

A clinical investigation of the association between perioperative oral management and prognostic nutritional index in patients with digestive and urinary cancers

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ABSTRACT

Background The prognostic nutritional index (PNI) is a simple metric calculated using serum albumin and the peripheral lymphocyte count. It was reported that a low PNI score is significantly associated with major postoperative complications and poor prognosis. The purpose of the present study was to investigate the effects of perioperative oral management (POM) on the perioperative PNI profiles of patients with digestive system or urinary cancers.

Study Design The medical records of 181 patients with cancer who underwent surgery and for whom a PNI could be calculated were retrospectively reviewed.

Results The intervention rate with POM was 34.8%. The median preoperative PNI score was 48.25 in all patients with a POM intervention [25% to 75% interquartile range (IQR): 44.38–54.13] and 47.25 in those without an intervention (IQR: 42.0–53.5). Compared with patients not receiving POM, those who received POM had significantly higher PNI scores from the early postoperative period ($p < 0.05$). Notably, of patients who could resume oral intake within 3 days after surgery, those who received POM intervention, compared with those who did not, had significantly higher PNI scores from the early postoperative period ($p < 0.05$).

Conclusions Perioperative oral management interventions might have positive effects on the postoperative PNI scores of patients with cancer.

Key Words Perioperative oral management, prognostic nutritional index, digestive cancer, urinary cancer, serum albumin, C-reactive protein, CRP

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INTRODUCTION

During cancer treatment, patients can experience various systemic and local complications, including oral complications. Some studies suggest that a patient's dental and oral condition is associated with systemic and surgical complications. In Japan, perioperative oral management (POM) became available under the national health insurance system in 2012. Patients with cancer, cardiovascular diseases, and organ transplantation can receive dental and oral POM during the perioperative period, and studies indicate that POM has positive effects in preventing complications such

as postoperative pneumonia, surgical site infection, and prolonged hospital stay, among others^{1–14}.

The prognostic nutritional index (PNI), first reported by Onodera *et al.*¹⁵, is a simple metric calculated using serum albumin and the peripheral lymphocyte count. Low PNI scores were reported to be significantly associated with major postoperative complications and poor prognosis in patients after gastrointestinal surgery¹⁵. Other reports have examined the clinical significance and usefulness of the PNI as a prognostic factor in some cancers^{16–20}.

Unfavourable dental and oral conditions, including increased oral bacteria, dental infections, oral mucositis,

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decreased saliva, missing teeth, masticatory disturbance, and neurosensory changes cause a decline of oral function, negatively affecting the nutrition condition in patients with cancer. However, no report has yet investigated the association between decline of oral function and the PNI. Perioperative oral management during cancer surgery could have a positive effect by maintaining or improving a patient's nutrition and immune condition, which might consequently reduce perioperative complications.

The purpose of the present study was to investigate the effects of POM on the perioperative PNI profile in patients with digestive system and urinary cancers. The oral cavity is a part of the digestive tract, which is essential to nutrition, and so the direct effects of POM were investigated in patients undergoing digestive system surgery for cancer. Given that urologic diseases are not directly related to functions of the oral cavity, the indirect effects of POM were also investigated in patients undergoing surgery for urologic cancer.

METHODS

The study protocol was approved by the Committee on Medical Research of Shinshu University (no. 3788). We published the research plan on the hospital Web site and guaranteed the opportunity for opt-out.

