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ARTICLE

Impact of skeletal muscle mass on postoperative delirium in patients undergoing free flap repair after oral cancer resection

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ABSTRACT

Postoperative delirium (POD) is a major risk factor for an extended hospital stay and higher costs, and is associated with increased mortality. The incidence of POD is high in free flap procedures, and POD may also be a risk factor for flap loss and complications. Sarcopenia is a condition characterized by skeletal muscle mass (SMM) depletion and a decrease in muscle power or physical activity. The aim of this study was to investigate risk factors for postoperative delirium (POD), including SMM, in 122 patients undergoing free flap repair after oral cancer resection. All patients underwent preoperative abdominal-lumbar CT or PET-CT. Cross-sectional areas (cm^2) of skeletal muscles at the third lumbar vertebra were measured on preoperative CT, normalized for height, and defined as the skeletal muscle index (SMI, cm^2/m^2). Risk factors for POD were investigated, including the value of SMI and taking the type of POD into consideration. POD occurred in 45 patients (36.9%), and was hyperactive in 28 (62.2%), mixed in 13 (28.9%), and hypoactive in 4 (8.9%). In multivariate analysis, high preoperative albumin ($p = 0.046$, adjusted odds ratio [OR] = 3.69) and postoperative insomnia ($p < 0.001$, OR = 6.79) were significant risk factors for POD. In a sub-analysis evaluating risk factors restricted to POD including the hypoactive type, lower SMI ($p = 0.035$, OR = 2.52 per 10-unit decrease) and postoperative insomnia ($p = 0.003$, OR = 6.37) were significant. We conclude that lower SMM increases the hypoactive and mixed types of POD. Increasing SMM by exercise and nutritional therapy preoperatively may prevent such POD in free flap repair for oral cancer.

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Sarcopenia; delirium; oral cancer; free flap; skeletal muscle mass

Introduction

Postoperative delirium (POD) is a major risk factor for an extended hospital stay and higher costs, and is associated with increased mortality [1–4]. The incidence of POD is 15–33% after oral cancer surgery, and multivariate analysis identified age, gender, pain control, minor tranquilizers, smoking, excessive hemorrhage and perioperative change of albumin as possible risk factors for POD [5–8]. Free flap reconstruction is now standard treatment after extended resection of oral cancer. However, the incidence of POD is high in free flap procedures because of the long and invasive surgery [5]. Furthermore, POD may also be a risk factor for flap loss and complications [9–11].

Sarcopenia is a condition characterized by skeletal muscle mass (SMM) depletion and a decrease in muscle power or physical activity [12–15]. Many recent reports have shown that sarcopenia in patients with a variety of malignancies, including head and neck cancer, leads to severe chemotherapy toxicity and a poorer survival rate [16–18]. Furthermore, a previous report showed that low SMM, which is strongly associated with sarcopenia, was a risk factor for POD in elderly patients undergoing colorectal cancer surgery [19].

Type of POD possibly differ between digestive cancer and head and neck cancers. Hypoactive type POD, where main symptom are apathy, impassiveness, somnolence and so on, is common after digestive cancer surgery, whereas hyperactive POD, where main symptom are agitation, hallucination, insomnia and so on, occurs more after head and neck surgery [4–7]. However, the relationship between SMM and POD in head and neck cancer surgery has not been examined. In aging society, cancer patients with sarcopenia are increasing. Thus, the aim of this study was to investigate risk factors, including SMM, in patients undergoing free flap repair after oral cancer resection, with the goal of using the results to reduce the occurrence of POD.

Patients and methods

The study was performed as a nonrandomized, retrospective cohort study, and thus, was granted exemption from institutional review board approval (approval No. 2017-154). Between February 2009 and February 2018, a total of 122 patients with oral cancer underwent resection surgery and free flap reconstruction, and were also examined by preoperative whole-body positron emission tomography (PET)-computed tomography (CT) or abdominal-lumbar area CT, 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, 4th edition (DSM-IV) [20]: 1) acute change in mental status with a fluctuating course; 2) inattention; 3) disorganized thinking; and 4) altered level of consciousness.

