standard deviation or number (%).
UR, urinary retention; UTI, urinary tract infection.
*$p < 0.05$.

and p = 0.33, respectively). **Table 4** compares functional status and improvement depending on tumor malignancy. **Table 5** compares functional status and improvement depending on whether the tumor included the frontal lobe or not, as this part of the brain is also involved in voiding function [14]. However, there were no statistically significant differences in functional status depending on tumor malignancy or location. Also, there was no statistically significant association between the presence of lesions involving the frontal lobe and the UR group (p = 0.90).

DISCUSSION

In this study, we have shown that initial UR after surgery is significantly associated with poor functional status in both the early stages of rehabilitation and after rehabilitation. Nevertheless, inpatient rehabilitation interventions can significantly improve functional outcomes in these patients, which is concordant with previous studies that rehabilitation is efficacious in patients with brain tumor [8,23-25], and the degree of improvement is comparable to that of patients without UR.

In a previous study, UR in the early stages of inpatient rehabilitation in stroke patients was significantly correlated with poorer early functional status evaluated by MMSE, MBI, BBS, and FAC [9]. In the study, the UR group showed significant functional improvement after

Table 2. Functional status before and after rehabilitation of UR and non-UR group

Variable	Non-UR (n = 37)		Intragroup difference	UR (n = 24)		Intragroup difference	Intergroup difference	
	Before	After		Before	After		Before	After
MMSE	20.2 (n = 37)	23.4 (n = 36)	< 0.05*	12.6 (n = 24)	16.5 (n = 21)	< 0.05*	< 0.05*	< 0.05*
FAC	1.4 (n = 37)	2.4 (n = 37)	< 0.05*	0.8 (n = 24)	1.7 (n = 24)	< 0.05*	< 0.05*	< 0.05*
mRS	4.0 (n = 37)	3.4 (n = 37)	< 0.05*	4.5 (n = 24)	3.7 (n = 24)	< 0.05*	< 0.05*	0.22
MI-lower	57.2 (n = 37)	62.1 (n = 31)	0.10	51.2 (n = 24)	56.2 (n = 23)	< 0.05*	0.29	0.23
MBI	39.4 (n = 37)			15.7 (n = 24)			< 0.05*	
BBS	15.4 (n = 24)			4.1 (n = 9)			< 0.05*	

Values are shown as mean.
UR, urinary retention; MMSE, Mini-Mental Status Examination; MBI, Modified Barthel Index; FAC, Functional Ambulation Category; mRS, Modified Rankin Scale; MI-lower, Motricity Index-lower limb; BBS, Berg Balance Scale.
*$p < 0.05$.