Medical records of patients who underwent cancer surgery at the departments of digestive surgery and urology of Shinshu University in 2016 were retrospectively reviewed. The primary outcome was an increase or decrease of the perioperative PNI score. Predictor variables were defined as patient factors (age, sex), surgical treatment factors (surgical site, operation time, blood loss, and postoperative time to the start of oral intake), and the presence or absence of a POM intervention. Pre- and postoperative blood parameters, including peripheral lymphocyte count and serum albumin, were obtained before the surgery (<1 week) and regularly afterward (until 6 weeks postoperatively). The PNI was calculated using the formula of Onodera *et al.*¹⁵:

$$10 \times \text{serum albumin (g/dL)} + 0.005 \times \text{peripheral lymphocyte count (per mm}^3\text{)}.$$

In our hospital, all patients with cancer are recommended and encouraged to receive POM before initiation of cancer treatments. The criteria for a POM intervention accorded with the report published by Yamagata *et al.*²¹. In general, POM was initiated at the time of the decision for hospitalization (before initiation of cancer therapy) and included oral health instruction, removal of dental calculus (scaling), professional mechanical tooth cleaning, removal of the tongue coating with a toothbrush, cleaning and adjustment of dentures, and extraction of teeth in cases of severe periodontitis showing pain, discharge of pus, mobility problems, or marked alveolar bone loss by radiographic examination. The POM interventions continued regularly after surgery.

Correlations between variables and PNI profiles were analyzed statistically using the Fisher exact test, the Wilcoxon test, and the univariate repeated-measures analysis least-squares method. Statistical analyses were performed using the JMP software application (version 13; SAS Institute, Cary, NC, U.S.A.), with *p* values less than 0.05 being considered significant.

RESULTS

Of the 349 patients who underwent cancer surgery at the departments of digestive surgery and urology, 168 were excluded because of insufficient data. The analysis therefore included 181 patients (132 men, 49 women; mean age: 67.8 ± 10.9 years; age range: 33–89 years; Table 1). Of those 181 patients, 63 (34.8%) received POM interventions. Of 74 patients who underwent surgery for digestive system cancers, 47 received POM (63.5%); and of the 107 who underwent surgery for urologic cancers, 16 received POM (15.0%). Patients with digestive system cancer received POM more frequently.

Table 1 summarizes the characteristics of the patients. No significant differences in sex and age were observed between the patients who did and did not receive POM. The median preoperative PNI score was 48.3 for patients who received POM [25%–75% interquartile range (IQR): 44.4–54.1], and 47.3 for those who did not (IQR: 42.0–53.5). The median preoperative PNI for patients with digestive system cancers was the same for patients who received POM (median: 49.5; IQR: 44.5–55.1) and for those who did not (median: 49.5; IQR: 40.3–57.3; Table 1). The median preoperative PNI for patients with urologic cancers was slightly lower in the patients who received POM (median: 44.5; IQR: 41.0–47.5) than in those who did not (median: 46.3; IQR: 42.0–51.1; Table 1). No significant differences in preoperative PNI were evident between the patients who did and did not receive POM (Wilcoxon *p* = 0.171). Operation times were significantly longer in patients who received POM than in those who did not, except when the operation was for urologic cancer (all patients, *p* < 0.001; patients with digestive system cancers, *p* < 0.05; patients with urologic cancers, *p* = 0.722). Blood loss was significantly greater in patients receiving POM than in those not receiving POM (all patients: Wilcoxon *p* < 0.01; patients with digestive system and urologic cancers: Wilcoxon *p* < 0.05). In the cohort overall, resumption of oral intake occurred significantly earlier in patients not receiving POM than in those receiving POM (*p* < 0.01). The result was the same for patients undergoing surgery for digestive system cancers, (*p* < 0.05), but not for those undergoing surgery for urologic cancer.

Figure 1 compares the perioperative PNI profiles during the perioperative period for all patients. Before surgery and throughout the postoperative period, PNI scores were significantly higher in patients receiving POM than in patients not receiving POM (univariate repeated-measures analysis least-squares method, *p* < 0.05). Figure 2 compares the perioperative PNI profiles for patients with digestive system and urologic cancers. In patients with digestive system cancers, the PNI score was higher during the early postoperative days, but later became lower, in patients who received POM compared with those who did not receive POM, although the difference was nonsignificant (univariate repeated-measures analysis least-squares method, *p* = 0.709). In contrast, in patients with urologic cancers, PNI scores throughout the perioperative period were higher in patients receiving POM than in those not receiving POM, although that difference also did not reach significance (univariate repeated-measures analysis least-squares method, *p* = 0.596).

