

Perioperative evaluation of the controlling nutritional status (CONUT) score in patients with N0 oral cancer

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Summary. The controlling nutritional status (CONUT) score has been considered to be an established assessment model for evaluating nutrition status in hospital. Here we show the results of perioperative evaluation of the CONUT score in patients with primary N0 oral cancer. The perioperative CONUT score and the prognostic nutritional index (PNI) of total 82 patients undergoing resection for primary oral cancer were analyzed to find the relationship between preoperative nutritional status and postoperative complications or prognosis. We classified these patients into two groups, high CONUT and low CONUT groups, as well as the patients were divided into two groups; low PNI and high PNI groups. 68 cases (82.9%) were divided into low CONUT group, and 14 cases (17.1%) were in high CONUT group. On the other hand, high PNI group has 80 cases (97.6%), and only 2 cases were in low PNI group. Moreover, 12 cases (14.6%) of high PNI were divided into high CONUT group. The CONUT score had a significant relationship with the Body Mass Index (BMI) ($P=0.0360$). In this study, patients who have a CONUT score of 3 or more are not at increased risk for postoperative complications. Further analyses are required for the evaluation of the complications rate and prognostic significance of the CONUT score in patients with N0 oral cancer.

Key words: controlling nutritional status (CONUT) score, enhanced recovery after surgery (ERAS), N0 oral cancer, perioperative evaluation, complication

Introduction

Enhanced Recovery After Surgery (ERAS) programs, which is a kind of new perioperative care strategies, have been developed in order to reduce the impact of surgery. ERAS programs has been applied successfully to the perioperative management in various kinds of fields for surgery. It has already been reported that the principles of ERAS programs can be potentially used for any surgery anywhere in the world (1,2). The evaluation for the possible application of ERAS programs to head and neck surgery patients and especially to those affected by head and neck cancer has also been reported

(1-3). It seems sensible to hypothesize that may also offer benefits to head and neck cancer patients, in terms of reducing complications, fastening recovery, decreasing hospital stay, and allowing earlier return to daily activities after hospital discharge.

The controlling nutritional status (CONUT) score and the prognostic nutritional index (PNI) have been widely used objective indexes for evaluating nutritional status. The CONUT score is an index calculated from the serum albumin concentration, the total peripheral lymphocyte counts and total cholesterol concentration. It is an efficient tool for continuous control of malnutrition in hospital, and allows assess-

ment of nutritional status in all inpatients (4). On the other hand, the PNI, which was calculated from the serum albumin concentration and the total peripheral lymphocyte count. Both CONUT score and the PNI have also been reported to correlate with the risk of perioperative complications and the survival (3,5-8). Recently, Kono et.al. has found the usefulness of CONUT score and the PNI for predicting severe adverse events (AE) in patients with head and neck cancer including oral cancer who underwent chemoradiotherapy. So they have suggested facilitating the planning of aggressive nutritional interventions prior to treatment (8).

However, regarding the PNI, it has also been reported that the serum albumin concentration tends to be excessively emphasized, and it is easily influenced by not only the nutritional status but changes in the body fluid volume including the dehydration/fluid retention status and inflammation. Moreover, total cholesterol concentration has been reported to correlate with the progression of cancer (9).

Therefore, this study is focused on analyzing the CONUT score (3,7,9).

The purpose of this study is, 1) to compare the accuracy of the CONUT score and the PNI as more efficient index for assessment of the nutritional status, and 2) to clarify whether the perioperative CONUT score could be a useful predictor for the incidence of complications in patients with N0 oral cancer.

Patients and Methods

Patients. We retrospectively reviewed the database of 82 patients who underwent curative surgery for N0 oral cancer at the Department of Oral and Maxillo-

facial Surgery, Tohoku University Hospital, between April 2012 and July 2015. None of the patients underwent neck dissection. There were no patients treated with preoperative chemotherapy or radiotherapy. This research protocol was approved by the ethics of committee at the Graduate School of Dentistry, Tohoku University. All patients have been followed up until Dec 2016, or until their deaths.

