Original Article

Impact of Prophylaxis Percutaneous Endoscopic Gastrostomy on the Survival Rate of Patients with Nasopharyngeal Cancer Stage II to IV Undergoing Definitive Concurrent Chemo-Radiation Therapy

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Background: The benefits of prophylaxis percutaneous endoscopic gastrostomy (PPEG) in term of survival and nutritional status in nasopharyngeal cancer (NPC) are still unknown.

Objective: To assess the impact of PPEG on the survival rate, completed treatment rate (CTR), and the nutritional status of patients with NPC stage II to IV, having been treated with concurrent chemo-radiation therapy (CCRT).

Materials and Methods: All of the computerized medical records of NPC stage II to IV patients treated with CCRT, without severe malnourishment (BMI <18.5 kg/m^2) from January 2007 to September 2011 were retrospectively reviewed. PPEG is defined as PEG tube placement prior to CCRT. The 1- and 3-year overall survival rates, completed treatment rate and nutritional status (body weight) during CCRT, between the PPEG group and the non-PPEG group, were compared. PEG utility rate and PEG related complications were collected.

Results: Two hundred and ninety-two patients (216 males, 76 females, with the mean age of 48.7±13.7 years) were enrolled, 192 (65%) in the PPEG group, and 100 patients in the non-PPEG group. The demographic data, tumor staging, and ECOG scores were similar between the 2 groups, and the 3-year overall survival rates of the PPEG and non-PPEG group were not significantly different. Mean weight reduction, and the proportion of patients with >10% weight reduction in the non-PPEG was significantly higher during weeks 4 to 7 of CCRT. The PPEG group showed a trend of having a higher CTR than the non-PPEG group (94.3% vs. 87%, p = 0.055). In the group of PPEG, PEG related complications occurred in 44 patients (23%) and severe complications were observed in 6 patients (3.1%). The utility rate of gastrostomy tube, as the route of feeding during CCRT, was 96.3% (155/161).

Conclusion: PPEG lessened weight reduction in NPC patients, stage II to IV during CCRT, and showed a trend of improving the completed treatment rate with minimal serious complications. However, there was no difference in terms of overall survival.

Keywords: Prophylaxis percutaneous endoscopic gastrostomy, Nasopharyngeal carcinoma, Concurrent chemo-radiation, Survival

J Med Assoc Thai 2019;102(Suppl.10): 124-9
Website: http://www.jmatonline.com

Nasopharyngeal carcinoma (NPC) is a high prevalence cancer in Southeast Asia, with an incidence rate of 4.7 per 100,000 populations in Thailand[1]. Most of NPC patients were found to be in stage II to IV, thus they required standard treatment with concurrent chemo-radiation therapy (CCRT), which can cause local complications, severe mucositis, dysphagia and severe xerostomia[2]. Furthermore, head and neck cancers per se could affect the alimentary tract causing poor clinical and nutritional status (tumor compression and painful) as well as general symptoms (anorexia). All of these contributing factors lead to impairment in nutritional status, treatment intolerance, and might shorten patient survival[3,4].

Weight loss in NPC patients, during CCRT, is severe with an average weight reduction of 5.5 to 12.3 kg, and 86% of patients have more than a 10% weight reduction[5,6] which commonly occurs during the first 3 weeks of the treatment course[7]. Percutaneous endoscopic gastrostomy (PEG) before CCRT, named prophylaxis PEG (PPEG), has shown effectiveness in maintaining body weight, increasing

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How to cite this article: Pattarapuntakul T, Chamroonkul N, Sripongpan P, Netinatsuton N, Tangthongkum M, Ovartlarnporn B. Impact of Prophylaxis Percutaneous Endoscopic Gastrostomy on the Survival Rate of Patients with Nasopharyngeal Cancer Stage II to IV Undergoing Definitive Concurrent Chemo-radiation Therapy. J Med Assoc Thai 2019;102(Suppl.10): 124-9.

treatment tolerance, and improving quality of life in head and neck cancer patients in prior studies[8]. However, no studies were conducted to access the benefit of PPEG on NPC patients' overall survival. Hence, this study aims to evaluate the effect of PPEG on the survival rate, completed treatment rate as well as the nutritional status in patients with nasopharyngeal carcinoma stage II to IV, who are undergoing CCRT.

Materials and Methods

This study is a retrospective cohort study. After ethical approval by the institutional review board, all data were maintained in an anonymized fashion on secure databases. We performed a retrospective review of computerized medical records of all stage II to IV npc patients undergoing CCRT between January 1, 2007 and September 30, 2011, in Songklanagarind Hospital, Hatyai, Songkhla, Thailand.

