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Case study

Scalp blocks for brain tumor craniotomies: A retrospective survival analysis of a propensity match cohort of patients

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A B S T R A C T

To test the association between the use of scalp blocks for malignant brain tumor craniotomy and survival. This is a retrospective study conducted in a tertiary academic center. Demographic, intraoperative and survival data from 808 adult patients with malignant brain tumors was included in the analysis. Patients were divided in those who received an Intraoperative use of scalp block or not. The progression free survival (PFS) and overall survival (OS) rates were compared in patients who had and had not scalp blocks. Kaplan-Meier method was used for time-to-event analysis including recurrence free survival and overall survival. Multivariate analyses before and after propensity score matching were conducted to test the association between different covariates including scalp blocks with PFS and OS. Five hundred and ninety (73%) of the patients had a scalp block. Before PSM, patients with a scalp block were more likely to have an ASA physical status of 3–4, recurrent tumors and receive adjuvant radiation. Patients with scalp block showed no significant reduction in intraoperative opioids. After adjusting for significant covariates, the administration of a scalp block was not associated with an increase in PFS (HR, 95%CI = 0.98, 0.8–1.2, p = 0.892) or OS (HR, 95%CI = 1.02, 0.82–1.26, p = 0.847) survival. This retrospective study suggests that the use of scalp blocks during brain tumor surgery is not associated with patients' longer survival.

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1. Introduction

Gliomas represent approximately 25% of the brain tumors in adults. Unfortunately, the survival of patients with malignant gliomas is poor [1]. Several factors including the world health organization (WHO) tumor grade, molecular features and modality of treatment play a role in the progression of gliomas and survival of patients [2]. For most patients, tumor resection followed by adjuvant chemotherapy, radiation or their combination represents the main treatment for low and high-grade gliomas [3,4].

The perioperative period is a critical moment for the survival of patients with cancer because excessive inflammation, a pro-angiogenesis state, and profound immunosuppression occur and can facilitate tumor growth and dissemination [5]. Therefore, there has been an increasing interest in finding perioperative interventions that can modulate those factors. Although it remains controversial, it has been speculated that regional analgesia might improve survival after cancer patients by reducing on opioid use, preserving the function of the innate immune system and decreasing inflammation and angiogenesis [6]. Some studies have shown an association between the use of regional analgesia and longer survival after breast, rectal and prostate cancer surgery [7–13]. On another hand, other groups of investigations demonstrated no beneficial effects on survival [7–13].

The scalp block is a commonly used regional analgesia technique for patients undergoing craniotomy [14]. Several studies and a *meta*-analysis indicate that scalp blocks effectively decrease opioid use and modulate the surgical stress response [15,16]. In a small cohort of patients, we have recently shown that the used of scalp blocks was associated with lower inflammatory scores, a reduction in peritumoral edema in postoperative imaging and longer progression free survival [17]. Therefore, we hypothesize

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that patients who have surgery for malignant gliomas and receive a scalp block are more likely to have a prolonged progression-free survival (PFS) and overall survival (OS) than those who do not have the block.

2. Material and methods

After obtaining institutional review board (IRB# PA12-0447), we conducted a retrospective study that included patients with malignant gliomas and underwent surgery between January 2000 and December 2016 at The University of Texas M.D. Anderson Cancer Center. We included patients who were 18 years or older, had surgery for primary or recurrent anaplastic astrocytoma, anaplastic oligodendroglioma or glioblastoma. Those patients who underwent craniotomy for benign tumors, awake craniotomies, infratentorial gliomas or had missing survival information were excluded from the analysis. The following variables were retrieved from our prospectively maintained registry database and included in the statistical analysis: patient age, gender, body mass index (BMI), American Society of Anesthesiology (ASA) physical status, tumor histology, scalp block use, dexamethasone administration, intraoperative opioid use, adjuvant temozolamide, adjuvant radiation and survival data.

2.1. Scalp blocks

The decision to perform a scalp block was based on surgeon's and anesthesiologist's preference or contraindications. All scalp block were performed by a group of experienced anesthesiologists who performed an average number of 135 blocks. Scalp blocks were done after induction of general anesthesia and before skull pinning. The most common solution of local anesthetic used in our patients it was a mixture of ropivacaine 0.5% with or without epinephrine 1:200,000. Typically, the volume of local anesthetic solution injected varied between 20 and 50 cc according to anesthesiologist clinical judgment. Fentanyl, sufentanil, remifentanil and hydromorphone were titrated during surgery according to clinical judgment. Intraoperative opioid consumption was calculated in fentanyl equivalents [9].