Methods. In our hospital, the CONUT score has been routinely evaluated as one of the preoperative examinations and as an efficient tool for assessment of nutritional status in all inpatients who undergo surgical treatment. The preoperative blood samples were gathered within one week before the operation. Followed by previous studies (7), CONUT score 3 was set as the cut-off value in this study. The perioperative CONUT score and the PNI of total 82 patients were calculated using data of blood test, and we classified these patients into high CONUT (≥ 3) and low CONUT (≤ 2) groups, as described in Table 1, as well as the patients were divided into two groups; low PNI (< 40) and high PNI (≥ 40) group.

We investigated the CONUT score regarding the relationship between preoperative nutritional status and gender, age, BMI, tumor location, tumor size, pathology and postoperative complications. Clinical staging was conducted according to the 7th edition of the International Union Against Cancer (UICC) for oral cancer. Complications were categorized with the use of Clavien-Dindo classification system.

Statistical analysis. Differences between the groups were verified by χ^2 test, Fisher's exact test or *t* test. Statistical significance was set at P-values of less than 0.05 ($p < 0.05$). The StatMate V software program (Version 5.01, ATMS Co. Ltd., Tokyo, Japan) as a standard statistical package was used to analyze these dates.

Table 1. Assessment of the nutritional status using the CONUT score.

Dysnutritional states (total)	Normal (0-1)	Mild (2-4)	Moderate (5-8)	Sever (9-12)
Parameter (score)				
Albumin (g/dL)	$\geq 3.5(0)$	3.0-3.4(2)	2.5-2.9(4)	$< 2.5(6)$
Total lymphocyte count (/ml)	$\geq 1,600(0)$	1,200-1,599(1)	800-1,199(2)	$< 800(3)$
Total cholesterol (mg/dL)	$\geq 180(0)$	140-179(1)	100-139(2)	$< 100(3)$

Add scores

≤ 2 Low CONUT group

$3 \geq$ High CONUT group

Table 2. The relationships between the CONUT score and the PNI and the clinicopathological factors of the patients.

	CONUT		p	PNI		p
	High (N =14)	Low (N=68)		>40 (N =79)	<40 (N =3)	
Gender						
Male	7	27		33	1	
Female	7	41	0.6788	46	2	0.6284
Age (years)						
Mean ± SD	72.57± 14.16	64. 79± 11 .93	0.0718	65.77± 12.69	75 .33± 8.38	0.2008
BMI (kg/m2)						
Mean ± SD	21.46± 3.56	23.71± 3.60	0.0360	23.81± 3.75	21.33±3.17	0.2625
Tumor location						
Tongue	4	36		40	0	
Maxilla gingiva	4	5		7	2	
Mandibular gingiva	3	11		14	0	
Buccal	1	11		12	0	
Oral floor	1	3		3	1	
Other	1	2	0.3242	3	0	0.2562
T classification						
T1, 2	11	60		69	2	
T3,4	3	8	0.9121	10	1	0.9540
Parhology						
SCC	13	66		76	3	
MC	1	2	0.9260	3	0	0.8929
Complications						
No	10	57		65	2	
Yes	4	11	0.9239	14	1	0.9154

SCC: Sguamous cell carcinoma; MC: Mucoepidermoid carcinoma; SD: Standard deviation

Results

Clinicopathological background. Clinicopathologic factors of these patients in this study were summarized in Table 2. The primary tumor was resected in all cases. Among them, 68 cases (82.9%) were divided into low CONUT group, and 14 cases (17.1%) were in high CONUT group, based on the cut-off value of 3. On the other hand, high PNI group had 79 cases (96.3%), and low PNI group had only 3 cases (3.7%). Then, 14 cases of high PNI were divided into high CONUT group. All patients with a low PNI were included in the high CONUT group.

There were no hospitalization deaths in this study. The number of cases with more than Clavien-Dindo classification 2 complications was 15 (18.3%). Among them 11 cases (13.4%) were in low CONUT group, and only 1 case (1.3%) was in low PNI group. In detail, 4 pa-

tients had postoperative bleeding, 2 patients had peptic ulcer, each one patient had hypertension, arrhythmia or pneumonia. 6 patients had other complications.

