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Original Research

Volume effect in paediatric brain tumour resection surgery: analysis of data from the Japanese national inpatient database



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Abstract Background: Paediatric brain tumours are the second most common type of malignancies that occur during childhood. Surgical resection is usually the first step in the treatment of these patients; however, evidence pertaining to a 'volume effect' in paediatric brain tumour resection surgery and the associations among the surgical volume, clinical features and treatments are not well characterised.

Methods: Data pertaining to paediatric patients (age ≤ 15 years) who underwent brain tumour resection surgery between April 2012 and March 2016 were retrieved from the Japanese administrative inpatient database and retrospectively analysed. Demographic characteristics, therapeutic procedures and in-hospital mortality were summarised according to the hospital surgical volume. Penalised logistic regression analysis was used to investigate the association between the hospital surgical volume and in-hospital mortality.

Results: A total of 1354 paediatric patients were included. About 40% of the patients were in the 11- to 15-year age group. The male:female ratio was 53:47, the overall crude in-hospital mortality was 1.8% (n = 24) and the 30-day postoperative mortality was 0.4% (n = 6). The crude mortality ratio was 3.3% in the lowest quartile and 0.8% in the highest quartile by volume. After adjusting for covariates, a higher hospital surgical volume was associated

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with lower in-hospital mortality (compared with 1–4 surgeries per 4 years, 15–25 surgeries, odds ratio [OR]: 0.25; 95% confidence interval [CI]: 0.05–0.90, $p = 0.033$; ≥ 26 surgeries, OR: 0.31; 95% CI: 0.08–0.96, $p = 0.042$).

Conclusions: The present study indicated a volume–outcome relationship in paediatric brain tumour resection surgery cases. Further centralisation of surgeries should be considered to achieve better outcomes.

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1. Introduction

Childhood cancer is a rare disease and is the leading cause of death from illness in children in developed countries [1]. In addition, paediatric brain tumours are the second most common malignancies in children. Owing to the rarity, the number of paediatric patients with brain tumour is relatively small, and studies related to paediatric brain tumours are largely lacking.

Surgical resection is usually the first step in the treatment of brain tumours in children. Individual hospitals typically have low exposure to paediatric patients with brain tumours. Current paediatric neurosurgery guidelines recommend that patients with central nervous system tumours should preferably be treated at specialised centres (including paediatric hospitals) that treat higher volumes of these patients and have specialised personnel along with well-established treatment protocols [2,3]. Furthermore, increasing evidence suggests that patient mortality and morbidity rates are typically lower in high-volume settings, including in the context of surgery for adult brain tumours and other adult cancers [4–10].

Nevertheless, data supporting this recommendation in the context of paediatric brain tumour resection surgery are limited. According to a previous review, studies that have investigated the association between institutional experience and outcomes of paediatric surgeries exhibit wide variability in methodologic quality [11]. Only a few studies have investigated the effect of the hospital surgical volume on the outcomes of paediatric brain tumour surgery using long-term data (>10 years) [12,13]. In addition, a previous review highlighted the need for more studies to characterise this relationship [14]. To assess this relationship, use of a national database may confer considerable leverage by overcoming the limitation of a small sample size.

Owing to the paucity of relevant epidemiological studies, evidence pertaining to the association of the hospital surgical volume with patient characteristics, procedures and outcomes is also scarce. Such investigations are likely to provide information that would enhance service provision, hospital function in terms of patient consolidation and the healthcare delivery system overall.

The aims of this study were (i) to describe the clinical features of patients who underwent paediatric brain tumour surgery, the procedural details and outcomes according to the hospital surgical volume and (ii) to examine the relationship between the hospital surgical volume and in-hospital mortality of these patients. We hypothesised that high-volume hospitals that specifically handle paediatric brain tumour resection surgery would be associated with lower in-hospital mortality compared with those with lower volumes.

2. Methods

2.1. Data source

This was a retrospective, observational study that used data from the Japanese administrative database entitled the Diagnosis Procedure Combination per-diem payment system (DPC/PDPS). The details of the DPC/PDPS have been described elsewhere [15]. In brief, the DPC/PDPS is a case-mix patient classification system that is linked to payments at acute-care and mixed-care hospitals in Japan. By 2016, the DPC/PDPS-based hospital reimbursement system had been adopted by more than 1600 hospitals, which accounted for more than half of the total 894,000 hospital beds nationwide.

