

Effect of Percutaneous Endoscopic Gastrostomy on Long-term Quality of Life in Patients with Locally Advanced Nasopharyngeal Carcinoma

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Research Article

Keywords: nasopharyngeal carcinoma, percutaneous endoscopic gastrostomy, chemotherapy, nutritional support, quality of life

Posted Date: October 21st, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-893910/v1>

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Abstract

Background: Previous study revealed that prophylactic percutaneous endoscopic gastrostomy (PEG) maintain nutritional status of patients with locally advanced nasopharyngeal carcinoma (LA-NPC). We aimed to further investigate the effect of PEG on the long-term quality of life of patients with LA-NPC.

Methods: Patients with LA-NPC were selected and divided into PEG and non-PEG groups. The QLQ-C30 scores, incidence of adverse effects, weight and xerostomia recovery were compared between the two groups.

Results: No statistically significant difference in the scores of each QLQ-C30 scales between the two groups ($P>0.05$). The incidence of xerostomia was higher in the PEG group than in the non-PEG group ($P=0.044$), but no significant difference in the incidence of the remaining adverse effects as well as in weight and dry mouth recovery ($P>0.05$).

Conclusion: PEG seems not to have a detrimental effect on long-term quality of life, including the swallowing function of NPC patients.

Introduction

Nasopharyngeal carcinoma (NPC) is a malignant epithelial cancer prevalent in southern China. Radiotherapy is the primary treatment for NPC owing to its high sensitivity to radiation and the complex anatomy of the nasopharynx[1]. