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Does postoperative non-sedation improve outcomes for patients after head and neck cancer reconstruction?

A STROBE compliant study

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Abstract

Whether a strategy of postoperative non-sedation produces better outcomes compared with sedation in patients after head and neck reconstruction remains controversial. Therefore, we retrospectively investigated outcomes in 150 of these patients in our institution.

Patients with head and neck cancer that received free anterolateral thigh flap were studied retrospectively, and were categorized in terms of their postoperative care into "sedation" and "non-sedation" groups. The related parameters of each patient were collected for analysis.

Overall, 150 patients were included (sedation protocol (N = 56) and non-sedation strategy (N = 94)). No significant differences were observed between groups in patient demographics or postoperative outcomes. Significantly shorter durations of mean and median intensive care unit (ICU) length of stay, mechanical ventilation, hospitalization, and operative time were observed in the non-sedation group than in the sedation group. Among all patients, the sedation and flap reopen were the common variables related to prolonged ICU stay, mechanical ventilator duration, and hospitalization.

The current study suggested the strategy of postoperative non-sedation is associated with a significant decrease in the duration of mechanical ventilation, ICU length of stay, hospitalization. Regardless of hospital stay, there were no differences in postoperative outcome between 2 groups.

Abbreviations: ALT = anterolateral thigh, ASA score = anesthesiologists score, BMI = body mass index, CT = chemotherapy, ICU = intensive care unit, RT = radiotherapy, TNM = tumor node metastasis.

Keywords: anterolateral thigh flap, head and neck reconstruction, hospitalization, non-sedation, sedation

1. Introduction

The use of microsurgical free tissue transfer is a well-established method to reconstruct the defects after head and neck cancer surgery but the survival of the free flap is affected by factors such as blood pressure and patient agitation. A postoperative sedation strategy may prevent disruption or kinking of flap vessels. A recent case series of patients after free ileocolon flaps for hypopharygeal defects managed with postoperative sedation using midazolam and dexmedetomidine had better outcomes.[1] Most patients with head and neck cancer have a higher incidence of alcohol abuse, and a sedation strategy may decrease the risk of alcohol withdraw during the postoperative period.[2]

Studies have suggested that early postoperative extubation decreased intensive care unit (ICU) stay, medical complications, and treatment for agitation and alcohol withdrawal syndrome.[3,4] Delayed mobilization was a risk factor for pneumonia in patients

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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undergoing oral cancer resection and free flap reconstruction.[5] So an early extubation policy may be beneficial for patients after head and neck reconstruction without increasing risks.

There have been few studies comparing postoperative non-sedation strategies so we retrospectively studied outcomes in patients after head and neck cancer reconstruction in our institution managed with and without postoperative sedation.

2. Materials and methods

This was a retrospective review at a single medical center between January 2017 and December 2018. Patients with head and neck cancer who received free anterolateral thigh (ALT) flap were included, and were categorized in terms of their postoperative care into sedation and non-sedation groups. The selection of sedation patients is mainly based on patient characteristics and intraoperative findings, such as: firstly, thrombosis formation during vessel anastomosis and re-anastomosis more than 3 times. Secondly, moderate calcification of anatomized vessels. Thirdly, intractable preoperative and postoperative hypertensive status. Fourthly, chronic sedative use. The operations were performed by boarded plastic surgeons (PK Shih, HC Chen, TC Huang). All patients received air-protective tracheostomy before operation. All the patients signed informed consent. This study was approved by the ethical committee of China Medical University.

In the non-sedation group, patients were transferred to the ICU for intensive monitoring of the free flap. Postoperative systolic blood pressure was kept in the range 120 to 150 mm Hg with the using of Nicardipine (Perdipine) bolus injection and postoperative pain was controlled by patient-controlled anesthesia. On the first day after surgery, the tracheostomy was connected to a T-piece tube when the patient was weaned from ventilator having regained clear consciousness. The flap perfusion was checked by a nurse every hour with a hand-held Doppler device. Later, once stable, patients were transferred to a general ward. We used Haloperidol (Haldol) (5 mg intramuscular injection) when there was delirium or extreme agitation during the ICU stay.