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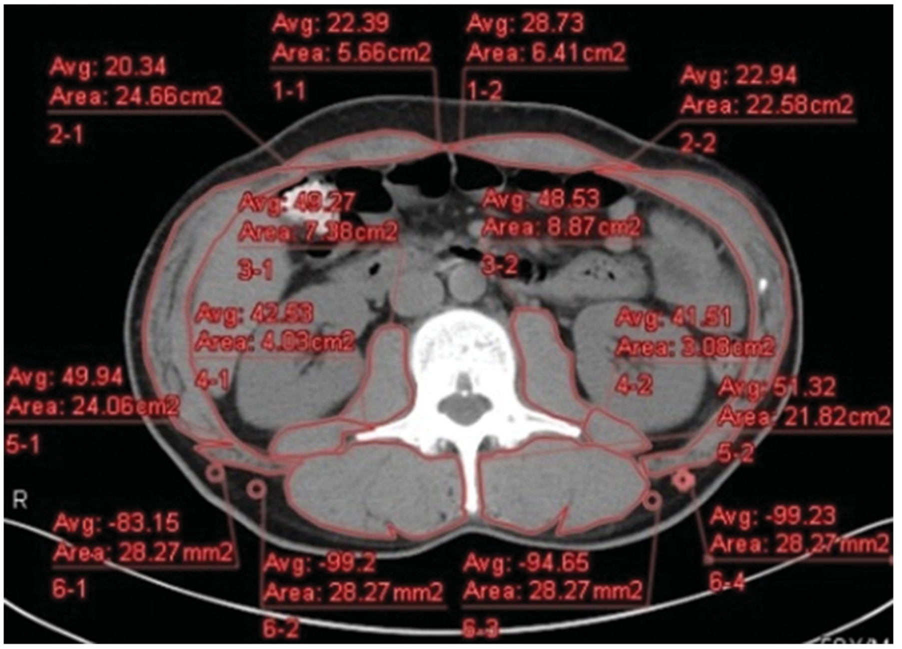

Figure 1. Evaluation of skeletal muscle in a transverse CT image at the third lumbar vertebra (L3).

Delirium was classified as hypoactive, hyperactive or mixed, and appropriate management was used [4,5].

Clinical data were collected for age, gender, history of smoking (current and ex-smoker), diabetes mellitus, alcohol consumption, use of hypnotics or antipsychotics, American Society of Anesthesiologists (ASA) classification of fitness before surgery, preoperative laboratory data (total protein [TP], albumin [ALB], hemoglobin [Hb] and hematocrit [Hct]) (preoperative factors); operation time, blood loss and intraoperative crystalloid infusion (intraoperative factors); and length of intensive care unit (ICU) stay, artificial ventilation period, sedation period, sedative used (fentanyl, propofol, dexmedetomidine), time until getting out of bed, postoperative insomnia (before onset of POD, not after onset), and postoperative laboratory data (TP, ALB, Hb and Hct) (postoperative factors). Changes in laboratory data (TP, ALB, Hb and Hct) from pre- to postoperatively were also analyzed.

A transverse CT image at the third lumbar vertebra (L3) in the inferior direction was assessed in each scan. SMM was quantified, including the psoas, erector spinae, quadratus lumborum, latissimus dorsi, transversus abdominis, external and internal oblique abdominal muscle, and rectus abdominis muscle by manual outline on CT images. Ziostation2 software (Ziosoft Inc., Tokyo) was used in SMM measurement (Figure 1) [5]. The obtained areas were normalized for height (cm^2/m^2), and the resulting value is referred to as the skeletal muscle index (SMI) [13,14,18].

In a study performed by the Asian Working Group for Sarcopenia (AWGS), a SMM cutoff based on a CT value was not proposed [14]. Cutoff values from Western studies have been used in some Japanese studies, but these may differ from the correct values in Asian subjects due to differences in weight, lifestyle, and ethnicity. Given the difficulty of establishing a cutoff, we treated SMI as a continuous value.

Variables associated with POD were identified using SPSS v.25 (SPSS, Chicago, IL, USA). Categorical data were analyzed by Fisher exact test, while continuous quantitative variables were compared by Mann-Whitney U-test or Student t-test, depending on the normality of the data distribution. Variables with a significant relationship with POD in univariate analysis were included in a multiple logistic regression model to identify factors with an independent association with POD. Multivariate odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. $p < 0.05$ was considered to be significant in all analyses. In a sub-analysis evaluating risk factors restricted to POD including hypoactive type (that is to say, hypoactive type and mixed type), factors related to POD were similarly evaluated.

Results

Background factors

A total of 122 patients (82 males and 40 females) with a mean age of 60.3 ± 11.2 years were included in the study. The site of the primary tumor was the tongue in 57 patients (46.7%), followed by the mandible in 39 (32.0%), oral floor in 11 (9.0%), and other sites in 15 (12.3%). The clinical stages (Union for International Cancer Control) were I in 1, II in 42, III in 23, and IV in 56 cases. The histological type was squamous cell carcinoma in 114 patients (93.4%).

Preoperative fortified diets or oral nutritional supplements were used for 6 patients with pain and obstruction because of the tumor, resulting in less intraoral intake. Preoperative enteral tube feeding using PEG or nasogastric tubes and parenteral nutrition were not used in any cases.

Reconstructive procedures used free rectus abdominis myocutaneous (RAM) flaps ($n = 61$), free radial forearm (RF) flaps ($n = 55$), free latissimus dorsi (LD) flaps ($n = 3$), and vascularized free fibula flaps ($n = 3$); and 116 patients (95.0%) underwent (modified) radical neck resection or supraomohyoid neck dissection. All except 11 patients underwent tracheotomy and all except one required intraoperative blood transfusions. Two patients received preoperative radiation therapy. Anastomosis thrombosis in the free flap procedure occurred in 2 cases (one at the vein site and the other at both artery and vein site). Vein thrombosis was salvaged in an immediate reoperation, giving a final free flap success rate of 99.2%. All patients were admitted to the ICU postoperatively.

POD occurred in 45 patients (36.9%), including 34 males and 11 females, and was hyperactive in 28 (62.2%), mixed in 13 (28.9%), and hypoactive in 4 (8.9%). The mean SMIs ± SD were

Table 1. Preoperative variables of patients who underwent oral cancer resection with free flap reconstruction and did and did not have postoperative delirium (POD).

Variable	non-POD ($n = 77$)	POD ($n = 45$)	p Value
Age (years)	59.6 ± 12.0	60.5 ± 11.3	0.222
Male	48 (62.3%)	34 (75.6%)	
Female	29 (37.7%)	11 (24.4%)	0.096
BMI (kg/m^2)	21.4 ± 2.7	22.1 ± 3.7	0.689
SMI (cm^2/m^2)	39.7 ± 8.5	39.6 ± 8.9	0.273
Diabetes mellitus	11 (14.3%)	15 (33.3%)	0.013*
History of smoking	38 (49.4%)	32 (71.1%)	0.018*
Alcohol consumption	50 (65.0%)	29 (64.4%)	0.554
Use of hypnotic or antipsychotic	2 (2.6%)	5 (11.1%)	0.066
ASA classification	1.9 ± 0.4	1.9 ± 0.4	0.984
ALB (g/dl)	3.9 ± 0.5	4.1 ± 0.3	0.032*
TP (g/dl)	6.7 ± 0.7	7.0 ± 0.5	0.229
Hb (g/dl)	12.9 ± 1.6	13.4 ± 1.3	0.511
Hct (%)	38.0 ± 4.4	38.9 ± 4.1	0.642

Data are expressed as the number of patients (%) or the mean ± SD.
Categorical data were analyzed by Fisher exact test. Comparisons of continuous quantitative variables were performed by Mann-Whitney U-test or Student t-test, depending on whether the data were normally distributed.
*$p < 0.05$ for non-POD vs. POD in univariate analysis.

39.9 ± 8.6 (range: 15.7 to 63.1) cm^2/m^2 in all patients, 42.8 ± 8.2 (15.7 to 63.1) cm^2/m^2 in males, and 33.8 ± 5.9 (21.8 to 47.3) cm^2/m^2 in females.