2.1.1. Statistical analysis

Summary statistics including mean, standard deviation, median, and range for continuous variables such as age and BMI, and frequency counts and percentages for categorical variables such as ASA are provided. The Chi-square test was used to evaluate the association between two categorical variables. Wilcoxon rank sum test or Kruskal-Wallis test was used to evaluate the difference in a continuous variable between/among patient groups.

2.1.1.1. Outcomes. PFS and OS were the primary endpoints of this study. PFS was defined as the time between the surgery date and the date of first evidence of progression (imaging) or the date of death (whichever occurred first). Patients were censored at the last known date if neither recurrence nor death occurred [18]. OS was defined as the time from the date of surgery to the date of death or last follow-up. Patients were censored at the last follow-up if death did not occur [18].

To adjust for selection bias, we conducted a propensity score matching analysis. The propensity score is the conditional probability of receiving a particular treatment (patients with scalp block) conditional on a set of observed covariates. We included the following prognostic covariates in the multicovariate logistic model to estimate the propensity scores: age at surgery, gender, BMI, ASA (1–2 vs. 3–4), tumor histology (non-glioblastoma vs. glioblastoma), and recurrent tumor (No vs. Yes). Among the 808 patients, the propensity score was calculated. The Greedy 5 → 1 digit match algorithm was used to match the baseline covariates, so that the two groups (with scalp block or without scalp block) would have similar propensity scores. Two hundred and seventeen patients with scalp block and with non-missing values for the covariates were matched with a 1:1 ratio to the patients without scalp block and with non-missing values for the covariates.

2.1.1.2. Survival analysis. Kaplan-Meier method was used for time-to-event analysis including progression free survival and overall survival. Median time to event in months with 95% confidence interval was calculated. The Log-rank test was used to evaluate the difference in time-to-event endpoints between patient groups. Univariate Cox proportional hazards models were fitted to evaluate the effects of continuous variables on time-to-event out comes. Multivariable Cox proportional hazards models were used for multivariate analysis to include important and significant covariates.

2.1.1.3. Sample size analysis. A Log-rank test of survival in two groups followed for fixed time and constant hazard ratio was used to estimate the sample size needed to demonstrate a significant difference in survival between patients without and with scalp block. With 208 patients in each treatment group and total number of events of 372, we would have 80% power to detect the difference using a 0.05 level two-sided log-rank test for equality of survival curves between a proportion p_1 at time 36 months of 0.062 (median PFS of 9 months) and a proportion p_2 at time 36 months of 0.125 (median PFS of 12 months). We assume a constant hazard ratio of 1.337 and no dropouts before time t.

A p value lower than 0.05 was considered statistically significant. Statistical software SAS 9.3 (SAS, Cary, NC) and S-Plus 8.2 (TIBCO Software Inc., Palo Alto, CA) were used for all the analyses.

3. Results

Among the 808 patients included in the study, there were more males (n = 502, 62%) than females (n = 306, 38%) and 84% (n = 684) had an ASA physical status of 3–4. The mean (standard deviation) age and BMI of the patients was 54.15 (13.88) years old and 28.23 (5.52).

The initial analysis demonstrated that 590 patients had a scalp block and 218 patients did not (Table 1). Before matching, a larger percentage of patients with a scalp block had ASA physical status of 1 or 2 (16.9% vs. 11%, p = 0.037), recurrent tumors (79.7% vs. 66.1%, p = 0.0001) and a non-glioblastoma histology (14.1% vs. 6%, p = 0.003) than those in the non-scalp block of patients. Although the duration of anesthesia was significantly longer in patients with a scalp block (445.46 ± 162.82 vs. 404.89 ± 152.11 min, p = 0.0001), their requirement of opioids (1427 ± 1073.58 fentanyl equivalents) was slightly but not statistically significant lower than those in the non-scalp block (1682 ± 2856.92 fentanyl equivalents, p = 0.517). A larger percentage of patients with a scalp block received adjuvant temozolamide (94.4% vs. 90.6%, p = 0.075) and radiation therapy (78% vs. 70%, p = 0.018) in comparison to those in the non-scalp group. As shown in Table 1, the overall tumor progression and mortality rates were slightly but not statistically higher in patients without scalp block (91.7% and 77.5%, respectively) than those with the block (87.5% and 73.9%, respectively).

To minimize the risk of bias, we conducted a propensity score matching. The standardized differences for all covariates were ≤ 7.54% in the post-matching cohort, suggesting substantial reduction of bias between the two groups. After matching the rates for tumor progression and death were slightly higher in patients with scalp block (Table 1).

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