Anonymous clinical and administrative claims data were collected annually for patients from participating hospitals. Clinical data consist of the baseline patient information, diagnostic aspects (based on International Statistical Classification of Diseases and Related Health Problems (ICD)-10) and detailed medical information such as all major or minor procedures, medication and device use. The database also includes the purpose of admission, discharge destination and the outcome at the time of hospital discharge. Hospital information is also available via the DPC/PDPS.

This study was approved by the institutional review board at the Tokyo Medical and Dental University and the National Center for Child Health and Development. The board waived off the requirement for informed patient consent because of the anonymous nature of the data.

2.2. Participants and variables

We identified paediatric patients aged ≤ 15 years who underwent brain tumour resection surgery (Japanese operative K-codes: K169-1 and K169-2) between April 1, 2012, and March 31, 2016, from the DPC/PDPS database. We considered patients with a length of stay (LOS) more than 365 days and who had a preoperative LOS more than 14 days as outliers and excluded them. Patients who only had a brain tumour biopsy and who underwent endoscopic endonasal surgery were also excluded. The inclusion criteria are described in Fig. 1.

Data pertaining to both individual- and hospital-level characteristics were extracted. Individual variables included age, sex, the admission status (planned, unplanned or urgent), use of an ambulance, tumour types according to the ICD-10 codes (Malignant: ICD-10 Cxx and Benign: ICD-10, Dxx), hydrocephalus at admission (ICD-10: G91x), LOS and discharge outcomes. Owing to the data availability on detailed subcategories in tumour classification such as ICD-Oncology, we used major categories ‘Malignant or Benign’ as previous studies have used similar classifications such as ‘malignant versus other’ [12] and ‘tumour low grade, high grade’ [16]. Data regarding the use of an intensive care unit (ICU) including step-down unit care, details of chemotherapy, radiation therapy, blood transfusion, duration of anaesthesia and shunt operation (Japanese operative K-code K1741, K1742 and K174-2) as the treatment for hydrocephalus were also obtained from the database.

Hospital-level characteristics included the academic status, cancer centre designation, paediatric inpatient volume and volume of paediatric brain tumour resection surgery. The Japanese government has designated several hospitals as core hospitals for different categories of cancer treatment: central, regional and child (401, 36 and 15, respectively, as of April 1, 2018). The

hospital paediatric inpatient volume was defined as the average annual number of discharged inpatients aged ≤ 15 years and was categorised into four groups: < 1200 , 1200 to 1799, 1800 to 2499 and ≥ 2500 . The hospital surgical volume was defined as the total number of paediatric brain tumour resection surgeries performed at each hospital and was categorised into quartile groups with approximately equal numbers of patients in each group. The primary outcome of this study was in-hospital mortality. The 30-day postoperative mortality was also reported.

2.3. Statistical analysis

Continuous variables are expressed as the mean \pm standard deviation or the median and interquartile range (IQR), depending on the overall variable distribution. The Mann–Whitney U test and Kruskal–Wallis one-way analysis of variance were used to assess between-group differences. Categorical variables are expressed as proportions and were compared using a Fisher’s exact test or Chi-squared test. Univariate logistic regression analysis and penalised logistic regression analysis were used to assess the relationship between in-hospital mortality and patient/hospital factors, given the low incidence rate of mortality [17].

Restricted cubic splines (RCSs) were generated assuming a non-linear relationship between the hospital surgical volume and in-hospital mortality. The cubic splines were adjusted for the same covariates that were included in the multivariable model. Cubic knots were set at 1 (5%), 8 (25%), 26 (75%) and 44 (95%) of the 4-year hospital surgical volume. All statistical analyses were performed using R statistical software, version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria) and SAS version 9.4 (SAS Institute, Cary, North Carolina, United States). The analyses were two tailed, and p -values < 0.05 were considered statistically