The reconstruction methods in the POD group used RF flaps in 16 cases (35.6%), RAM flaps in 26 cases (57.8%), vascularized free fibula flaps in 2 cases (4.4%), and a LD flap in 1 case (2.2%). Those in the non-POD group used RF flaps in 39 cases (50.6%), RAM flaps in 35 (45.5%), LD flaps in 2 cases (2.4%), and a vascularized free fibula flap in 1 case (1.2%). In the POD group, use of RAM flaps was slightly higher and use of RF flaps was slightly lower than in the non-POD group, but neither difference was significant.

Risk factors for POD

In univariate analysis, POD was significantly associated with diabetes mellitus, smoking history, high preoperative albumin (Table 1), postoperative insomnia (Table 2), and a decrease in TP after surgery (Table 3) in univariate analysis. In a multiple logistic regression model including these factors, high preoperative ALB and postoperative insomnia were identified as significant independent risk factors for POD (Table 4). Adjusted ORs and 95% CIs for these variables are given in Table 4. The discriminant hit ratio was 79.0% in this analysis.

In a sub-analysis, risk factors of POD including hypoactive type were similarly evaluated. In univariate analysis, hypoactive and mixed type POD was significantly associated with a lower SMI, use of hypnotics or antipsychotics, and insomnia (Tables 5–7). In multivariate analysis of these variables, a lower SMI and postoperative insomnia were identified as significant independent risk factors (Table 8).

Discussion

Sarcopenia is characterized by muscle mass depletion and a decrease in muscle power or physical activity [12–15]. Sarcopenia in patients with malignancies including hepatic, lung, bladder, colorectal and breast cancer results in more postoperative complications, severe chemotherapy toxicity, and a lower survival rate, compared to those without sarcopenia [15,18]. A few recent reports have shown that head and neck cancer patients with sarcopenia also have severe chemotherapy toxicity and poorer survival [16,17]. However, the impact of sarcopenia on POD after resection of head and neck cancer has not been examined. To our knowledge, this is the first study to evaluate the relationship of SMM, which is the main pathology of sarcopenia, with POD in head and neck cancer.

We evaluated SMM using the most common method of L3 level CT. However, some recent studies have used CT at the third cervical (C3) vertebra level for measuring SMM [21], which is particularly useful in patients with head and neck cancer. We also measured C3 level CT in the current same population. A further analysis showed that SMI at C3 was related to that at L3 (Pearson correlation coefficient: 0.715, $p < 0.001$). Thus, C3 level CT is also useful for evaluating SMM in patients with head and neck disease or trauma.

In this study, lower SMM was not associated with POD after oral cancer resection with free flap repair. However, lower SMM was significantly associated with POD including symptoms of the hypoactive type, as also shown by Mosk *et al.* in colorectal cancer surgery [19]. The article by Mosk et al. [19] is the only previous assessment of the relevance of low SMM to POD. Thus, lower SMM is possible to associate with hypoactive type POD, although it might not increase hyperactive type POD. This suggests that the influence of SMM might differ among the types of POD, and that increasing SMM by active intervention such as exercise and nutritional therapy from early before surgery may prevent postoperative hypoactive or mixed type POD although further study is needed.

Hypoactive POD is common after digestive cancer surgery, whereas hyperactive POD occurs more after head and neck surgery [4–7]. The reason for this difference is unclear. In patients with POD after oral cancer surgery in the current study, the rate of hyperactive POD was 62.2%, which is much higher than the rates after thoracic or digestive cancer surgery. Younger patients are more likely to have hyperactive delirium, whereas patients with hypoactive delirium more frequently have preoperative anemia [4,22]. The current study showed that low muscle mass volume was associated with hypoactive or mixed type POD, but not with all POD, including the hyperactive type. These findings seem to imply that relatively physically durable patients tend to have hyperactive type POD, whereas relatively frail patients tend to have hypoactive type. This is just speculation, but head and neck surgery may be less invasive or there were more physically durable patients preoperatively in our study compared to those before digestive surgery such as cardiac or hepatic surgery, and patients after head and neck surgery may also be relatively stronger. Thus, hyperactive type POD might occur more in head and neck surgery. A further study is needed to examine these suggestions.