In the sedation group, continuous infusions of midazolam (Midazo, 0.25–0.5 $mg\,kg^{-1}\,h^{-1}$) and the muscle relaxant cis-atracurium (Nimbex, 1–2 $mcg\,kg^{-1}\,min^{-1}$) were used directly when the patient was transferred to ICU. The sedation lasted for 3 days and progressively diminished on the fourth postoperative day. After patients regained consciousness, the tracheostomy was connected to a T-piece tube then the patients were transferred once stable the next day to a general ward.

2.1. Data collected

The following data were extracted from the case records retrospectively: age, gender, American Society of Anesthesiologists (ASA) score, body mass index (BMI), malignancy location, tumor node metastasis (TNM) stage of malignancy, operative time, flap size, previous treatments (including operation, radiotherapy (RT), chemotherapy (CT)), smoking, betel nut consumption, alcohol consumption, comorbidities, ICU length of stay, duration of mechanical ventilation, duration of hospitalization, free flap re-operation and salvage, systemic and flap complications, and the need for RT or CT at 30 days or 1 year after surgery.

Sizes of harvested flaps varied and were graded as 0 (<100 cm^2), 1 (100–199 cm^2), 2 (200–299 cm^2), and 3 (>300 cm^2).

The comorbidities included cardiovascular disease (such as arrhythmia, hypertension, acute myocardial infarction), endocrine disease (gout, diabetes mellitus, goiter, hypothyroidism), hepatic disease (hepatitis B/C, liver cirrhosis), psychological disorders, nephrotic disease (nephritis, renal stones, chronic kidney disease), respiratory disease (asthma, chronic obstructive pulmonary disease, tuberculosis infection), orthopedic disease (knee osteoarthritis, spine herniation of inter-vertebral disc), neurological disease (stroke, Parkinsonism, chronic subdural hematoma), anemia, malignancy (colon cancer, esophageal cancer, lung cancer, hepatocellular carcinoma, nasopharyngeal carcinoma).

The circumstances for flap re-operation included for artery occlusion, vein occlusion, and bleeding. Life-threatening systemic complications were cardiovascular failure (pump failure needing supportive apparatus), respiratory failure (needing re-intubation), or sepsis.

2.2. Statistical analysis

We presented the baseline characteristic factors by number (%), mean (SD), and median (IQR). Chi-square test and fisher exact test were applied to compare the difference between sedation and non-sedation group for categorical variable; Student's *t* test and Mann–Whitney *U* test were used to compare the mean and median difference between 2 groups for continuous variable, respectively. In this study, stepwise linear regression analysis was performed using ICU stay, mechanical ventilator duration, and hospitalization as dependent variables and the baseline characteristics were set as independent variables. Significance levels for entry and to remain were set at 0.05 to extract potential variables. All statistical analyses were performed using SAS statistical software, version 9.4 (SAS Institute Inc., Cary, NC) and two-tailed $P<.05$ was considered statistically significant.

3. Results

Among 150 patients after head and neck cancer reconstruction, 56 patients with sedation strategy. The mean age of sedation and non-sedation group was 59.1 and 58.1, respectively and male were in the majority (92%). The distribution of age, gender, ASA level, BMI, malignancy position, TNM stage, operative time, flap size, previous treatments (OP, RT, CT), smoking, betel nut consumption, alcohol consumption, and comorbidities are summarized in Table 1. There were no significant differences between groups except for the operation time which was shorter in the non-sedation group (12.3 hours vs 14.2 hours; $P<.001$).

The duration of ICU stay, mechanical ventilation duration, and hospitalization are summarized in Table 2. There were significantly shorter durations in the non-sedation group of mean ICU length of stay (2.5 days vs 6.3 days, $P<.001$), mean duration of mechanical ventilation (1.3 days vs 5.1 days, $P<.001$), and mean hospitalization (15.8 days vs 19.0 days, $P=.04$) and also showed shorter duration in non-sedation group when calculated median ICU stay (2.0 days vs 5.0 days, $P<.001$), median duration of mechanical ventilation (1.0 days vs 4.0 days, $P<.001$), and median hospitalization (15.0 days vs 17.0 days, $P<.001$).

