



# Perioperative Anesthesia Management and Mortality Predictors in Pediatric Patients Undergoing Craniotomy for Cranial Tumors

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## Abstract

**Aim:** Studies investigating the effects of perioperative anesthesia management on outcomes in patients undergoing craniotomy for pediatric intracranial tumors are limited in the literature. Our aim in this study was to investigate the effects of perioperative anesthesia management on mortality. Secondly, other mortality predictors were investigated.

**Material and Method:** A total of 165 patients aged <18 years who underwent craniotomy due to intracranial tumor in our hospital were included in the retrospective study between 01/2018 and 09/2024. Patients were divided into two groups according to the intraoperative anesthetic agents used. There were 58 patients in the sevoflurane group and 107 patients in the remifentanyl and propofol groups. The primary endpoint was in-hospital mortality.

**Results:** In the sevoflurane group, the mean age (2.5 [3] vs. 7 [8],  $p < 0.001$ ) and body weight (15 [13] vs. 25 [8],  $p < 0.001$ ) of the patients were lower. Sevoflurane was the preferred anesthetic agent instead of remifentanyl in the younger age group. Therefore, the perioperative vital signs of the patients also differed at a statistically significant level ( $p < 0.05$  for each). In the univariable logistic regression analyses; weight (OR=0.866, 95% CI=0.771-0.971,  $p=0.014$ ), blood transfusion (OR=13.143, 95% CI=1.624-106.333,  $p=0.016$ ), need for inotropes (OR=19.125, 95% CI=2.378-153.835,  $p=0.006$ ), and comorbid diseases (OR=4.681, 95% CI=1.080-20.297,  $p=0.039$ ), were parameters associated with mortality.

**Conclusion:** Our study found no link between perioperative anesthesia management and in-hospital mortality in pediatric patients who underwent craniotomy for intracranial tumors. However, low body weight, comorbidities, intraoperative blood transfusion, and inotropic support were associated with in-hospital mortality. Our study may help clinicians assess perioperative risk for patients who planned craniotomy.

**Keywords:** Pediatric anesthesia, craniotomy, mortality

## INTRODUCTION

The most frequent solid tumor in children is a brain tumor. The incidence rate of all primary brain and central nervous system cancers in children (ages 0–19) is 4.71 per 100,000 person-years, according to the US Central Brain Tumor Registry (1). Surgery is the mainstay of treatment for children's brain tumors. In addition to removing as many tumors as feasible to increase survival and reduce the tumor burden for other treatment modalities, surgery aims to diagnose the tissue accurately. Relieving symptoms, improving quality of life, increasing lifespan, and occasionally even curing the tumor are all possible advantages of tumor excision.

Compared to adult neurooncological surgical procedures, pediatric neurological tumor operations have a higher risk due to several factors, such as a higher frequency of big tumors, complicated midline tumors, and posterior fossa tumors. Various variables, such as the large heterogeneity in tumor kind and site, the small number of patients, and the absence of widely accepted reporting guidelines, exacerbate this in pediatric neurooncological surgery. Furthermore, other significant variables affect results that are not always connected to the quality of surgery, such as differences in the patient's state at diagnosis, the location and severity of the illness at presentation, and any delays in diagnosis. There aren't many extensive series in the

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pediatric neurosurgical literature that discuss morbidity outcomes in pediatric neurooncological surgery, and they all employ rather different metrics. There is no published systematic study on the subject, nor is there a metric that is widely accepted for measuring surgical morbidity in pediatric neurooncology.

Pediatric patients undergoing craniotomy for tumor resection present unique challenges in perioperative anesthesia management due to their physiological and anatomical differences compared to adults. Hemodynamic instability, often caused by significant blood loss during surgery, is a critical concern, as children have a smaller blood volume and are more susceptible to rapid decompensation. Additionally, positioning during craniotomy, such as the prone or sitting position, can lead to ventilation difficulties, including impaired oxygenation and increased risk of airway obstruction. These factors necessitate meticulous monitoring and tailored anesthetic strategies to ensure hemodynamic stability and adequate ventilation. Anesthesiologists must also consider the potential for postoperative complications, such as cerebral edema or seizures, which further complicate perioperative care (2).

Although 30-day mortality rates in pediatric tumor surgery generally range from 0.5% to 5%, these rates may vary depending on various factors such as the type of surgery, the hospital's level of experience, the patient's age, the size of the tumor, the histopathological type of the tumor, and the health status of the patients (3-6).

There are no sufficient studies investigating perioperative anesthesia management and its relationship with mortality. Our aim in this study was to investigate the effect of perioperative anesthesia management on in-hospital mortality in pediatric patients who underwent craniotomy for intracranial tumors. Our second aim was to investigate other mortality predictors.