https://doi.org/10.12786/bn.2023.16.e11

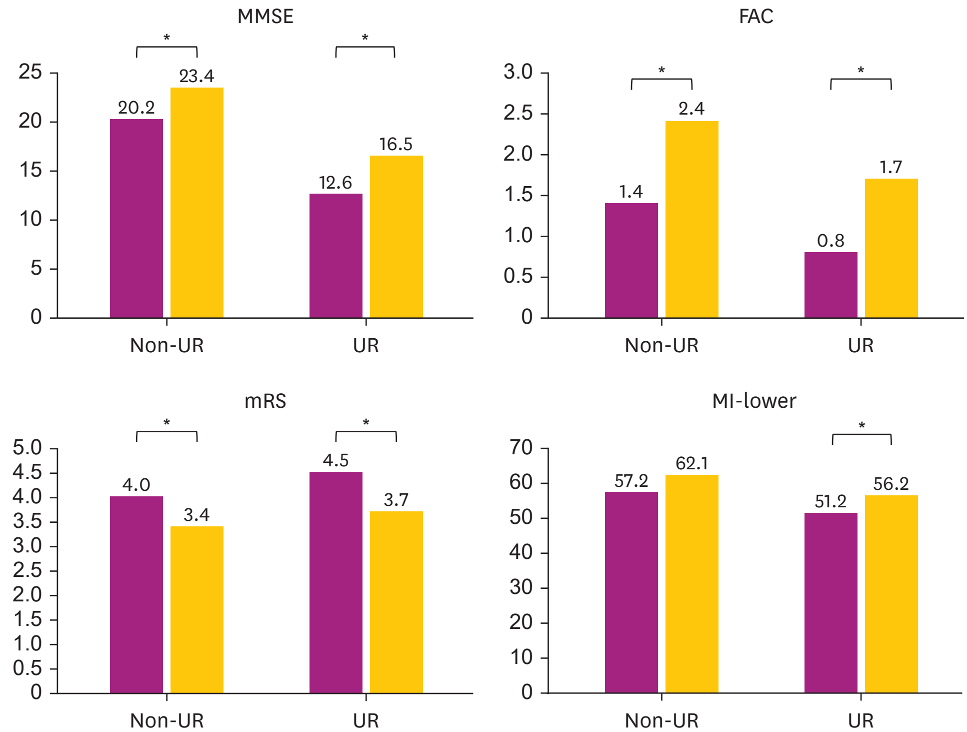

Fig. 2. Comparison of improvement in functional outcomes throughout a rehabilitation program.
UR, urinary retention; MMSE, Mini-Mental State Examination; FAC, Functional Ambulation Category; mRS, Modified Rankin Scale; MI-lower, Motricity Index-lower limb.
*$p < 0.05$.

Table 3. Functional improvement during rehabilitation of UR and non-UR group

Variable	Non-UR (n = 37)	UR (n = 24)	p value
ΔMMSE	3.52 ± 5.47 (n = 36)	4.00 ± 4.58 (n = 21)	0.75
ΔFAC	1.03 ± 0.87 (n = 37)	0.92 ± 0.72 (n = 24)	0.54
ΔmRS	−0.64 ± 0.68 (n = 37)	−0.83 ± 0.56 (n = 24)	0.21
ΔMI-lower	3.52 ± 11.78 (n = 31)	6.09 ± 8.41 (n = 23)	0.33

Values are shown as mean ± standard deviation.
UR, urinary retention; MMSE, Mini-Mental Status Examination; FAC, Functional Ambulation Category; mRS, Modified Rankin Scale; MI-lower, Motricity Index-lower limb.

Table 4. Functional outcomes for benign and malignant brain tumor groups

Variable	Benign (n = 23)	Malignant (n = 38)	p value
MMSE at transfer	16.52 (n = 23)	17.63 (n = 38)	0.44
FAC at transfer	0.91 (n = 23)	1.24 (n = 38)	0.20
mRS at transfer	4.3 (n = 23)	4.13 (n = 38)	0.43
MI-lower at transfer	58.3 (n = 23)	52.71 (n = 38)	0.28
MMSE after rehabilitation	21.71 (n = 21)	20.41 (n = 36)	0.85
FAC after rehabilitation	1.87 (n = 23)	2.24 (n = 38)	0.19
mRS after rehabilitation	3.65 (n = 23)	3.37 (n = 38)	0.15
MI-lower after rehabilitation	59.17 (n = 18)	59.81 (n = 36)	0.76
ΔMMSE	4.71 (n = 21)	3.11 (n = 36)	0.23
ΔFAC	0.96 (n = 23)	1 (n = 38)	0.75
ΔmRS	(−)0.65 (n = 23)	(−)0.76 (n = 38)	0.50
ΔMI-lower	1.28 (n = 18)	6.28 (n = 36)	0.17

Values are shown as mean (%).
MMSE, Mini-Mental Status Examination; FAC, Functional Ambulation Category; mRS, Modified Rankin Scale; MI-lower, Motricity Index-lower limb.

Table 5. Functional outcomes and urinary retention depending on whether brain tumor lesion includes frontal lobe

Variable	Including frontal lobe (n = 35)	Not including frontal lobe (n = 26)	p value
MMSE at transfer	18 (n = 35)	16.15 (n = 26)	0.35
FAC at transfer	1 (n = 35)	1.27 (n = 26)	0.33
mRS at transfer	4.29 (n = 35)	4.08 (n = 26)	0.29
MI-lower at transfer	51.54 (n = 35)	59.23 (n = 26)	0.08
MMSE after rehabilitation	20.94 (n = 34)	20.83 (n = 23)	0.81
FAC after rehabilitation	1.9 (n = 35)	2.27 (n = 26)	0.45
mRS after rehabilitation	3.51 (n = 35)	3.42 (n = 26)	0.63
MI-lower after rehabilitation	57.31 (n = 32)	62.91 (n = 22)	0.28
ΔMMSE	3.29 (n = 34)	4.3 (n = 23)	0.47
ΔFAC	0.97 (n = 35)	1 (n = 26)	0.90
ΔmRS	(−)0.77 (n = 35)	(−)0.65 (n = 26)	0.48
ΔMI-lower	5.53 (n = 32)	3.27 (n = 22)	0.32
UR group	14	10	0.90
Non-UR group	21	16	