Postoperative PNI profiles were influenced by surgical intensity and the postoperative alimentation method. The

TABLE 1 Patient characteristics

Variable	Overall cohort		Digestive system cancer subgroup		Urologic cancer subgroup	
	POM	No POM	POM	No POM	POM	No POM
Patients [n (%)]	63 (34.8)	118 (65.2)	47 (63.5)	27 (36.5)	16 (15.0)	91 (85.0)
Mean age (years)	67.0±10.4	68.1±10.5	66.3±11.3	69.7±11.1	69.0±9.7	67.6±9.8
	NS ^a (p=0.430)		NS ^a (p=0.724)		NS ^a (p=0.341)	
Sex (men:women)	42:21	90:28	27:20	17:10	15:1	75:16
	NS ^b (p=0.219)		NS ^b (p=0.806)		NS ^b (p=0.459)	
Preoperative PNI score						
Median	48.3	47.3	49.5	49.5	44.5	46.3
IQR	44.4–54.1	42.0–53.5	44.5–55.0	40.3–57.3	41.0–47.5	42.0–51.1
	NS ^a (p=0.171)		NS ^a (p=0.797)		NS ^a (p=0.166)	
Operation time (minutes)						
Median	297	212	336.5	100	223	207
IQR	233–404	165.5–268	278.3–412.5	215–330	166–244.5	165–244.5
	p<0.001 ^a		p<0.05 ^a		NS ^a (p=0.722)	
Blood loss (mL)						
Median	100	55	100	30	150	100
IQR	40–350	10–200	20–330	10–160	77.5–712.5	10–200
	p<0.05 ^a		p<0.05 ^a		p<0.05 ^a	
Resumption of oral intake after surgery [n (%)]						
Within 3 days	23 (12.7)	91 (50.3)	9 (12.2)	12 (16.2)	14 (13.1)	79 (73.8)
At 4 days or more	40 (22.1)	27 (14.9)	38 (51.4)	15 (20.3)	2 (1.9)	12 (11.2)
	p<0.01 ^b		p<0.05 ^b		NS ^b (p=1.000)	

^a By Wilcoxon rank-sum test.

^b By Fisher exact test.

POM = perioperative oral management; PNI = prognostic nutritional index; IQR = 25%–75% interquartile range.

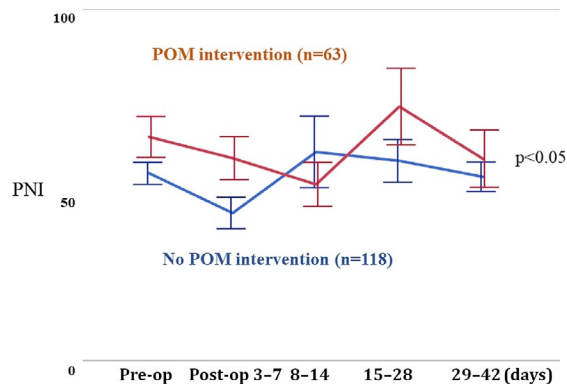


FIGURE 1 Perioperative change of the prognostic nutritional index (PNI) profile in 181 patients. Compared with those who did not receive perioperative oral management (POM) interventions, those who did had significantly higher PNI scores from the early postoperative period ($p < 0.05$).

PNI profiles of patients who resumed oral intake within 3 days after surgery were therefore compared separately (Figure 3). The PNI scores from the early postoperative period were significantly higher in patients who received POM than in patients who did not receive POM (univariate repeated-measures analysis least-squares method, $p < 0.05$).