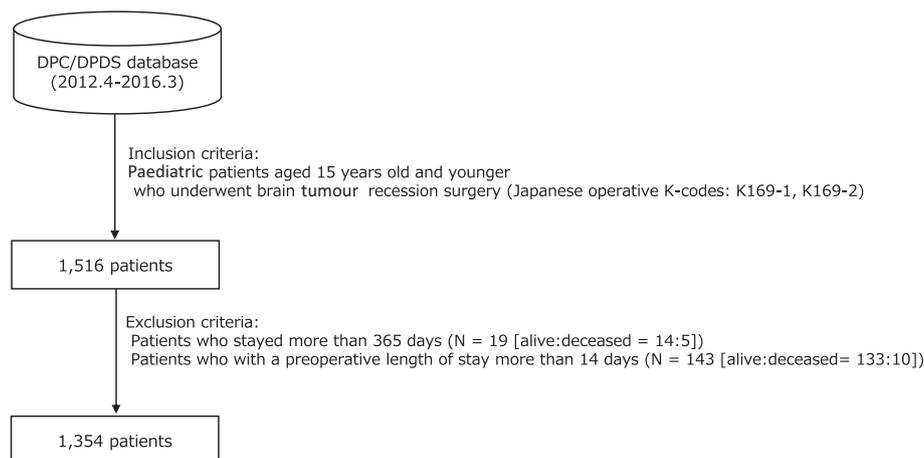


Fig. 1. Schematic illustration of the study population and the selection criteria. DPC/PDPS, Diagnosis Procedure Combination per-diem payment system.

significant. We did not impute any missing data in the present study.

3. Results

3.1. Patient and hospital characteristics

A total of 1354 paediatric patients who underwent brain tumour resection surgery were qualified for our study

based on the inclusion criteria (Fig. 1). Table 1 shows the characteristics of the patients and hospitals. Almost two-fifths of the patients were aged 11–15 years (39.3%), and nearly half of the patients were women (46.5%). The median (IQR) LOS was 24 days (15–65 days), whereas the median preoperative LOS was 4 days (2–7 days). The overall crude in-hospital mortality ratio was 1.8% (24/1354), and the 30-day postoperative mortality ratio was 0.4% (6/1354). On comparing patient

Table 1
Characteristics of patients and hospitals disaggregated by the hospital surgical volume.

Characteristics	Overall cohort	Number of surgeries (4 years)				p value
		Lowest quartile	Second quartile	Third quartile	Highest quartile	
		1–7 surgeries	8–14 surgeries	15–25 surgeries	26+ surgeries	
N	1354	333	329	335	357	
Age						0.014
0–2	200(14.8%)	47(14.1%)	38(11.6%)	57(17.0%)	58(16.2%)	
3–5	232(17.1%)	42(12.6%)	57(17.3%)	60(17.9%)	73(20.4%)	
6–10	390(28.8%)	91(27.3%)	106(32.2%)	104(31.0%)	89(24.9%)	
11–15	532(39.3%)	153(45.9%)	128(38.9%)	114(34.0%)	137(38.4%)	
Sex						0.379
Female	630(46.5%)	154(46.2%)	166(50.5%)	153(45.7%)	157(44.0%)	
Male	724(53.5%)	179(53.8%)	163(49.5%)	182(54.3%)	200(56.0%)	
Confirmed ICU use	870(64.3%)	224(67.3%)	215(65.3%)	178(53.1%)	253(70.9%)	0.000
ICU length of stay, days						
Patients who used the ICU, median (IQR)	2(2–5)	2(2–8)	2(1–4)	2(2–4)	2(1–4)	0.023
Overall cohort, median (IQR)	1(0–3)	2(0–4)	1(0–2)	1(0–2)	2(0–3)	< 0.001
Use of ambulance	144(10.6%)	41(12.3%)	36(10.9%)	22(6.6%)	45(12.6%)	0.040
Admission setting						<0.001
Planned	823(60.8%)	158(47.4%)	205(62.3%)	231(69.0%)	229(64.1%)	
Unplanned or urgent	531(39.2%)	175(52.6%)	124(37.7%)	104(31.0%)	128(35.9%)	
Type of tumour						0.016
Malignant (ICD-10, Cxx)	828(61.2%)	188(56.5%)	200(60.8%)	228(68.1%)	212(59.4%)	
Benign (ICD-10, Dxx)	526(38.8%)	145(43.5%)	129(39.2%)	107(31.9%)	145(40.6%)	
Hydrocephalus at admission	279(20.6%)	69(20.7%)	78(23.7%)	69(20.6%)	63(17.6%)	0.278
Academic hospitals	939(69.4%)	109(32.7%)	279(84.8%)	256(76.4%)	295(82.6%)	<0.001
Cancer centre						
Child	263(19.4%)	6(1.8%)	8(2.4%)	85(25.4%)	164(45.9%)	
Central, region	849(62.7%)	216(64.9%)	283(86.0%)	215(64.2%)	135(37.8%)	
None	242(17.9%)	111(33.3%)	38(11.6%)	35(10.4%)	58(16.2%)	
Paediatric inpatient volume (per year)						<0.001
0–1199	460(34.0%)	138(41.4%)	163(49.5%)	89(26.6%)	70(19.6%)	
1200–1799	343(25.3%)	128(38.4%)	83(25.2%)	57(17.0%)	75(21.0%)	
1800–2499	329(24.3%)	47(14.1%)	75(22.8%)	147(43.9%)	60(16.8%)	
2500+	222(16.4%)	20(6.0%)	8(2.4%)	42(12.5%)	152(42.6%)	
Length of stay, days	24(15–65)	23(15–51)	25(16–68)	22(15–62)	26(15–73)	0.141
Preoperative length of stay, days	4(2–7)	4(2–7)	4(2–7)	3(2–6)	3(2–6)	0.093
In-hospital deaths	24(1.8%)	11(3.3%)	8(2.4%)	2(0.6%)	3(0.8%)	0.021
30-day mortality after surgery	6(0.4%)	4(1.2%)	1(0.3%)	0(0.0%)	1(0.3%)	0.131
Summary of hospital information						
Number of hospitals	208	149	32	17	10	
Academic	76(36.5%)	29(19.5%)	26(81.3%)	13(76.5%)	8(80.0%)	
Cancer centre						
Child	12(5.8%)	2(1.3%)	1(3.1%)	4(23.5%)	5(50.0%)	
Central, region	132(63.5%)	91(61.1%)	27(84.4%)	11(64.7%)	3(30.0%)	
None	64(30.8%)	56(37.6%)	4(12.5%)	2(11.8%)	2(20.0%)	
Paediatric inpatients volume (per year)						
0–1199	95(45.7%)	73(49.0%)	15(46.9%)	5(29.4%)	2(20.0%)	
1200–1799	67(32.2%)	54(36.2%)	8(25.0%)	3(17.6%)	2(20.0%)	
1800–2499	31(14.9%)	14(9.4%)	8(25.0%)	7(41.2%)	2(20.0%)	
2500+	15(7.2%)	8(5.4%)	1(3.1%)	2(11.8%)	4(40.0%)	

