Research Paper
Reconstructive Surgery

Risk factors for postoperative delirium in patients undergoing free flap reconstruction for oral cancer

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Abstract. The aim of this study was to investigate risk factors for postoperative delirium in patients undergoing free flap reconstruction for defects after oral cancer resection. This was a non-randomized, retrospective cohort study involving 102 patients who underwent oral cancer resection and free flap reconstruction. Data were collected from the medical records. Postoperative delirium occurred in 34 patients (33.3%), of whom 27 were male and seven were female. High preoperative total protein and albumin, diabetes mellitus, history of smoking, use of hypnotics or antipsychotics, time until getting out of bed after surgery, and postoperative insomnia were significantly related to delirium in the univariate analysis ($P < 0.05$). In a multiple logistic regression model, high preoperative albumin (odds ratio 4.45), postoperative insomnia (odds ratio 10.72), and history of smoking (odds ratio 2.91) were significant risk factors for delirium ($P < 0.05$). The analysis of laboratory data before and after surgery showed greater decreases in albumin, total protein, and haemoglobin after surgery in patients with postoperative delirium than in those without this condition. These results show that the perioperative maintenance of nutritional status and early postoperative management of the sleep cycle are important to prevent delirium after oral cancer resection and free flap reconstruction.

Postoperative delirium (POD) is a major risk factor for an extended hospital stay and higher costs, and is associated with increased mortality[1–4]. Free flap reconstruction is standard treatment after extended resection of oral cancer, and POD may also be a risk factor for flap loss and complications[5–7]. An incidence of POD of 15–26% after oral cancer surgery has been reported[8–11], and multivariate analysis has identified age, sex, pain control, use of minor tranquilizers, and excessive haemorrhage as risk factors for POD. However, there has been no study on the risk factors for POD after extended resection of oral cancer and free flap reconstruction. Therefore, the aim of this study was to investigate these risk factors in patients

undergoing this procedure, with the goal of using the results to reduce the occurrence of POD.

Patients and methods

This study was performed as a non-randomized, retrospective cohort study, and was thus granted exemption from institutional review board approval. Between October 2010 and March 2017, a total of 102 patients with oral cancer underwent resection surgery and free flap reconstruction at the Department of Oral and Maxillofacial Surgery and Plastic and Reconstructive Surgery, Gunma University Hospital. Patients were diagnosed with POD when symptoms corresponded to one of the criteria in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV)[12]: (1) acute change in mental status with a fluctuating course; (2) inattention; (3) disorganized thinking; and (4) altered level of consciousness. Delirium was classified as hypoactive, hyperactive, or mixed, and appropriate management was used[4,10].

Clinical data were collected for the preoperative, intraoperative, and postoperative periods. Preoperative data included age, sex, history of smoking (including current and ex-smoker), diabetes mellitus, alcohol consumption, use of hypnotics or antipsychotics, American Society of Anesthesiologists (ASA) classification of the fitness of patients before surgery (range 1–5), and preoperative laboratory data (total protein (TP), albumin (ALB), and haemoglobin (Hb)). Intraoperative data included operation time, blood loss, and intraoperative crystalloid infusion. Postoperative data included length of intensive care unit (ICU) stay, duration of artificial ventilation, sedation period, sedative used (fentanyl, propofol, dexmedetomidine), time until getting out of bed, postoperative insomnia (that occurred before the onset of POD, not after onset), arterial blood gas analysis (pH, PaO_2, $PaCO_2$, SaO_2, Na, K, Cl, Ca, Blood Sugar (BS), lactate), and postoperative laboratory data (TP, ALB, and Hb). Changes in laboratory data (TP, ALB, and Hb) from pre- to postoperative were also analyzed. Data for all of these parameters are listed in Tables 1–3.