Inclusion criteria were all patients with stage II to IV npc according to AJCC/TNM 6th, 7th editions (2002, 2009), undergoing CCRT, with an age above 15 years, Eastern Cooperative Oncology Group (ECOG) performance status 0 to 2, and no clinical severe malnourished status before treatment (BMI >18.5 kg/m^2). Patients were excluded if they had any serious medical illness (pulmonary, cardiovascular, renal or liver disease), or a history of other malignancy.

Data were collected on age, gender, comorbidities, TNM stage of disease, ECOG, treatment regimen, completed treatment, treatment duration, PEG insertion, PEG complications, PEG utility, and body weight at initial and then subsequent body weight during CCRT.

PPEG was defined by PEG tube placement (pull technique) before CCRT. Non PPEG was defined by oral intake or nasogastric tube (NG) placement during CCRT and some patients was placed PEG tube when they could not oral feeding or NG tube problems. Completed treatment rate (CTR) was defined by patients, who received a total of 35 fractions radiation and cisplatin 100 mg/m^2, or carboplatin AUC6 given every 3 weeks for 3 cycles during radiation time. During the CCRT period, patients were evaluated weekly, or more frequently if clinically indicated. Toxicity during treatment was assessed according to CTCAE (version 4). Severe weight loss was defined by weight loss during the treatment of more than 10% of initial body weight. PEG related complications were classified as early (<2 weeks after procedure), and late (>2 weeks after procedure), and severe PEG related complications were defined as complications that required hospitalization.

Statistical analysis

Patients baseline characteristics (demographical, clinical, and laboratory data) were compared between the two groups as; non-normal distributed data, using Wilcoxon's test, and via student's t-test for normal distributed data. Categorical data were compared by Chi-square test, or Fisher's exact test. The 3-year overall survival rate of the whole cohort was obtained by the Kaplan-Meier method, and the significance of differences between curves was classified by variable category, being evaluated using the log-rank test for univariate analysis. Weight change in each cycle of weekly radiation was defined as the difference in current weight from the baseline. Severe weight loss was defined as more than a 10% weight loss from the baseline body weight. Statistical significance was defined with p-value <0.05. Analysis was performed using R program (Apical package R foundation for statistical Computing, 2008).

Results

During the study period, there were a total of 292 patients with NPC stage II to IV who underwent treatment with CCRT. They were categorized into either a PPEG group (192 patients), or non-PPEG group (100 patients). Patient characteristics for each group are shown in Table 1. The mean age of the patients was 48.7±13.7 years, with 216 patients being male. Eighty-six per cent of patients presented with stage III to IV, whilst 92% of the patients had an ECOG

Table 1. Demographic data

	PPEG	Non-PPEG	p-value
Total patients	192	100	-
Gender (male), (n, %)	138 (71.9)	78 (78)	0.321
Age (y), mean (SD)	48.2 (13.1)	49.6 (13.8)	0.377
Disease TNM stage (n, %)			0.115
Stage II	25 (13)	14 (14)	
Stage III	79 (41.1)	29 (29)	
Stage IV	88 (45.8)	57 (57)	
ECOG score (n, %)			0.824
0	97 (50.5)	48 (48)	
1	83 (43.2)	42 (42)	
2	12 (6.2)	8 (8)	
Baseline body weight (kg), mean (SD)	58.7 (12.8)	58.0 (12.7)	0.639

PPEG = prophylaxis percutaneous endoscopic gastrostomy, ECOG = Eastern Cooperative Oncology Group

score 0, and 1 equally in both groups. There was no significance difference in the patients' demographic data between the PPEG group and the non-PPEG group.

Overall survival and treatment completion

Both 1- and 3-year overall survival rates of NPC patients, stage II-IV, CCRT in the PPEG and the non-PPEG group (88.5% vs. 84%, $p = 0.234$) and (59.4% vs. 58%, $p = 0.709$) were not statistically different. NPC patients, who were in PPEG group, had higher complete treatment rate than those in the non-PPEG group (94.3% vs. 87% $p = 0.055$); however, this finding was not statistically significant (Table 2).

Weight reduction in NPC patients during treatment with CCRT

Mean body weight reduction during weeks 4 to 7 of CCRT in the non-PPEG group was significantly higher than in the PPEG group (week 4: 4.2 kg vs. 3.3 kg, $p = 0.028$; week 5: 4.9 kg vs. 3.9 kg, $p = 0.017$; week 6: 5.6 kg vs. 4.2 kg, $p = 0.004$; week 7: 6.4 kg vs. 4.4 kg, $p<0.001$, respectively) (Figure 2). More than 10% weight reduction occurred more frequently in the non-PPEG group during weeks 4 to 7 of CCRT (week 4: 25% vs. 13.6%, $p = 0.017$; week 5: 37% vs. 21%, $p = 0.003$; week 6: 48% vs. 30%, $p<0.001$; week 7: 52% vs. 32.4%, $p<0.001$) (Figure 3).