Correlation analysis. The CONUT score had only a significant relationship with the BMI (p=0.0360). On the other hand, the CONUT score did not correlate with the complication rate (p=0.4456) (Table 2). There was a significant correlation between the CONUT score and PNI (p=0.0041) (Table 3).

Table 3. The correlation between the CONUT score and the PNI

	the CONUT score					
		Low	%	High	%	p
PNI	Low	0	0	3	2.5	
	High	68	82.9	11	14.6	0.0041

Discussion

It has recently been reported that new strategies have required for perioperative management to reduce the impact of surgery and treatment. The principles of ERAS programs can be potentially used for any surgery anywhere in the world. This program is a combination of elements of perioperative care, which aims to: 1) optimise preoperative preparation for surgery, 2) prevent postoperative complications, 3) minimise the stress response to surgery, and 4) speed recovery and return to normal function (1-4). In addition, the overall strategy has been reported as below: 1) to bring patients in the best health status before surgery, 2) to provide protocolled evidence based care throughout their hospital stay, and 3) to offer the best possible rehabilitation (1,3,4,10).

The CONUT score was developed to evaluate the nutritional status more easily and more clearly (4). However, there have been no previous reports about the preoperative nutritional status using the CONUT score in patients with N0 oral cancer, nor the relationship between the CONUT score and rates for the incidence of complications or prognosis. Therefore, this is the first report to evaluate the CONUT score in patients with N0 oral cancer.

The PNI, which is one of the immune-nutritional index, has previously been reported to be associated with survival in many types of human cancer (5-7). In addition, some papers reported the CONUT score more accurately predicted the survival than that of the PNI (4,7). Therefore, we examined whether the CONUT score was superior to the PNI in evaluation for nutrition status in patients with oral cancer.

All of the patients with a low PNI were included in the high CONUT group (Table 3). The patients with a high CONUT score who were not included in the low-PNI group had a low peripheral lymphocyte count and/or hypocholesterolemia. In the CONUT score, there is a higher emphasis placed on the peripheral lymphocyte count. In addition, total cholesterol concentration is also evaluated, which is not included in the PNI. This time we found that the CONUT score was correlated with the BMI. This is also one of the reason why the CONUT score is considered to be more favorable to assess nutrition status.

Recently, Chiara et al. reported the advantage of ERAS program in the field of head and neck surgery in terms of fastening recovery, reducing hospital stay, and favoring early return to daily activities. Apart from the general principles of ERAS methodology presented above, the head and neck protocol addresses specific issues and includes the following (3,13):

- 1) Preoperative assessment of the nutritional status of the patient, to allow the early recognition of developing malnutrition, and its correction;
- 2) A psychological evaluation;
- 3) A meeting with the speech therapist before surgery;
- 4) Early postoperative patient mobilization;
- 5) Early execution of speech and breathing exercises, and swallowing exercises;
- 6) Early return to oral feeding between the sixth and the tenth day after surgery, depending on the type of surgical intervention and on the postoperative course (13).

It has also reported that patients of head and neck cancer including oral cancer, who undergoing not only surgery but in need of radiotherapy and/or chemotherapy, could possibly benefit from the application of principles of ERAS protocols (3,14,15), because these programs should aim to improve quality of life and enhance the beneficial effects of treatment.

As one of the ERAS methodology, therefore, evaluations of perioperative nutrition status with useful tools such as CONUT score seems sensible to hypothesize that may also offer benefits to oral cancer patients, in terms of reducing complications, fastening recovery, decreasing hospital stay, allowing earlier return to daily activities after hospital discharge and improve the prognosis. Among them, CONUT score and the PNI have been reported as predictors for severe AE in head and neck cancer patients undergoing chemoradiotherapy (8).

We could not clarify the significant difference between the CONUT score and the rate of complications in patients with N0 oral cancer.

There are some limitations in this study. First, it is a retrospective study with a relatively small number of patients. Further studies, such as prospective studies with a larger number of patients, should be required. Second, although the CONUT is revealed to be su-

perior to the PNI, this result is based on an analysis of 14 patients with the high CONUT and only 3 patients with low PNI. Therefore, it may be difficult to conclude exactly. Third, patients with N0 oral cancer who underwent neck dissections are not included. Therefore, surgical stress is low, and this may reveal no significant difference between CONUT score and complications rate. And forth, the observation period was less than five years.