The flap re-operation and salvage, flap complications (including dehiscence, partial loss, and infection), systemic complications, in-hospital mortality, and received radiotherapy/chemotherapy at 30 days or 1 year after surgery are summarized in Table 3. There were no significant differences between the sedation and non-sedation groups.

Table 1

Characteristics of patients.

Variable	Sedation No N = 94 n (%)/mean (SD)	Sedation Yes N = 56 n (%)/mean (SD)	P
Age at baseline			.49
<50	14 (14.9)	8 (14.3)	
50–65	64 (68.1)	34 (60.7)	
>65	16 (17.0)	14 (25.0)	
Mean (SD)[a]	58.1 (8.6)	59.1 (9.6)	.50
Gender			1.00
Female	7 (7.5)	4 (7.1)	
Male	87 (92.6)	52 (92.9)	
ASA			.37
I	2 (2.1)	0 (0.0)	
II	46 (48.9)	33 (58.9)	
III	46 (48.9)	23 (41.1)	
BMI (kg/m^2)			.18
<18.5	4 (4.3)	5 (8.9)	
18.5–24	52 (55.3)	23 (41.1)	
>24	38 (40.4)	28 (50.0)	
Location			
Tongue	18 (19.2)	7 (12.5)	.23
Buccal	43 (45.7)	33 (58.9)	.12
Lip	2 (2.1)	3 (5.4)	.36
Palate	3 (3.2)	3 (5.4)	.67
Gingival	23 (24.5)	9 (16.1)	.22
Hypopharygeal	5 (5.3)	1 (1.8)	.41
Stage			
T1	11 (11.7)	5 (8.9)	.59
T2	26 (27.7)	21 (37.5)	.21
T3	13 (13.8)	3 (5.4)	.10
T4	43 (45.7)	27 (48.2)	.77
N0	57 (60.6)	30 (53.6)	.40
N1	12 (12.8)	9 (16.1)	.57
N2	25 (26.6)	17 (30.4)	.62
M0	94 (100.0)	56 (100.0)	–
OP time[a]	12.3 (1.9)	14.2 (1.7)	<.001***
Flap size			.37
0	29 (30.9)	16 (28.6)	
1	44 (46.8)	22 (39.3)	
2	21 (22.3)	17 (30.4)	
3	0 (0.0)	1 (1.8)	
Previous treatments			
OP	20 (21.3)	19 (33.9)	.09
RT	17 (18.1)	16 (28.6)	.13
CT	13 (13.8)	14 (25.0)	.09
Smoking	69 (73.4)	42 (75.0)	.83
Betel nut	66 (70.2)	46 (82.1)	.10
Alcohol use	33 (35.1)	28 (50.0)	.07
Comorbidities			
Cardiovascular disease	34 (36.2)	21 (37.5)	.87
Endocrine disease	26 (27.7)	17 (30.4)	.72
Hepatic disease	9 (9.6)	6 (10.7)	.82
Psychological disorders	2 (2.1)	1 (1.8)	1.00
Nephrotic disease	10 (10.6)	4 (7.1)	.48
Respiratory disease	4 (4.3)	1 (1.8)	.65
Orthopedic disease	1 (1.1)	1 (1.8)	1.00
Neurological disease	6 (6.4)	4 (7.1)	1.00
Anemia	1 (1.1)	1 (1.8)	1.00
Malignancy	5 (5.3)	1 (1.8)	.41

Statically analysis: Student's *t* test[a], Chi-square test, Fisher exact test. ASA = anesthesiologists, BMI = body mass index, CT = chemotherapy, OP = operation, RT = radiotherapy.
*** $P < .001$.

Table 2

ICU stay, mechanical ventilation duration, and hospitalization of patients.