Many recent reports have shown that sarcopenia leads to a poorer survival rate in patients with a variety of malignancies, including head and neck cancer [16–18]. The Kaplan–Meier method was used to compare mortality in the current study between patients with and without low muscle mass volume (using a cut off value from our previous Japanese population study: male <36.02, female <31.76) [23]. Patients with low skeletal muscle mass tended to have higher all-cause mortality, but the difference was not significant ($p = 0.172$ by log-rank test). Of all investigated parameters, preoperative low hemoglobin (<13 g/dL for males, <12 g/dL for females), hypoalbuminemia (serum albumin <4.0 mg/dL) and a poor performance status (ASA-PS >2) were associated with significantly higher mortality ($p = 0.002$, $p = 0.001$, $p = 0.006$ by log-rank test, respectively).

Table 2. Intraoperative and postoperative variables of patients who underwent oral cancer resection with free flap reconstruction and did and did not have postoperative delirium (POD).

Variable	non-POD ($n = 77$)	POD ($n = 45$)	p Value
Blood loss (g)[a]	1114.0 ± 1145.2	1206.9 ± 642.6	0.096
Operation time (min)[a]	874.9 ± 129.4	855.0 ± 205.8	0.592
Crystalloid infusion (ml)[a]	6919.5 ± 2219.4	6635.8 ± 1861.2	0.306
ICU stay (days)	4.3 ± 1.3	4.5 ± 1.2	0.878
Period with sedation (days)	2.3 ± 1.0	2.7 ± 0.7	0.474
Sedation with propofol	75 (97.4%)	45 (100.0%)	0.396
Sedation with fentanyl	68 (88.3%)	42 (93.3%)	0.442
Sedation with dexmedetomidine	36 (46.8%)	23 (51.1%)	0.391
Period with artificial ventilator (days)	2.3 ± 1.0	2.2 ± 0.9	0.951
Time until getting out of bed (days)	4.0 ± 1.4	4.8 ± 1.4	0.070
Insomnia	21(27.3%)	33 (73.3%)	<0.0001***
ALB (g/dl)	2.6 ± 0.4	2.6 ± 0.4	0.534
TP (g/dl)	4.6 ± 0.7	4.4 ± 0.7	0.055
Hb (g/dl)	10.7 ± 1.3	10.5 ± 1.0	0.457
Hct (%)	30.9 ± 3.6	30.0 ± 3.0	0.159

Data are expressed as the number of patients (%) or the mean ± SD.
[a]Intraoperative variable. All other data are postoperative.
Categorical data were analyzed by Fisher exact test. Comparisons of continuous quantitative variables were performed by Mann-Whitney U-test or Student t-test, depending on whether the data were normally distributed.
***$p < 0.001$ for non-POD vs. POD in univariate analysis.

Table 3. Decreases in laboratory data from before to after surgery in patients with and without postoperative delirium (POD).

Variable	non-POD	POD	p Value
ALB (g/dl)	1.2 ± 0.7	1.5 ± 0.5	0.088
TP (g/dl)	2.1 ± 1.0	2.7 ± 0.7	0.006**
Hb (g/dl)	2.2 ± 1.7	2.9 ± 1.5	0.152
Hct (%)	6.9 ± 4.5	8.9 ± 3.8	0.114

Data are expressed as the mean ± SD.
**$p < 0.01$ for non-POD vs. POD by Mann-Whitney U-test.

Table 4. Significant risk factors for postoperative delirium identified in multiple logistic regression analysis.

		95% CI		
Variable	Odds ratio	Lower	Upper	p Value
Preoperative high albumin	4.94	1.01	24.11	0.048*
Postoperative insomnia	7.38	2.50	21.76	<0.0001***
Smoking	2.6	0.89	7.50	0.081
Diabetes	1.95	0.61	6.3	0.262

*$p < 0.05$ ***$p < 0.001$.

Postoperative insomnia was also found to be a risk factor for POD, consistent with previous studies [5,24]. Insomnia could be both a cause and effect of POD. However, our definition of insomnia was limited to a postoperative event before onset of POD [5], and not after onset; therefore, such an event could only be a cause of POD. Insomnia that occurred with or after symptoms of POD, such as hyperactive behaviour, hallucinations, slowing or lack of movement, or unresponsiveness were excluded from 'insomnia' as a possible risk factor, but 'insomnia', which we defined as occurring before onset of POD, cannot be completely excluded as a possible early symptom of POD (that is, as an effect of POD). Generally, these findings suggest that prevention of insomnia may be useful for prevention of POD. The association of use of a minor tranquilizer with delirium is unclear: some studies show that this medication increases delirium [25] and others suggest that it decreases delirium [8,26]. Our results suggest that early management of the sleep cycle using a minor tranquilizer and environmental improvement may prevent hyperactive or hypoactive POD after free flap repair for oral cancer resection.