Further studies should be encouraged to investigate the relationships between the nutrition status using CONUT score and complications rate and/or prognosis, as one of the ERAS methodology, in patients with N0 oral cancer.

Conclusion

These findings of this study suggest that, although the perioperative CONUT score is no predictor for the incidence of complications, it may be more efficient index for assessment of the nutritional status than that of the PNI even if in patients with N0 oral cancer.

References

1. Melnyk M, Casey RG, Black P, Koupparis AJ: Enhanced recovery after surgery (ERAS) protocols: time to change practice? *Can Urol Assoc J* 5: 342–348, 2011.
2. Wind J, Polle SW, Fung Kon Jin PH et al: Systematic review of enhanced recovery programmes in colonic surgery. *Br J Surg* 93:800–809, 2006.
3. Chiara B, Stefano P, Antonio P, Carlo VF, Andrea C: Enhanced recovery after surgery (ERAS) strategies: possible advantages also for head and neck surgery patients? *Eur Arch Otorhinolaryngol* 271: 439–443, 2014.
4. de Ulibarri JI, Gonzalez-Madrono A, de Villar NG, Gonzalez P, Gonzalez B, Mancha A, et al: CONUT: A tool for Controlling Nutritional Status. First validation in a hospital population. *Nutr Hosp*. 20: 38–45, 2005.
5. Nozoe T, Kohno M, Iguchi T, Mori E, Maeda T, Matsukuma A, et al: The prognostic nutritional index can be a prognostic indicator in colorectal carcinoma. *Surg Today* 42: 532–535, 2012.
6. Mohri Y, Inoue Y, Tanaka K, Hiro J, Uchida K, Kusunoki M: Prognostic nutritional index predicts postoperative outcome in colorectal cancer. *World J Surg*. Nov 37: 2688–92, 2013.
7. Iseki Y, Shibutani M, Maeda K, Nagahara H, Ohtani H, Sugano K, Ikeya T, Muguruma K, Tanaka H, Toyokawa T, Sakurai K, Hirakawa K: Impact of the Preoperative Controlling Nutritional Status (CONUT) Score on the Survival after Curative Surgery for Colorectal Cancer. *PLoS One* 10(7): e0132488. 2015.
8. Kono K, Sakamoto K, Shinden S, Ogawa K: Pre-therapeutic nutritional assessment for predicting severe adverse events in patients with head and neck cancer treated by radiotherapy. *Clin Nutr*. 1-5, 2016.
9. de Ulibarri Perez JI, Fernandez G, Rodriguez Salvanes F, Diaz Lopez AM: Nutritional screening control of clinical undernutrition with analytical parameters. *Nutr Hosp* 29: 797–811, 2014.
10. Abraham N, Albayati S: Enhanced recovery after surgery programs hasten recovery after colorectal resections. *World J Gastrointest Surg* 3: 1–6, 2011.
11. Varadhan KK, Neal KR, Dejong CH, Fearon KC, Ljungqvist O, Lobo DN: The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective open colorectal surgery: a meta-analysis of randomized controlled trials. *Clin Nutr* 29: 434–440, 2010.
12. Srinivasa S, Sammour T, Kahokehr A, Hill AG: Enhanced recovery after surgery (ERAS) protocols must be considered when determining optimal perioperative care in colorectal surgery. *Ann Surg* 252: 409, 2010.
13. Italian perioperative program: <http://www.italianperioperativeprogram.it/>
14. Bianchini C, Ciorba A, Stomeo F, Pelucchi S, Pastore A: Immunonutrition in head and neck cancer: have a look before surgery! *Eur Arch Otorhinolaryngol* 269: 5–8, 2012.
15. Kahokehr AA, Thompson L, Thompson M, Soop M, Hill AG: Enhanced recovery after surgery (ERAS) workshop: effect on attitudes of the perioperative care team. *J Perioper Pract* 22: 237–241, 2012.

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