## MATERIAL AND METHOD

All patients under the age of 18 who underwent craniotomy due to intracranial tumor at Dicle University Faculty of Medicine Hospital between 01.01.2018 and 30.09.2024 were retrospectively included in our study. Only individuals treated with a surgical technique compatible with tumor biopsy or craniotomy were included in the sample, and spinal cord tumors were excluded. All parameters such as age, sex, ASA classification, preoperative laboratory parameters, operation duration, anesthesia duration, perioperative vital signs, perioperative blood transfusion, or inotropic needs of the patients were obtained from hospital records. We defined mortality as in-hospital mortality. Patients with a history of previous surgery (3), those with serious systemic disease (such as advanced heart disease, liver failure, and other systemic diseases) (5), patients with active infection (4), those who received chemotherapy or radiotherapy before surgery (6), and patients with missing data (22) were excluded. The entire population was divided into two groups according to perioperative anesthesia management. There were 58 patients in the sevoflurane group and 107 patients

in the remifentanyl and propofol combination remifentanyl group. The patient flow chart is schematized in Figure 1. Ethical approval was obtained from the ethics committee of Dicle University Faculty of Medicine for the study (295-16/10/2024). Our study was conducted in accordance with the principles of the Helsinki Declaration.

## Perioperative Anesthesia Management

All patients were evaluated according to the American Society of Anesthesiologists (ASA) classification. In this retrospective study, patients who had undergone a uniform perioperative anesthetic approach were selected to ensure comparability in assessing mortality factors. Every patient had a preoperative evaluation that comprised a comorbidity assessment, imaging investigation, and neurological examination. All surgeries were carried out under general anesthesia, and the attending anesthesiologist chose between inhalation and intravenous anesthesia induction based on whether the patient had signs of intracranial hypertension. Following endotracheal intubation, general anesthesia was maintained with an intravenous infusion of either sevoflurane (Sevoflurane Liquid 100%, Queensborough) at a concentration  $<1$  MAC or propofol (Propofol, Fresenius Kabi, Sweden) (6–12 mg/kg/h) and remifentanyl (0.02–0.2  $\mu\text{g}/\text{kg}/\text{min}$ ). Comorbid diseases were defined as cardiovascular, respiratory, hematological, endocrinological, metabolic, neurological, congenital diseases, and others. The goal of both regimens was to minimize intracranial pressure while maintaining stable hemodynamics and cerebral perfusion pressure. Electrocardiography, invasive arterial pressure, end-tidal  $\text{CO}_2$ , pulse oximetry, and temperature were all monitored during the procedure. Mannitol or hypertonic saline was used as necessary to control intracranial pressure, and fluids were carefully given to avoid cerebral edema. Transfusions were given and blood loss was tracked. To maintain appropriate hematocrit levels, blood loss was tracked and transfusions were given in accordance with institutional procedures. For postoperative follow-up, every patient was sent to the intensive care unit. Postoperative hemoglobin and hematocrit measurements, length of hospital stays, length of intensive care unit stay, and whether the patients were intubated or extubated were all documented during the postoperative phase.

## Statistical Analysis

The data was analyzed using SPSS version 26.0 for Windows (Armonk, NY, USA: IBM Corporation). The normal distribution of continuous data was assessed using histograms and the Kolmogorov-Smirnov and Shapiro-Wilks tests. The mean  $\pm$  standard deviation (SD) was used to represent normally distributed continuous data, whereas the median (interquartile range [IQR]) was used to represent non-normally distributed continuous variables. When comparing continuous variables with a normal distribution across two groups, the student t-test was employed; for continuous variables that were not normally distributed, the Mann-Whitney U test was employed. Categorical variables were shown as percentages, and the chi-square test or Fisher-

Freeman-Halton test was used for comparison between groups. Mortality factors were identified using univariable logistic regression analysis. Statistical significance was defined as a p-value of less than 0.05.

## RESULTS

A total of 165 patients under the age of 18 were included in the study. There were 58 patients in the sevoflurane group and 107 patients in the remifentanil group. 49.7% (82) of the population were female.

In the sevoflurane group, the mean age (2.5 [3] vs. 7 [8],  $p<0.001$ ) and body weight (15 [13] vs. 25 [8],  $p<0.001$ ) of the patients were lower. Sevoflurane was the preferred anesthetic agent instead of remifentanil in the younger age group. Therefore, the preoperative, intraoperative and postoperative vital signs (mean arterial pressure and heart

rate) of the patients also differed at a statistically significant level ( $p<0.05$  for each). No significant difference was observed between the groups in terms of gender, duration of anesthesia, duration of intensive care follow-up, tumor size, rate of emergency surgery, perioperative oxygen saturation, blood transfusion, comorbid disease, and in-hospital mortality ( $p>0.05$  for each). In the sevoflurane group, preoperative hemoglobin, urea, and creatinine values were lower, and white blood cell and potassium levels were higher ( $p<0.05$  for each).