Low preoperative serum ALB has been identified as a risk factor for delirium, which is generally caused by poor nutrition and metabolic disturbance [27]. However, conversely, in our patients we found that increased preoperative ALB was a significant risk factor for POD, as also shown in our previous study [9]. Pre- and postoperative blood tests showed that decreases in ALB after surgery tended to be greater in patients with POD compared to non-POD cases, although without a significant difference ($p = 0.088$) (Table 3). Therefore, patients with elevated preoperative ALB may develop POD because of a larger perioperative decrease in nutrition. High preoperative ALB is beneficial for wound healing and reducing complications, but a large perioperative decrease in ALB can cause POD. This suggests that maintenance of the ALB level might be important to prevent POD, especially the hyperactive type [11]. The European Working Group on Sarcopenia in Older People (EWGSOP) and the AWGS recommend diagnosis of sarcopenia based on muscle weakness or reduced physical ability, in addition to reduced muscle mass [13,14]. There is no established method for SMM measurement, and criteria vary among reports. In this study, SMM at L3 was evaluated on CT. Grip strength is a useful index of muscle weakness, and walking speed is similarly an index of reduced physical function. However, in this study, we could not evaluate muscle weakness and physical function because of the retrospective design. Thus, diagnosis of sarcopenia using the criteria of the EWGSOP and AWGS was not possible, and age was not restricted to >65 years, which is a cutoff in the EWGSOP and AWGS criteria. However, all ages are included in the definition of sarcopenia of the Working Group on Sarcopenia of the Japan Society of Hepatology, and SMM loss may have an impact on hypoactive or mixed type POD, regardless of age. Strictly speaking, we cannot conclude that sarcopenia is a risk factor for hypoactive and mixed type POD after oral cancer surgery. However, a reduction of muscle mass, which is the main pathology of sarcopenia, was found to be such a risk factor.

Several other limitations of the study should also be noted, including the retrospective design and the relatively small number of patients, which may have led to selection bias and a lack of statistical power. The small sample of patients with purely hypoactive or hyperactive delirium did not allow for statistical comparison of this motor subtype of delirium with the other groups. Also, we could not evaluate differences in severity of POD between groups using a tool such as the Delirium Rating Scale (DRS) due to the retrospective study design.

Table 5. Preoperative variables of patients who underwent oral cancer resection with free flap reconstruction and did and did not have hypoactive or mixed type postoperative delirium (POD) (sub-analysis excluding hyperactive subtype).

Variable	non-POD ($n = 77$)	Hypoactive or mixed POD ($n = 17$)	p Value
Age (years)	59.5 ± 12.1	59.1 ± 12.8	0.698
Male	48 (62.3%)	10 (58.8%)	
Female	29 (37.7%)	7 (41.2%)	0.497
BMI (kg/m^2)	21.4 ± 2.7	20.9 ± 3.5	0.212
SMI (cm^2/m^2)	39.6 ± 8.5	36.9 ± 6.4	0.019*
Diabetes mellitus	11 (14.3%)	3 (17.6%)	0.486
History of smoking	38 (49.4%)	10 (58.8%)	0.349
Alcohol consumption	50 (64.9%)	11 (64.7%)	0.597
Use of hypnotic or antipsychotic	2 (2.6%)	3 (17.6%)	0.041*
ASA classification	1.9 ± 0.4	1.8 ± 0.6	0.196
ALB (g/dl)	3.9 ± 0.5	4.1 ± 0.3	0.248
TP (g/dl)	6.7 ± 0.7	6.9 ± 0.4	0.380
Hb (g/dl)	12.9 ± 1.6	12.9 ± 1.1	0.363
Hct	38.0 ± 4.4	37.8 ± 3.3	0.408

Data are expressed as the number of patients (%) or the mean ± SD.
Categorical data were analyzed by Fisher exact test. Comparisons of continuous quantitative variables were performed by Mann-Whitney U-test or Student t-test, depending on whether the data were normally distributed.
*$p < 0.05$for non-POD vs. hypoactive or mixed POD in univariate analysis.