All except four patients underwent a tracheotomy and all received intraoperative blood transfusions. No patient developed severe cerebrovascular disease, coronary heart disease, or renal dysfunction; this is because free flap reconstruction is not performed for patients with these disorders in the study department. All patients were managed postoperatively in the ICU. Blood tests were performed within 5 days before surgery and on the day after surgery. Laboratory data obtained before and after surgery were compared to examine changes in nutritional status and blood loss.

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY, USA). Categorical data were analyzed using Fisher's exact test. Comparisons of continuous quantitative variables were performed with the Mann–Whitney U-test or Student t-test, depending on whether or not the data were normally distributed. Variables associated with POD in the univariate analysis were included in a multiple logistic regression model. The forward selection method was used, and the multivariate odds ratio (OR) and 95% confidence interval (CI) were calculated for all variables. $P < 0.05$ was considered to be significant in all analyses.

Results

The 102 patients who underwent oral cancer resection and free flap reconstruction were aged 30 to 75 years, with a mean age of 59.6 ± 11.4 years. All patients were ≤75 years old, because this age is used as an operative indication for free flap reconstruction due to the risk of anastomotic thrombosis in older patients[13].

The site of the primary tumour was the tongue in 46 patients (45.1%), followed by the mandible in 32 (31.4%), buccal mucosa in nine (8.8%), and other sites in 15 (14.7%). The histological type was squamous cell carcinoma in 95 patients (93.1%). POD occurred in 34 patients (33.3%), including 27 male subjects and seven female subjects, and was hyperactive in 20 (58.8%), mixed in 12 (35.3%), and hypoactive in two (5.9%). Anastomotic thrombosis in the free flap procedure occurred in two cases (one each at the vein and artery site). The vein thrombosis was salvaged in an immediate reoperation, giving a final free flap success rate of 99.0%.

Risk factors for POD

In the univariate analysis, POD was significantly associated with high preoperative TP and ALB, diabetes mellitus, history of smoking, and use of hypnotics or antipsychotics (Table 1), and with postoperative time until getting out of bed and insomnia (Table 2).

Analysis of the laboratory data obtained before and after surgery showed that decreases in TP and Hb after surgery were significantly greater in patients with POD than in patients without POD (Table 3). In the multivariate analysis of these variables using a logistic regression model, high preoperative ALB, a history of smoking, and postoperative insomnia were identified as significant risk factors for POD. The adjusted OR and 95% CI of these variables are given in Table 4. The discriminant hit ratio was 80% in this analysis.

Discussion

The incidence of POD after oral cancer surgery was 33.3% in this study, which is

Table 1. Preoperative variables for patients who underwent oral cancer resection with free flap reconstruction, according to the presence of postoperative delirium (POD).

Variable	POD		*P*-value
	No (*n* = 68)	Yes (*n* = 34)	
Age (years)	59.2 ± 11.6	60.6 ± 11.0	
Sex			
Male	42 (61.8%)	27 (79.4%)	0.642[a]
Female	26 (38.2%)	7 (20.6%)	0.056[b]
Diabetes mellitus	9 (13.2%)	22 (64.7%)	0.011*[b]
History of smoking	34 (50.0%)	24 (70.6%)	0.038*[b]
Alcohol consumption	43 (63.2%)	19 (55.9%)	0.307[b]
Use of hypnotic or antipsychotic	2 (2.9%)	5 (14.7%)	0.040*[b]
ASA classification	1.9 ± 0.3	1.9 ± 0.4	0.730[a]
ALB (g/dl)	3.8 ± 0.5	4.1 ± 0.3	0.023*[a]
TP (g/dl)	6.6 ± 0.8	7.0 ± 0.5	0.038*[a]
Hb (g/dl)	13.0 ± 1.5	13.5 ± 1.3	0.102[c]

ALB, albumin; ASA, American Society of Anesthesiologists; Hb, haemoglobin; SD, standard deviation; TP, total protein. Data are expressed as the number of patients (%) or the mean ± SD.
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ for no POD vs. POD in the univariate analysis.
[a] Mann–Whitney U-test.
[b] Fisher's exact test.
[c] Student t-test.