Variable	Sedation No N = 94 n (%)/mean (SD)	Sedation Yes N = 56 n (%)/mean (SD)	P
ICU stay, d			
Mean (SD)[a]	2.5 (1.6)	6.3 (2.8)	<.001***
Median (IQR)[b]	2.0 (1.0)	5.0 (1.0)	<.001***
Mechanical ventilation duration, d			
Mean (SD)[a]	1.3 (1.2)	5.1 (2.6)	<.001***
Median (IQR)[b]	1.0 (0.0)	4.0 (1.0)	<.001***
Hospitalizations, d			
Mean (SD)[a]	15.8 (4.3)	19.0 (11.0)	.04*
Median (IQR)[b]	15.0 (3.0)	17.0 (3.5)	<.001***

ICU = intensive care unit.
[a] Student's *t* test.
[b] Mann–Whitney *U* test.
* $P < .05$.
*** $P < .001$.

Table 3

Flap and systemic complications of patients.

Variable	Sedation No N = 94 n (%)/mean (SD)	Sedation Yes N = 56 n (%)/mean (SD)	P
Flap reopen	2 (2.1)	5 (8.9)	.10
Reopen for artery	1 (1.1)	1 (1.8)	
Reopen for vein	0 (0.0)	2 (3.6)	
Reopen for bleeding	1 (1.1)	2 (3.6)	
Flap salvage	2 (2.1)	5 (8.9)	.10
Success	0 (0.0)	2 (3.6)	
Failure	2 (2.1)	3 (5.4)	
Flap complications	1 (1.1)	4 (7.1)	.06
Systemic complications	2 (2.1)	6 (10.7)	.05
CV failure (pump failure need supportive apparatus)	2 (2.1)	1 (1.8)	
Respiratory failure (re-intubation)	0 (0.0)	4 (7.1)	
Sepsis	0 (0.0)	1 (1.8)	
In hospital mortality	0 (0.0)	0 (0.0)	–
RT 30 days	59 (62.8)	28 (50.0)	.13
CT 30 days	30 (31.9)	18 (32.1)	.98
RT 1 year	2 (2.1)	1 (1.8)	1.00
CT 1 year	30 (31.9)	18 (32.1)	.98

Chi-square test, Fisher exact test. RT 30 days: radiotherapy at 30 d after surgery, CT 30 days: chemotherapy at 30 d after surgery. RT = radiotherapy.

After performing stepwise linear regression, the significant predictor of ICU days, mechanical ventilator duration, and hospitalization days were shown in Tables 4–6, respectively.

Sedation and reopen were common factors in each stepwise regression model, revealing the significant predictors of ICU stays, mechanical ventilator duration, and hospitalization days ($P < .05$). Other factors such as cardiovascular disease was a significant predictor for the length of ICU days ($P = .001$) and mechanical ventilator duration ($P < .001$); the increasing age was significantly associated with prolonged ICU stay ($P = .003$).

Table 4

Stepwise regression analysis for ICU days.

Variable	Parameter estimate	Standard error	95% CI	P
Intercept	−0.85	0.98	(−2.79, 1.08)	.385
Sedation	3.45	0.31	(2.85, 4.06)	<.001
Reopen	3.57	0.71	(2.16, 4.97)	<.001
CV	1.06	0.31	(0.45, 1.67)	.001
Age	0.05	0.02	(0.02, 0.08)	.003

CV = cardiovascular disease, ICU = intensive care unit.

4. Discussion

There has been inconsistency in postoperative care of head and neck cancer patients after free flap reconstruction with most studies focused on the degrees of intensive care, monitoring for flap perfusion, respiratory tract patency, and stabilization of hemodynamics. Recent evidence suggests that intensive care and specialty care produced similar postoperative hospital stay, complication rates, and outcomes.[6,7]

It is logical to assume that the earlier the flap is explored, the lower is the chance of flap failure.[8] Therefore, the patients in this study received ICU care directly after surgery where there is a higher nurse/patient ratio thus giving direct and in-time evaluation of flap discoloration. In addition, patients with alcohol withdrawal syndrome may experience a higher rate of flap failure.[9] In our series, there were 33 cases (35.1%) in the non-sedation group and 28 cases (50%) in the sedation groups with chronic alcohol use, respectively. Therefore, integrated ICU care with a multidisciplinary approach helps with rapid diagnosis of problems.