Table 6. Intraoperative and postoperative variables of patients who underwent oral cancer resection with free flap reconstruction and did and did not have hypoactive or mixed type postoperative delirium (POD) (sub-analysis excluding hyperactive subtype).

Variable	non-POD ($n = 77$)	Hypoactive or mixed POD ($n = 17$)	p Value
Blood loss (g)[a]	1121.9 ± 1153.0	909.3 ± 523.9	0.514
Operation time (min)[a]	874.2 ± 130.3	787.3 ± 175.4	0.350
Crystalloid infusion (ml)[a]	6916.6 ± 2237.7	6090.8 ± 1286.1	0.208
ICU stay (days)	4.3 ± 1.3	4.5 ± 1.1	0.931
Period with sedation (days)	2.3 ± 1.0	2.4 ± 1.0	0.889
Sedation with propofol	75 (97.4%)	17 (100.0%)	0.669
Sedation with fentanyl	68 (88.3%)	16 (94.1%)	0.554
Sedation with Dexmedetomidine	36 (46.8%)	9 (52.9%)	0.422
Period with artificial ventilator (days)	2.3 ± 1.0	2.3 ± 1.0	0.388
Time until getting out of bed (days)	4.0 ± 1.3	4.3 ± 1.1	0.706
Insomnia	21(27.3%)	12 (70.6%)	0.001**
ALB (g/dl)	2.6 ± 0.5	2.6 ± 0.4	0.248
TP (g/dl)	4.6 ± 0.7	4.5 ± 0.9	0.380
Hb (g/dl)	10.7 ± 1.2	10.3 ± 0.9	0.363
Hct	31.0 ± 3.6	29.4 ± 2.9	0.408
ALB (g/dl)	2.6 ± 0.4	2.6 ± 0.4	0.739
TP (g/dl)	4.5 ± 0.7	4.5 ± 0.8	0.720
Hb (g/dl)	10.7 ± 1.2	10.4 ± 0.9	0.277
Hct (%)	30.7 ± 3.5	29.8 ± 2.7	0.336

Data are expressed as the number of patients (%) or the mean ± SD.
[a]Intraoperative variable. All other data are postoperative. Categorical data were analyzed by Fisher exact test. Comparisons of continuous quantitative variables were performed by Mann-Whitney *U*-test or Student *t*-test, depending on whether the data were normally distributed.
**$p < 0.01$for non-POD vs. hypoactive or mixed POD in univariate analysis.

Table 7. Decreases in laboratory data from before to after surgery in patients with and without postoperative delirium (POD).

Variable	non-POD	POD	p Value
ALB (g/dl)	1.2 ± 0.7	1.5 ± 0.5	0.379
TP (g/dl)	2.1 ± 1.0	2.5 ± 0.9	0.238
Hb (g/dl)	2.2 ± 1.7	2.6 ± 1.1	0.788
Hct (%)	7.0 ± 4.5	8.4 ± 2.7	0.705

Data are expressed as the mean ± SD.

Table 8. Significant risk factors for hypoactive or mixed type postoperative delirium identified in multiple logistic regression analysis.

		95% CI		
Variable	Odds ratio	Lower	Upper	p Value
Lower SMI (cm^2/m^2)	2.52[a]	1.01	1.19	0.035*
Postoperative insomnia	5.53	1.79	20.23	0.004**
Use of hypnotics or antipsychotics	3.05	0.40	23.6	0.284

[a]odds ratio per 10 cm^2/m^2 decrease.
*$p < 0.05$, **$p < 0.01$.

In conclusion, the association between reduction of muscle mass, the main cause of sarcopenia, and POD was investigated, along with other possible risk factors. In multivariate logistic regression analysis, decrease of SMI was not a significant risk factor for POD in all subjects, but was a significant independent risk factor for hypoactive and mixed type POD. This finding suggests that increasing SMM by active intervention, such as exercise and nutritional therapy, from early before surgery may prevent hypoactive or mixed POD.

Disclosure statement

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