Values are shown as mean (%).
MMSE, Mini-Mental Status Examination; FAC, Functional Ambulation Category; mRS, Modified Rankin Scale; MI-lower, Motricity Index-lower limb; UR, urinary retention.

rehabilitation, but still demonstrated significantly worse functional outcomes compared to the non-UR group even after rehabilitation. Our study also showed that the initial MMSE and FAC were significantly worse in the UR group than in the non-UR group, and this difference persisted even after rehabilitation. Although mRS and MI-lower were also worse in the UR group, this was not statistically significant. These results are similar to previous study on stroke and UR [9], and are concordant with other studies that have found comparable degrees of improvement in rehabilitation for brain tumors and stroke [23,25]. Specifically, this study demonstrated, as in Son et al.'s study [9], that the presence of early UR in brain tumor patients is associated with worse functional outcomes in both mobility and cognition domains before and after rehabilitation compared to non-UR patients. Therefore, this study is significant in extending the correlation between stroke and UR to the brain tumor patient population, as demonstrated in previous studies. The representative brain regions responsible for harmonious urination include the prefrontal cortex and pons [14,15]. Prefrontal cortex, which produces important projections to the regions responsible for urination, is also involved with projections to other brain regions responsible for cognition integration. In addition, motor function is mediated through a complex interconnection of cortical and subcortical pathways, and these pathways also play an important role in urinary continence [16]. Therefore, considering the commonality of such pathways of the brain, it can be anticipated that the recovery of neurogenic continence due to damage to urinary center is paralleled with the improvement of cognitive and motor dysfunction as shown in our study [17-19].

We further investigated whether the degree of functional improvements could be correlated with the initial UR. However, we cannot find significant difference between the 2 groups on improvements in functional outcomes. This result can be attributed to the low number of patients and the ceiling effect of functional measures used in the study. Only FAC improved more in the non-UR group than UR group, which is consistent with the hypothesis of our study. However, in the case of MMSE, mRS and MI-lower, the UR group showed a greater degree of improvement after rehabilitation than the non-UR group. This may be due to the ceiling effect of evaluation measures. Specifically, it can be inferred that a ceiling effect was observed in MMSE, mRS, and MI-lower. Since the UR group showed worse initial functional scores, there was more room for numerical improvement of the functional measures than in the non-UR group. Indeed, upon calculation of proportional recovery of functional measures, it becomes evident that the UR group has exhibited a more favorable outcome than

https://doi.org/10.12786/bn.2023.16.e11

non-UR group (UR vs. non-UR; MMSE: 131% vs. 116%, FAC: 213% vs. 171%, mRS: 82% vs. 85%, MI-lower: 110% vs. 109%). We anticipate that further statistical significance would be secured in a future larger study.

We explored the association of malignancy status on any possible differences in functional outcomes or improvement through rehabilitation, but there were no statistically significant differences. We also divided patients depending on whether their tumor included the frontal lobe or not, as this part of the brain is involved in controlling urination, and analyzed if there was any functional difference between the 2 groups [14]. However, we cannot find significant difference in functional outcome depending on whether the tumor involves frontal lobe. As the regulation of urination is mediated not only by the frontal lobe, but also by the complex interconnections between the pons and cortex [14,15], we assumed that more factors should be taken into account in future study focusing on differences regarding anatomical locations.

There are several limitations to this study. First, it was conducted with a small number of patients. It is considered that statistical significance might be achieved if a larger scale study were to be conducted. Second, there is the possibility of selection bias. Since patients transferred to rehabilitation units after brain tumor surgery are likely to be functionally worse and require more intensive inpatient rehabilitation than those who are not transferred and therefore discharged, we cannot yet generalize our results to all patients who have received brain tumor surgery. Moreover, since 397 out of 458 patients were excluded, it is difficult to claim that the results are unbiased. Finally, urine retention cannot be representative of lower urinary dysfunction. Often cerebral lesions cause not just UR but also disinhibition of bladder emptying. We could not address this aspect of urinary dysfunction due to limitations of retrospective data collection. In future research, it will be necessary to address and overcome these limitations.

Rehabilitation was shown to be effective for brain tumor patients regardless of UR. Initial UR after brain tumor surgery was significantly associated with poor functional status in the early stages of rehabilitation and functional outcomes after rehabilitation. Therefore, by evaluating easy-to-check initial UR, one is able to partly predict functional outcomes after rehabilitation in brain tumor patients. We expect that statistically significant results will be derived from a further larger scale study.

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