Inotropic agent requirement (4 [6.9] vs. 0 [0],  $p=0.006$ ) was lower, and rate of intubated removal from the operating room to intensive care (31 [53.4] vs. 84 [78.5],  $p<0.001$ ) was higher in the sevoflurane group. While ASA 2-3 rates were higher in the sevoflurane group, ASA 1-4 rates were lower ( $p=0.038$ ) (Table 1).

**Table 1. Baseline characteristics of the total population**

| Parameters                                      | Sevoflurane group (n=58) | Remifentanil and propofol group (n=107) | Total (n=168) | p-value          |
|---|--------------------------|---|---------------|------------------|
| Age (month) (IQR)                               | 2.5 (3)                  | 7 (8)                                   | 5 (8)         | <b>&lt;0.001</b> |
| Weight (kg) (IQR)                               | 15 (13)                  | 25 (8)                                  | 20 (19)       | <b>&lt;0.001</b> |
| Female gender, n (%)                            | 23 (39.7)                | 59 (55.1)                               | 82 (49.7)     | 0.058            |
| Preoperative SaO <sub>2</sub> (%)               | 97.8±2.4                 | 98.3±1.3                                | 98.1±1.8      | 0.165            |
| Intraoperative SaO <sub>2</sub> (%)             | 99±1.9                   | 99.3±0.8                                | 99.2±1.2      | 0.234            |
| Postoperative SaO <sub>2</sub> (%)              | 98.2±2.3                 | 98.8±1                                  | 98.6±1.6      | 0.056            |
| Preoperative heart rate (bpm)                   | 118.6±19.4               | 107.2±17.5                              | 111.2±18.9    | <b>&lt;0.001</b> |
| Intraoperative heart rate (bpm)                 | 117.4±20.1               | 99.6±16.3                               | 105.9±19.6    | <b>&lt;0.001</b> |
| Postoperative heart rate (bpm)                  | 117.9±29.9               | 100±20.6                                | 106.3±24.9    | <b>&lt;0.001</b> |
| Preoperative MAP (mmHg)                         | 66.8±11.1                | 76.5±10.1                               | 73.1±11.4     | <b>&lt;0.001</b> |
| Intraoperative MAP (mmHg)                       | 63.5±8.8                 | 72.5±9.5                                | 69.3±10.2     | <b>&lt;0.001</b> |
| Postoperative MAP (mmHg)                        | 62.1±8.5                 | 72±9.1                                  | 68.6±10.1     | <b>&lt;0.001</b> |
| Anesthesia time (min)                           | 373±217                  | 542±218                                 | 483±231       | 0.344            |
| ICU hospitalization time (month)(IQR)           | 14.5 (21)                | 16 (19)                                 | 16 (20)       | 0.743            |
| Tumor size (mm)                                 | 44.2±14.9                | 41.4±14.7                               | 41.8 (14.7)   | 0.598            |
| In-hospital mortality, n (%)                    | 2 (3.4)                  | 8 (7.5)                                 | 10 (6.1)      | 0.300            |
| ASA, n (%)                                      |                          |   |               | <b>0.038</b>     |
| 1   | 4 (6.9)                  | 25 (23.6)                               | 29 (17.7)     |                  |
| 2   | 39 (67.2)                | 50 (50)                                 | 92 (56.1)     |                  |
| 3   | 14 (24.1)                | 24 (22.6)                               | 38 (23.2)     |                  |
| 4   | 1 (1.7)                  | 4 (3.8)                                 | 5 (3)         |                  |
| Blood transfusion, n (%)                        | 28 (48.3)                | 44 (41.1)                               | 72 (43.6)     | 0.376            |
| Emergency operation, n (%)                      | 19 (32.8)                | 29 (27.1)                               | 48 (29.1)     | 0.445            |
| Comorbid disease, n (%)                         | 3 (5.2)                  | 13 (12.1)                               | 16 (9.7)      | 0.148            |
| Need for inotropes, n (%)                       | 4 (6.9)                  | 0 (0)                                   | 4 (2.4)       | <b>0.006</b>     |
| Unable to extubate in the operation room, n (%) | 31 (53.4)                | 84 (78.5)                               | 115 (69.7)    | <b>&lt;0.001</b> |
| <b>Preoperative laboratory parameters</b>       |                          |   |               |                  |
| Hemoglobin (mg/dL)                              | 11.4±1.2                 | 12.1±1.5                                | 11.8±1.4      | <b>0.003</b>     |
| White blood cell (mg/dl)                        | 12.2±6.2                 | 9.7±4.6                                 | 10.7±5.4      | <b>0.023</b>     |
| Urea (mg/dl)                                    | 20.4±8.9                 | 24.3±9                                  | 22.9±9.1      | <b>0.015</b>     |
| Creatinine (mg/dl)                              | 0.37±0.13                | 0.42±0.13                               | 0.39±0.13     | <b>0.020</b>     |
| Natrium (mol/L)                                 | 135.4±3.9                | 136.4±2.9                               | 136.1±3.3     | 0.057            |
| Potassium (mmol/L)                              | 4.4±0.5                  | 4.2±0.5                                 | 4.3±0.5       | <b>0.011</b>     |
| Clora (mmol/L)                                  | 104.6±4.2                | 104±3.2                                 | 104.2±3.6     | 0.343            |
| Aspartate transaminase (IU/L)-IQR               | 31 (14)                  | 27 (13)                                 | 29 (14)       | 0.159            |
| Alanine transaminase (IU/L)-IQR                 | 14 (9)                   | 15 (6)                                  | 15 (8)        | 0.703            |
| Lactate (mmol/L)-IQR                            | 3 (3)                    | 1 (2)                                   | 1.5 (3)       | 0.058            |