PEG complications and PEG utility rate

In all 192 patients who underwent PPEG before CCRT, PEG procedure was performed successfully. Two patients (1%) had immediate complications of bleeding at the PEG insertion site. Twenty-two percent of patients in the PPEG group developed late PEG related complications; 30 patients (15.6%) had local infections, 16 patients (6.2%) had PEG malposition and 3 patients (1.6%) had feeding problems. Among the patients, who developed PEG related complications, only 6 patients (3.1%), who had severe complications, required hospitalization. One hundred sixty-one of the 192 patients (83.8%) were available for interviews, and the utility rate of PEG as a major route of feeding (>80% route of feeding) during CCRT was; 96.3% (155/161) (Table 2).

Discussion

This study enrolled 192 patients in the PPEG group and 100 patients in the non-PPEG group. There was no significant difference in baseline characteristics, including stage of disease and ECOG. Our study showed no significant difference in either the 1- or 3-year overall survival rates in both the PPEG and non-PPEG groups respectively.

Table 2. Overall survival, completed treatment rate and nutritional status of nasopharyngeal cancer patients undergoing treatment with CCRT

Outcomes	PPEG (n = 192)	Non-PPEG (n = 100)	*p*-value
3-year overall survival rate (%)	59.4	58	0.709
Median survival time (year)	5.1	4.6	0.883
Complete treatment rate, n (%)	181 (94.3)	87 (87)	0.055
Mean of weight reduction (kg), mean (SD)			
Week 1	1.1 (2.2)	0.9 (1.8)	0.329
Week 2	2.1 (2.5)	2.4 (2.8)	0.392
Week 3	2.9 (3.0)	3.2 (2.8)	0.392
Week 4	3.3 (3.3)	4.2 (3.3)	0.028
Week 5	3.9 (3.6)	4.9 (3.4)	0.017
Week 6	4.2 (4.0)	5.6 (4.0)	0.004
Week 7	4.4 (4.3)	6.4 (4.2)	<0.001
Number of patient with weight loss >10%, n (%)			
Week 1	5 (2.6)	1 (1)	0.668
Week 2	7 (3.7)	9 (9)	0.104
Week 3	19 (9.9)	14 (14)	0.350
Week 4	26 (13.6)	25 (25)	0.017
Week 5	40 (21.1)	37 (37)	0.003
Week 6	57 (30.2)	48 (48)	<0.001
Week 7	64 (34.2)	52 (52)	<0.001
PEG related complications, n (%)	44 (23)		
Early complication	2 (1)		
Late complication	42 (22)		
Need hospitalization	6 (3)		
PEG utility, n (%)			
Used >80% of feeding	155 (96.3)		
Not used	6 (3.7)		

CCRT = concurrent chemo-radiation therapy, PPEG = prophylaxis percutaneous endoscopic gastrostomy, SD = standard deviation

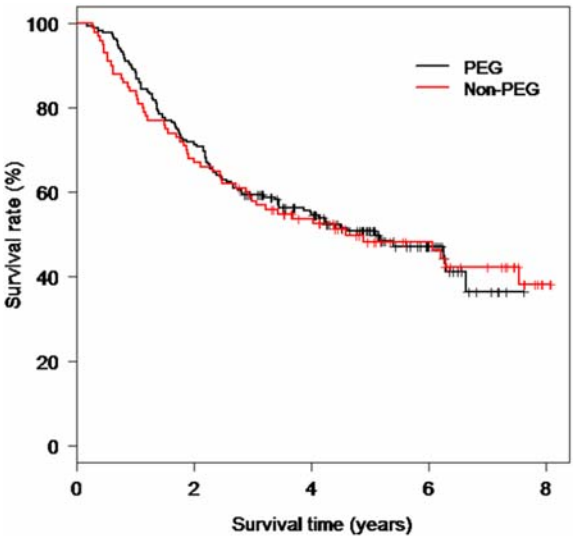

Figure 1. Three-year overall survival of nasopharyngeal cancer patients undergoing concurrent chemo-radiation therapy.

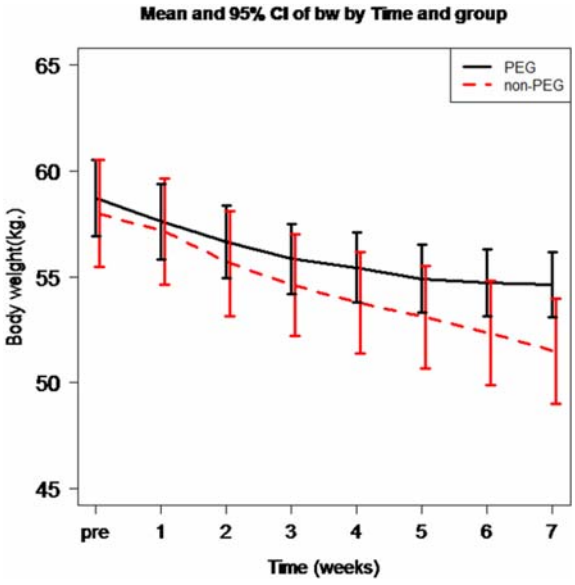

Figure 2. Mean weight (kg) of nasopharyngeal cancer patients during concurrent chemo-radiation therapy.