ICU, intensive care unit; ICD, International Classification of Diseases; IQR, interquartile range.

characteristics according to the hospital surgical volume group, high-volume hospitals covered younger patients, the proportion of unplanned admissions was higher in the lowest surgical volume hospitals and the crude in-hospital mortality ratio was inversely correlated with the hospital surgical volume.

In terms of hospital characteristics, a total of 208 hospitals provided paediatric brain tumour resection surgery during the study reference period. The top 10 hospitals in terms of the surgical volume covered more than one-fourth of all patients (26.4%), whereas 149 hospitals had 1–7 surgeries during the 4-year study period (24.6%). Thus, the distribution of hospitals according to the surgical volume was right skewed (Fig. 2).

3.2. Details of in-hospital deaths and its risk factors

Table 2 shows patient characteristics by the final outcome and the results of univariate logistic regression analysis. Compared with patients who were discharged, patients who died in hospital were younger, female, used the ICU longer, experienced unplanned/urgent admission and had a longer LOS. Multivariate penalised logistic regression analysis showed that unplanned/urgent admission was associated with an increased risk of in-hospital mortality (odds ratio [OR]: 5.42; 95% confidence interval [CI]: 2.06–17.67; $p < 0.001$), whereas a higher hospital surgical volume was associated with a decreased risk of in-hospital mortality (15–25 surgeries, OR: 0.25 [95% CI: 0.05–0.90], $p = 0.033$; ≥ 26 surgeries, OR: 0.31 [95% CI: 0.08–0.96], $p = 0.042$) (Table 3).