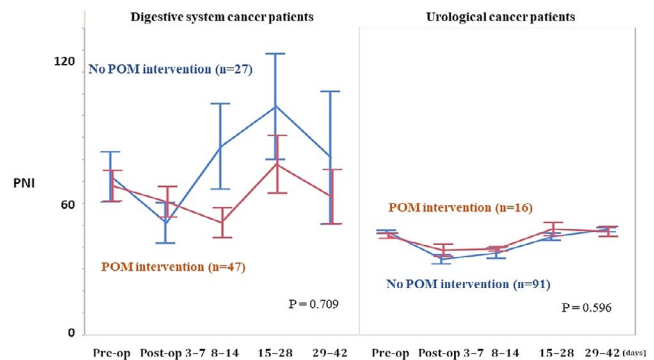


FIGURE 2 Perioperative change of the prognostic nutritional index (PNI) profile in 74 patients with digestive system cancers and 107 patients with urologic cancers. Perioperative PNI scores were not significantly different in patients who received perioperative oral management (POM) and in those who did not (digestive cancer: $p = 0.709$; urologic cancer: $p = 0.596$).

DISCUSSION

In Japan, POM has been available under the national health insurance system since 2012 for patients receiving cancer treatment, organ transplantation, cardiovascular surgery, and orthopedic implant surgery. The oral cavity has been

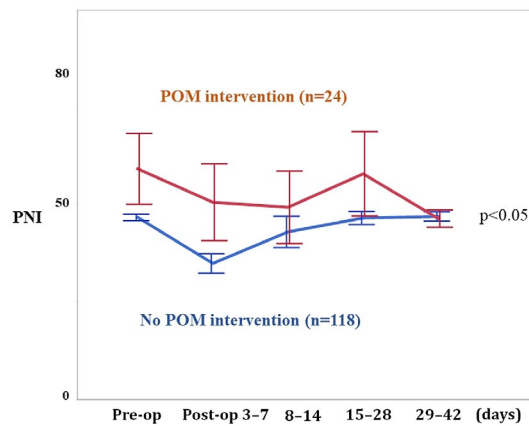


FIGURE 3 Perioperative change of the prognostic nutritional index (PNI) profile in 142 patients who could resume oral intake by postoperative day 3. Of the patients who could resume oral intake within 3 days postoperatively, PNI scores were significantly higher for those who received perioperative oral management (POM) from the early postoperative period, compared with those who did not ($p < 0.05$).

reported to possibly be a large reservoir of pathogenic bacteria that can cause infections in multiple organs^{22–25}, and professional oral care has been reported to reduce microbial counts in the oropharynx, aiding in the prevention of aspiration pneumonia²⁶. However, because of a lack of prospective randomized clinical trials investigating POM, evidence of its efficacy has not been fully established. Several recent reports have described positive effects of POM in patients with cancer, with many studies indicating that POM interventions might reduce the prevalence of postoperative pneumonia in patients who undergo cancer surgery^{1,2,4,5,8,10–12,14}. Other reported effects of POM include reduced numbers of bacteria and bacterial species detected by endotracheal bacteriologic examination³, shortened postoperative systemic inflammatory response syndrome³, fewer postoperative hospitalization days^{6–9,11}, a shorter postoperative fasting period^{6,7,9}, lower C-reactive protein¹¹, and a reduced prevalence of surgical site infections¹³. It is easy to understand that the reduction of oral and dental bacteria and infections could lead to reductions in local and systemic infections. Perioperative oral management includes not only oral care, but also dental and functional restoration of the oral cavity. That functional and dental management might improve a patient's nutrition status and, consequently, their immunologic condition. However, no reports about the association between POM and change in perioperative nutrition markers have been published. In the present study, we therefore examined the possible effects of POM on nutrition status and immunologic condition.

The PNI has been reported to be an easy and useful prognostic factor for survival and postoperative complications in some patients with cancer. A low PNI score has been reported to be significantly associated with poor survival^{15,17–20} and to be useful for predicting nutrition status and mortality in patients undergoing peritoneal dialysis¹⁶. Additionally, low PNI scores have been associated with postoperative complications in colorectal and lung cancer^{15,17,20}.