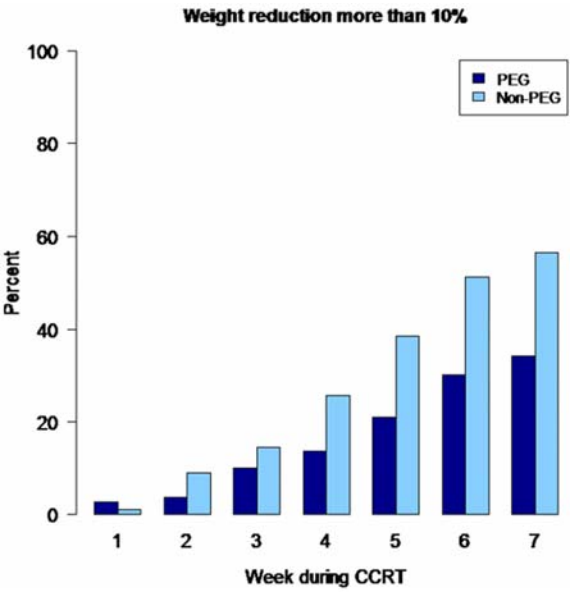

Figure 3. Nasopharyngeal cancer patients who had a weight reduction more than 10% during concurrent chemo-radiation therapy.

According to previous studies, in PPEG in head and neck cancer patients who underwent CCRT, there was a decrease in weight reduction, but no effect to the overall survival rate. However, they included all types of head and neck cancer and NPC patients were a small populations[9-11]. Many studies demonstrate nutritional status as an independent factor that affects prognosis, the completed treatment rate, and may affect to the overall survival rate in NPC patients[3,12-14]. Our study demonstrated a benefit of PPEG during CCRT in terms of lesser weight reduction during weeks 4-7 of CCRT compared to patients who PEG was placed when they indicated need of PEG. Furthermore, patients in PPEG group tended to have a higher completed treatment rate (CTR) than those in non-PPEG group, but this finding was not statistically significant that might be caused by small sample size.

All patients within the PPEG group had successful PEG insertion, and 83% of all patients received antibiotic prophylaxis before procedure. About 22% in the PPEG group had complications. Most of these complications were not serious; however, 3% required hospitalization. This result is the same as previous studies that reported serious PEG complications at a rate of about; 2 to 7.4%[15-17].

To demonstrate the PEG utility rate, our team interviewed patients or his/her close relatives by telephone. The PEG utility rate was more than 90% during CCRT. This finding was different from previous studies, in which the rate of unused PEG in head and neck cancer patients was about 18 to 47% which was much higher than in our study[18]. This finding could be an effect of using different treatment protocols for NPC patients in Songklanagarind Hospital, and conducting good educational programs for patients, before PEG placement in our center.

This study has strength in that it enrolled patients with NPC, stage II to IV, undergoing CCRT in a tertiary hospital in Southern Thailand, where there is a high prevalence of NPC patients. Since 2005, PPEG procedure in NPC patients in Songklanagarind Hospital has been inserted routinely for prophylaxis feeding problems, before CCRT.

The follow-up data from computerized medical records are more accurate in weight, survival, treatment compliance and admissions. This study had a high phone contact rate (>80%) for interviews concerning PEG utility.

The limitations are that it is a retrospective cohort study with a rather small power of sample size, approximately 60%. Therefore, it cannot represent the benefits of PPEG in overall survival, and completed treatment rates.

Conclusion

PPEG lessened weight reduction in NPC patients, stage II to IV during CCRT, and showed a trend of improving the completed treatment rate with minimal serious complications. However, there was no difference in terms of overall survival.

What is already known on this topic?

PPEG is a procedure of choice in NPC patients, who received treatment with CCRT. The benefit of PPEG is demonstrated in weight reduction and complete treatment rate during treatment.

What this study adds?

This study needs further investigations with randomized and prospective design and larger sample size.

Acknowledgements

The authors would like to give our grateful thanks to the patients in this study, and our gastroenterologists, Head and Neck oncologist, medical staffs and native speaker for approval this manuscript.

Potential conflicts of interest

The authors declare no conflicts of interest.

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