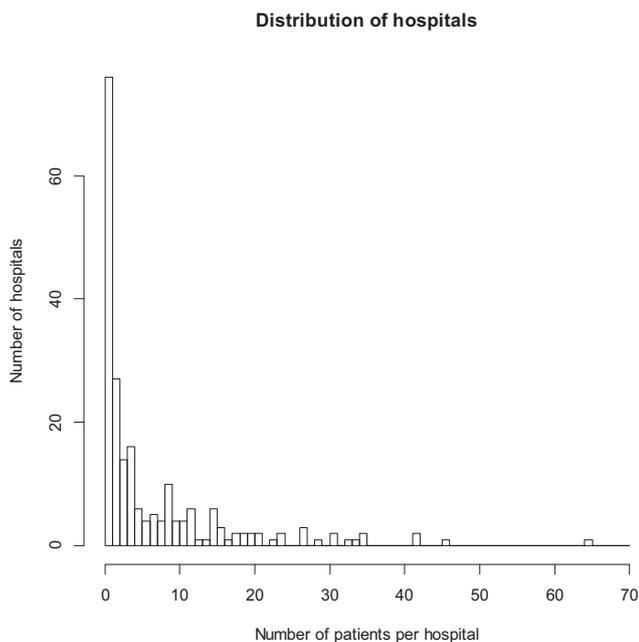


Fig. 2. Distribution of the case volume of paediatric brain tumour resection surgeries.

The adjusted RCS plot demonstrated a non-linear association between the hospital surgical volume and in-hospital mortality (Fig. 3). This plot showed that an increase in the hospital surgical volume was associated with a decrease in the odds of an in-hospital death by up to four cases per year (16 cases per 4 years).

We also compared the final outcome, hospital surgical volume and type of brain tumour according to ICD-10 codes (Supplemental Table S1).

3.3. Differences in other therapeutic procedures according to the hospital surgical volume

The association between other therapeutic procedures and the hospital surgical volume is summarised in Supplemental Table S2. Although the results were not based on the histopathological tumour classification, low-volume hospitals had fewer instances of both chemotherapy and radiation therapy. However, some of the procedures were not dramatically affected by the hospital surgical volume. Among unplanned/urgent admission patients, about 6% of the patients underwent a shunt operation (33/531) and more than 10% of these patients (14/128) were treated by a shunt operation in the highest surgical volume hospitals. Detailed chemotherapy information according to the hospital surgical volume subgroups is presented in Supplemental Table S3.

3.4. Mortality and hospital surgical volume in paediatric patients and patients of all ages

Table 4 summarises the in-hospital mortality ratio associated with the hospital surgical volume in paediatric patients and in patients of all ages. In-hospital mortality of paediatric patients who underwent brain tumour resection surgery showed a decreasing trend when the brain tumour resection surgery volume increased; however, this phenomenon was not observed when the hospital surgical volume was based on patients of all ages in the analysis.

3.5. Subgroup analysis for young patients (aged ≤ 5 years) and high-volume centres

Subgroup descriptive analysis for patients aged ≤ 5 years is shown in Supplemental Table S4. There was higher crude in-hospital mortality in the lowest surgical volume hospitals (5.6%, 5/89) compared with that in the highest surgical volume hospitals (0.8%, 1/131).

Subgroup descriptive analysis for high-volume centres (≥ 10 cases per year) is shown in Supplemental Table S5. There were four high-volume centres (1.9%, 4/208), covering more than 13% of the patients (179/1354). None were considered very high-volume centres that would have involved at least 20 cases per year (Fig. 2).

Table 2
Univariate logistic regression analysis for in-hospital death.