MAP: mean arterial pressure, ICU: intensive care unit, ASA: American Society of Anesthesiologists

## Logistic Regression Analyses

Univariable logistic regression analyses were performed to determine mortality predictors. The univariable logistic regression analysis included variables that differed statistically between groups and parameters whose relationship with mortality is discussed in the literature. In the univariable logistic regression analysis; weight (OR=0.866, 95% CI=0.771-0.971, p=0.014), blood transfusion (OR=13.143, 95% CI=1.624-106.333, p=0.016), need for inotropes (OR=19.125, 95% CI=2.378-153.835, p=0.006), and comorbid disease (OR=4.681, 95% CI=1.080-20.297,

p=0.039), were parameters associated with mortality.

No statistically significant relationship was observed between age (OR=0.811, 95% CI=0.655-1.004, p=0.054), anesthesia duration (OR=1.002, 95% CI=0.999-1.004, p=0.173), intubated removal from operating room (OR=1.794, 95% CI=0.367-8.768, p=0.470), ICU hospitalization time (OR=0.980, 95% CI=0.933-1.029, p=0.412), tumor size (OR=1.044, 95% CI=0.968-1.125, p=0.265), GFAP positivity (OR=3.164, 95% CI=0.906-12.062, p=0.070), vimentin positivity (OR=3.160, 95% CI=0.835-11.968, p=0.090) and mortality (Table 2).

**Table 2. Logistic regression analysis for mortality predictors**

| Parameters                               | OR (95% CI)            | p-value      |
|--|------------------------|--------------|
| Age                                      | 0.811 (0.655-1.004)    | 0.054        |
| Weight                                   | 0.866 (0.771-0.972)    | <b>0.014</b> |
| Anesthesia time                          | 1.002 (0.999-1.004)    | 0.173        |
| Unable to extubate in the operating room | 1.794 (0.367-8.768)    | 0.470        |
| ICU hospitalization time                 | 0.980 (0.933-1.029)    | 0.412        |
| Tumor size                               | 1.044 (0.968-1.125)    | 0.265        |
| Blood transfusion                        | 13.143 (1.624-106.333) | <b>0.016</b> |
| Need for inotropes                       | 19.125 (2.378-153.835) | <b>0.006</b> |
| GFAP positivity                          | 3.164 (0.906-12.062)   | 0.070        |
| Vimentin positivity                      | 3.160 (0.835-11.968)   | 0.090        |
| Comorbid disease                         | 4.681 (1.080-20.297)   | <b>0.039</b> |

## DISCUSSION

In this study, we investigated the effect of perioperative anesthesia management on mortality. In addition, we investigated other predictors of mortality in our patient group. In our study, the number of patients who died during postoperative in-hospital follow-up was 10 and therefore multivariable logistic regression analyses could not be performed. According to the results of our study, we think that perioperative anesthesia management has no significant effect on mortality. According to our study, the predictors of mortality were; comorbid disease, low weight, blood transfusion, and need for inotropes.