There have been few studies of sedation versus non-sedation after complicated free flap surgery for head and neck cancer but, for other surgical sites, outcomes were better when a postoperative sedation policy was used.[1,6] The postoperative sedation protocol provides advantages of better blood pressure fluctuation control, avoid ICU stress, and prevent delirium related drainage tube dislocation or flap injury. In the current series, we use midazolam and cisatracurium for sedation instead of dexmedetomidine because that the expense of dexmedetomidine was not covered by the health insurance policy in Taiwan.

Some studies have shown a lower incidence of pneumonia, fewer hospitalizations, and reduced ICU length of stay using a non-sedation strategy,[4] probably because mechanical ventilation increases respiratory tract secretions and decreases effective coughing, resulting in ICU-acquired pneumonia.[9] In our study, we found that the non-sedation policy significantly decreased the duration of mechanical ventilation, ICU length of stay, and hospitalization compared with sedated patients (Table 2). These results assume that the non-sedation policy might decline medical cost due to reduced hospitalization and ICU length of stay.

In a study of ALT flap reconstruction after oral cancer ablation, Chen et al demonstrated comparable flap outcomes between ward and ICU patients.[6] Their ward patients group discontinued mechanical ventilation in the operation room and were transferred to the ward after stabilization, similar to our non-sedation group.[6] In comparison with Chen's study, our study showed similar outcomes in flap success rate (our study vs Chen's study: 98.9% vs 98.3%) with lower flap re-operation rates (2.1% vs 8.4%) and shorter hospitalization (15.8 days vs 24.2 days) in our series. This might be attributed to flap checking in the ICU and in-time postoperative medication in our study.

There were concerns that a postoperative non-sedation regimen might bring about the risk of ICU-related delirium due to disruption of circadian rhythms by hourly flap monitoring. Hence, patients were advised transferring to ordinary ward shortly after stabilized conditions.

There was a longer operative time in sedation group while compared with non-sedation group (Table 1). This might be attributed to a more severe operative condition in sedation group, which is a bias in patient selection in this study. Although there were significant differences between ICU stay, mechanical ventilator duration, and hospitalization between 2 groups, no significant differences on systemic complications were found in the current studies (Table 3). Another concern has to be raised about the higher incidences of respiratory failure in postoperative sedation group than in non-sedation group (4 cases vs 0 case). However, the case number was so insufficient that further studies were necessary.

In the current study, we also found some predictors including sedation, flap reopen, cardiovascular disease, and older age were closely related the prolonged ICU stay, mechanical ventilator duration, and hospitalizations. In stepwise regression model, sedation and reopen were common and significant predictors of outcome. The flap reopen may require intense flap monitoring, adequate sedation with ventilator protection, and multidisciplinary approach, which made prolonged hospitalization inevitable.

We recognize the limitations of this study, including its retrospective nature, small sample size, the bias in case selection, and single-center nature that restricts its generalizability. We also acknowledge that there were missing data because meticulous daily data collection was not always obtained in the busy clinical setting. We recommend a prospective, multicenter approach to this issue in future including a randomized controlled study.

In summary, our study suggested that for head and neck cancer patients who received free ALT flap reconstruction, a strategy of postoperative non-sedation is associated with a significant decrease in the duration of mechanical ventilation, ICU length of stay, hospitalization. Regardless of hospital stay, there were no differences in postoperative outcome between 2 groups. This could have important resource implications for health care institutions and services.

Table 5

Stepwise regression analysis for mechanical ventilator duration.

Variable	Parameter estimate	Standard error	95% CI	P
Intercept	0.82	0.20	(0.43, 1.21)	<.001
Sedation	3.54	0.28	(2.98, 4.10)	<.001
Reopen	3.02	0.65	(1.75, 4.30)	<.001
CV	1.14	0.28	(0.58, 1.69)	<.001

Table 6

Stepwise regression analysis for hospitalization.

Variable	Parameter estimate	Standard error	95% CI	P
Intercept	15.64	0.77	(14.13,17.16)	<.001
Sedation	2.83	1.27	(0.33, 5.33)	.027
Reopen	6.34	2.90	(0.60, 12.08)	.031

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