Characteristics	Alive	Deceased	Mortality rate	Unadjusted odds ratio(95% CI)	p value
N	1330	24	1.8%		
Age					
0-2	192(14.4%)	8(33.3%)	4.0%	2.73(1.01–7.37)	0.048
3-5	228(17.1%)	4(16.7%)	1.7%	1.15(0.34–3.85)	0.822
6-10	386(29.0%)	4(16.7%)	1.0%	0.68(0.20–2.27)	0.529
11-15	524(39.4%)	8(33.3%)	1.5%	reference	
Sex					
Female	616(46.3%)	14(58.3%)	2.2%	1.62(0.72–3.68)	0.246
Male	714(53.7%)	10(41.7%)	1.4%	reference	
Confirmed ICU use	852(64.1%)	18(75.0%)	2.1%	1.68(0.66–4.27)	0.273
ICU length of stay, days					
Patients who used the ICU, median (IQR)	2(2–4)	5(5–22)	–	–	–
Overall cohort, median (IQR)	1(0–2)	10(1–14)	–	–	–
Use of ambulance	141(10.6%)	3(12.5%)	2.1%	1.20(0.35–4.08)	0.767
Admission setting					
Planned	819(61.6%)	4(16.7%)	0.5%	reference	
Unplanned or urgent	511(38.4%)	20(83.3%)	3.8%	8.01(2.72–23.58)	<0.001
Type of tumour					
Malignant (ICD-10, Cxx)	810(60.9%)	18(75.0%)	2.2%	1.93(0.76–4.88)	0.167
Benign (ICD-10, Dxx)	520(39.1%)	6(25.0%)	1.1%	reference	
Hydrocephalus at admission	271(20.4%)	8(33.3%)	2.9%	1.95(0.83–4.61)	0.126
Academic hospitals	923(69.4%)	16(66.7%)	1.7%	0.88(0.37–2.08)	0.774
Child	261(19.6%)	2(8.3%)	0.8%	0.30(0.06–1.51)	0.144
Central region	833(62.6%)	16(66.7%)	1.9%	0.76(0.29–1.95)	0.563
None	236(17.7%)	6(25.0%)	2.5%	reference	
Paediatric patient volume (per year)					
0-1199	454(34.1%)	6(25.0%)	1.3%	reference	
1200-1799	336(25.3%)	7(29.2%)	2.0%	1.58(0.52–4.73)	0.417
1800-2499	320(24.1%)	9(37.5%)	2.7%	2.13(0.75–6.04)	0.156
2500+	220(16.5%)	2(8.3%)	0.9%	0.69(0.14–3.44)	0.648
Hospital surgical volume (4 years)					
1-7	322(24.2%)	11(45.8%)	3.3%	reference	
8-14	321(24.1%)	8(33.3%)	2.4%	0.73(0.29–1.84)	0.503
15-25	333(25.0%)	2(8.3%)	0.6%	0.18(0.04–0.80)	0.024
26+	354(26.6%)	3(12.5%)	0.8%	0.25(0.07–0.90)	0.034
Length of stay, days	24(15–64)	62(33–176)	–	1.01(1.00–1.01)	<0.001
Preoperative length of stay, days	4(2–7)	2(0–8)	–	0.96(0.85–1.09)	0.560
Number of hospitals	207		20		

CI, confidence interval; ICU, intensive care unit; ICD, International Classification of Diseases; IQR, interquartile range.

4. Discussion

The present study characterised the differences in the clinical features of paediatric patients who underwent brain tumour resection surgery, the procedures performed and the outcomes between hospitals disaggregated by the level of the surgical volume, using a nationally representative inpatient database in Japan. This study also characterised the volume–outcome relationship in the context of surgery in paediatric patients. Although there are several unmeasured confounders such as histopathological classification, depth and the tumour size, our results represent some of the best available evidence pertaining to paediatric brain tumour resection surgery.

In terms of surgical settings (Table 1), an interesting finding was the higher proportion of unplanned/urgent admissions observed in the lowest surgical volume hospitals. On one hand, this may reflect a difference with

respect to hospital function and location; for example, hospitals in rural regions may treat more patients in an emergency setting. On the other hand, this may also indicate that low-volume hospitals tend to provide the surgery themselves rather than refer the patient to more specialised centres. Our results also showed that the consolidation of younger patients with brain tumour is progressing, although the consolidation level was lower than that in other countries. For example, 81.5% of the paediatric patients (aged ≤ 20) were treated in high-volume centres (four cases per year) in the United States [13], whereas 26.3% of the patients (aged ≤ 15) in the present study were treated in hospitals with a similar volume of cases (26 cases in 4 years). Surprisingly, in 75 of the hospitals analysed in our study, only one surgery was performed over the 4-year period (Fig. 2).

The crude in-hospital mortality ratio of 1.8% was comparable to that reported from other countries (1.2%–2.7%) [12,13], whereas the 30-day postoperative

Table 3
Multivariate penalised logistic regression analysis for in-hospital death.