Hemodynamic stability and cerebral perfusion optimization are the main goals of perioperative anesthesia management for patients undergoing pediatric intracranial tumor surgery. Children are more vulnerable to hypoxia and hypotension because of their elevated cerebral metabolic oxygen rate (6). While muscle relaxants and analgesics are chosen depending on the patients' pharmacological reaction, inhalational anesthetic, and balanced anesthesia procedures are typically recommended (7,8). Positioning and blood loss reduction strategies are not widely used. Although anesthetic management does not directly impact survival rates, our study revealed that it had no obvious effect on mortality, highlighting the significance of management in attaining the best possible surgical results.

Previous studies have shown significant relationships between young age groups and short-term mortality.

Children less than one year at diagnosis had a considerably greater short-term death rate (OR 6.7) than children between the ages of one and twenty-one, according to a study by Hankinson TC et al (3). A study by O'Kane et al. found a similar outcome, with a statistically significant 30-day mortality rate of 7.1% for children under the age of two and 2.0% for those between the ages of two and fourteen (2). In our study, mortality was investigated without separating patients according to age group, and no significant relationship was found between age and in-hospital mortality. We attribute this to the small size of our total patient population. The total number of patients who died in our population was only ten. We think that this rate may change with a higher number of patients who develop mortality.

Although there was no significant relationship between age and mortality in our study, we found that weight, which showed a significant positive correlation with age, was associated with mortality. According to a study by Liu et al., the risk of postoperative mortality and BMI have a nonlinear association (9). They demonstrated that in male patients (>18 years old) having a craniotomy for brain tumors, a low preoperative weight (BMI<18.5 kg/m<sup>2</sup>) increased the chance of postoperative mortality. Many previous studies have discussed the obesity paradox in cancer patients. In these studies, patients were classified according to BMI and it was shown that underweight and overweight patients were at risk for mortality (10-12). In our study, BMI was not used, but the body weight of the patients was taken into account. In the pediatric age group,

percentile curves are used instead of BMI. In our study, we associate the relationship between body weight and mortality with lower body weight in young children.

The effect of blood transfusion on mortality in pediatric intracranial tumor surgeries is a critical area of research, as transfusions can influence postoperative outcomes significantly. Studies indicate that while blood transfusions are often necessary, they are associated with increased risks of complications, including infections (13) and longer hospital stays (14), which can ultimately affect mortality rates. In our study, we determined the relationship between blood transfusion and overall mortality, although it was not an independent predictor.

Because the use of inotropic agents can vary greatly depending on the patient's health and the surgical context, the impact of these drugs on mortality in pediatric brain tumor procedures is complex and has not been adequately studied. Although inotropes are frequently used to treat hemodynamic instability, some studies have associated them with higher mortality rates (15-17). Although a relationship was observed between inotropic need and mortality in our study, we believe that this result should be investigated further, as only four patients in total required inotropic support.

Numerous studies demonstrating the influence of comorbid diseases on surgical outcomes have demonstrated the substantial correlation between comorbidity and mortality in pediatric patients having tumor surgery (18-20). Comorbidities can raise the risk of death and worsen treatment-related side effects. Similar to previous studies, comorbid diseases were associated with mortality in our study too.

### Limitations

As in many studies, our study has many limitations. The most notable limitation is the small number of patients, which prevents us from performing detailed statistical analysis. Since our study was designed retrospectively, bias cannot be eliminated. We do not have data on the cause of death in patients who died; all-cause deaths were investigated in the study. In addition, we did not have data on factors that could affect mortality, such as the surgical technique used and operator experience. These deficiencies may have affected the results of the study. Although the mortality rates in our study are similar to previous studies, they are not generalizable because they included patients who underwent surgery at a single center. Univariable logistic regression was used, but multivariable analysis was not performed. This is an important limitation of our larger study because univariable analysis does not account for interdependencies among variables. We do not have data on the patient's preoperative chemotherapy or radiotherapy treatments. Preoperative neoadjuvant treatments may have affected the results because they reduce the tumor diameter and decrease blood flow. Another limitation of our study is the lack of data on tumor histology types. Tumor histology

types may potentially alter the results regarding total mortality. In our study, we do not have data on the extent of surgical resection, which would be expected to alter outcomes related to mortality and hospitalization. This may have affected the results of the study.

### CONCLUSION

In our study, we found that perioperative anesthesia management was not associated with in-hospital mortality in patients undergoing craniotomy for pediatric intracranial tumors. In addition, we found that factors such as low body weight, comorbid diseases, need for intraoperative blood transfusion, and need for intraoperative inotropic support were associated with in-hospital mortality. Our study may guide clinicians in perioperative risk assessment in patients scheduled for craniotomy due to intracranial tumors.

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