The PNI is calculated using serum albumin and the peripheral lymphocyte count¹⁵. Lymphocytes act as activators in the adaptive immune system to clear tumour from the body and to halt its development and dispersion²⁶. Serum albumin has been reported to reflect an individual's nutrition and inflammatory status²⁷. Low levels of serum albumin and lymphocytes have been reported to promote inflammatory tumour development and the spread and metastasis of cancer²⁸. In patients with colorectal cancer, hypoalbuminemia was found to reflect malnutrition and immunosuppression, increasing disease severity, progression of the tumour, and poor prognosis²⁹. Additionally, early postoperative reduction in serum albumin was found to be an independent risk factor for severe postoperative complications and poor prognosis^{30,31}.

Our results suggested that POM interventions might have the positive effects of preserving and improving the perioperative PNI score in patients with cancer. The number of decayed teeth was reported to correlate with lower serum albumin³². A significant association between mean clinical attachment loss and lower serum albumin was reported in elderly patients³³, and a close relationship between periodontitis and lower serum albumin has been demonstrated^{33–36}. Tooth loss was reported to possibly be a predictor of low energy and protein intake, and low serum albumin³⁷, and prosthodontic treatments such as partial dentures were reported to significantly increase serum albumin³⁸. Those results suggest that POM—including oral care, abatement of chronic dental infections, and prosthodontic treatments—has a positive effect on maintaining and increasing perioperative nutrition status, including serum albumin and lymphocyte counts, resulting in higher perioperative PNI scores.

However, in digestive cancer surgery, the PNI level more than a week after surgery was higher in patients who did not receive POM than in those who received POM. In the present retrospective study, our investigations showed that POM had been applied in patients who underwent long and intensive surgery (with more blood loss). It is logical to speculate that the patients who did not receive POM underwent less-intensive surgery, and thus their PNI scores recovered better than did those for patients who received POM. Additionally, oral intake was resumed significantly later in patients who received POM than in those who did not receive POM.

Postoperative parenteral nutrition might have a significant influence on the postoperative PNI score. The patients who resumed oral intake within 3 days after surgery were therefore analyzed separately, with PNI profiles being compared for those who did and did not receive POM (Figure 3). A better PNI profile was observed in the patients who received POM than in those who did not. In addition, in patients with digestive system cancers, PNI scores were lower in the patients who received POM than in those who did not, especially in the early postoperative period when the postoperative alimentation method was not different between the groups. Those results also suggest that POM has a positive effect on the perioperative PNI profile.

Our report is the first to examine the effects of POM interventions on the perioperative PNI score in patients who undergo cancer surgery. However, the study has some limitations. One limitation is the retrospective nature of the

study, which was based on a relatively small case series at a single institute. Because of insufficient data, especially lack of laboratory data before surgery (<1 week) and postoperatively (regularly until 6 weeks postoperatively), more than half of the 349 eligible patients had to be excluded from the study. Those exclusions might have affected the study results. Although our study detected positive effects of POM interventions on the perioperative PNI score, other factors, such as the primary site and surgical method, might have affected the PNI score. Although the patients who received POM underwent more intensive surgery, their PNI profiles were better than those of the patients who did not receive POM. Further prospective investigations, with larger numbers of cases and multicentre analyses, will be needed to clarify the significant independent risk factors for perioperative PNI score in patients with cancer.

CONCLUSIONS

Positive effects of POM interventions in patients undergoing cancer surgery were demonstrated. In the early postoperative period, PNI scores were significantly higher in patients receiving POM than in patients not receiving POM. Of patients who could resume oral intake within 3 days after surgery especially, PNI scores from the early postoperative period were significantly higher for those who received POM than for those who did not receive POM. Those results suggest that POM interventions have positive effects on the postoperative improvement of the PNI score in patients with cancer. We intend to conduct a nationwide retrospective study to investigate the efficacy of POM for perioperative serum albumin using data from the Japanese Stomatological Society.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare that we have none.

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