Characteristics	Adjusted odds ratio (95% CI)	p value
N		
Age		
0-2	2.19(0.79–6.08)	0.131
3- 5	0.98(0.27–3.08)	0.973
6-10	0.60(0.17–1.85)	0.375
11-15	reference	
Sex		
Female	1.43(0.63–3.34)	0.388
Male	reference	–
Admission setting		
Planned	reference	
Unplanned or urgent	5.42(2.06–17.67)	<0.001
Type of tumour		
Malignant (ICD-10, Cxx)	1.68(0.7–4.57)	0.253
Benign (ICD-10, Dxx)	reference	
Hospital surgical volume (4 years)		
1-7	reference	
8-14	0.89(0.34–2.22)	0.804
15-25	0.25(0.05–0.9)	0.033
26+	0.31(0.08–0.96)	0.042

ICD, International Classification of Diseases; CI, confidence interval.

mortality of 0.4% was lower than that in other countries (1.2%–1.7%) [16,18,19]. These data implied possible improvements in postoperative care in Japan, although the surgical and discharge criteria could vary in each country. Among the factors that were significantly

associated with in-hospital mortality (Table 3), younger age was not consistent with those reported by previous studies [16,18]. Patients with unplanned/urgent admissions showed an increased risk of mortality; this is partly because such admissions reflect severe conditions, and less information is available compared to that with planned admissions.

The hospital volume effect in paediatric surgery has also been reported in the context of other paediatric surgeries [20–23]. High-volume hospitals are more likely to have a higher number of specialists, including surgeons and anaesthesiologists, which contributes to better outcomes. The present study showed volume–outcome relationship in paediatric brain tumour resection surgery, which is consistent with a previous study [12]. The adjusted analysis indicated that a hospital surgical volume threshold of four cases per year was associated with a higher risk of in-hospital mortality. This threshold suggests that low-volume hospitals should preferably refer paediatric patients with brain tumour to high-volume centres for surgery after providing symptomatic treatment. Our results also imply that consolidation of paediatric patients with brain tumours, rather than patients with brain tumour of all ages, contributes to improved outcomes (Table 4). Nevertheless, some studies have not found that the hospital volume effects surgery outcomes in settings where consolidation of such patients has already progressed [13] and in neurosurgical centres with variable volumes of specialists for treatment of children [24]. Further studies investigating why the surgical volume contributes to better outcomes are needed.

Regarding other major procedures, low-volume hospitals may be associated with an inability to provide multidisciplinary treatments (Supplemental Table S2). In addition, the proportion of shunt operations to urgent admission patients differed among hospital surgical quartiles, indicating the difference of treatment procedures among these hospitals. However, our study did not include data pertaining to the need of these therapies or treatment delays. Further investigations are needed to better assess the process of care owing to the limited evidence.

Findings from a subgroup analysis of young patients indicated several interesting implications. First, the centralisation of young patients may be in progress as indicated by higher rates of admission of patients using ambulance, which is likely to reflect the transfer of these patients to high-volume centres (Supplemental Table S4). Second, the proportion of unplanned/urgent patients was higher in the case of young patients (49.5%, Supplemental Table S4) compared with that in the overall cohort (39.2%, Table 1). Interventions to improve diagnostic support may help avoid delayed diagnosis in some cases. Finally, in-hospital mortality showed a remarkable increase associated with a decreased hospital volume, which indicates the need for

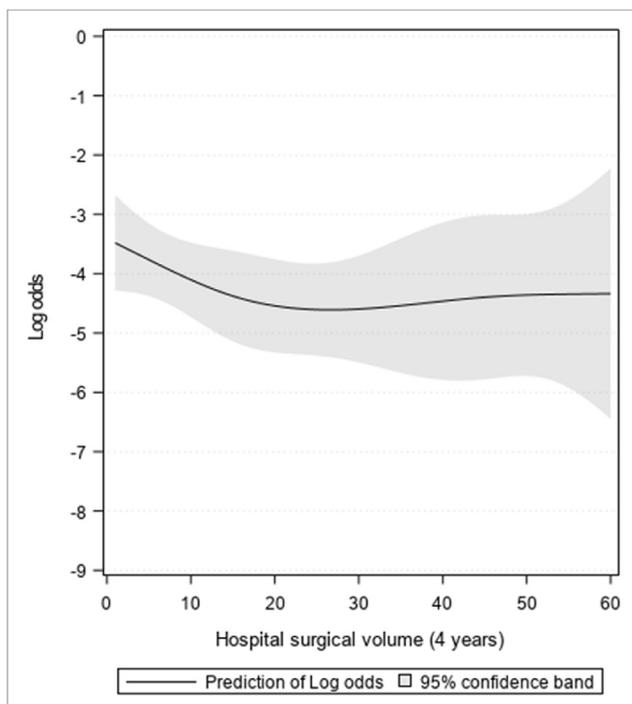


Fig. 3. Adjusted restricted cubic spline showing the relationship between the hospital surgical volume and in-hospital mortality in paediatric brain tumour resection surgery. (The curve was adjusted for age, sex, admission setting and the type of tumour).

Table 4

Cross tabulation for in-hospital death and in-hospital mortality ratio according to the hospital surgical volume in all ages and the group ≤ 15 years old.

Number of surgeries (4 years)	Overall cohort	Lowest quartile	Second quartile	Third quartile	Highest quartile
		Number of surgeries (4 years)			
		1–7 surgeries	8–14 surgeries	15–25 surgeries	26 + surgeries
Mortality ratio (N: deaths/N: patients)					
Brain tumour resection surgery hospital volume (4 years, in all ages)					
Overall cohort	1.8% (24/1354)	3.3% (11/333)	2.4% (8/329)	0.6% (2/335)	0.8% (3/357)
1–49 surgeries	1.3% (2/151)	2.7% (2/54)	0.0% (0/8)	0.0% (0/42)	0.0% (0/26)
50–99 surgeries	2.2% (3/136)	2.4% (2/82)	0.0% (0/17)	2.7% (1/37)	
100–249 surgeries	1.8% (9/487)	4.0% (6/150)	1.6% (3/183)	0.0% (0/87)	0.0% (0/67)
250 + surgeries	1.7% (10/580)	3.8% (1/26)	4.1% (5/121)	0.6% (1/169)	1.1% (3/264)

immediate measures to improve the quality of care at low-volume hospitals.

This study has major strengths: it is the largest reported study on this subject in terms of patient numbers based on a national administrative database. Also, the analysis included detailed data pertaining to medical services and clinical features associated with mortality and the hospital surgical volume; our results may inform future interventions to improve medical services and the healthcare delivery system.

Several limitations of the present study must be considered. First, this investigation was based on an administrative database. The database covers more than 80% of surgeries conducted across Japan; however, a few paediatric hospitals do not participate in the DPC/PDPS system. Exclusion of these hospitals may have introduced an element of sampling bias.

Second, the study did not consider postdischarge outcomes. Data regarding the cause of death, detailed discharge settings (e.g. the hospital to which the patient was transferred) and long-term outcomes were not considered either. Further analysis that considers the overall treatment flow of the patients would provide additional insights.

Third, data pertaining to several potential confounding variables are not available in the DPC/PDPS database. Therefore, factors such as histopathological classification, depth and tumour size, diagnosis timing and tumour metastasis were not included in the analysis. There are wide variations among brain tumour types and various malignancy grades, which would contribute to the risk of in-hospital mortality and therapeutic procedures. In addition, the following potential confounders were not considered: (1) detailed operative information including the difficulty level of each surgery, (2) information pertaining to surgeons/anaesthesiologists including their experience levels, (3) neurosurgical subspecialisation, which is associated with surgical outcomes of malignant brain tumours in children [25] and (4) regional factors including healthcare resources.

Fourth, the exclusion criteria eliminated patients with a higher mortality ratio, especially those with a

preoperative LOS > 14 days (Fig. 1), although the penalised logistic regression analysis including these patients showed a volume–outcome relationship (data not shown). We assume that some of these patients had complications or more severe diseases including metastatic brain tumours, or were admitted to hospitals that lacked specialists, which led to a delayed diagnosis and surgery. However, detailed data were not available to assess this hypothesis. Outcome analysis for this kind of surgery is inherently complex owing to considerable heterogeneity.

5. Conclusions

Evidence pertaining to brain tumour resection surgery in paediatric patients is not well characterised. Although there are several unmeasured confounding variables, our results indicate the existence of a volume–outcome association in the context of paediatric brain tumour resection surgery. This study highlights the need to consolidate paediatric patients with brain tumour to high-volume hospitals. Further efforts, including analysis of more detailed data, are required to help achieve better outcomes of paediatric brain tumour resection surgery.

Author contributions

D.S. participated in the study design, analysis and interpretation of data, drafting the article and revising the article for intellectual content. K.M., K.T. and T.T. participated in the study design, interpretation of data, drafting the article and revising the article for intellectual content. T.O. and T.N. participated in the study design and revising the article for intellectual content. K.F. participated in the study design, interpretation of data and revising the article for intellectual content. All authors read and approved the final manuscript.

Conflict of interest statement

We declare that we have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejca.2018.12.030>.

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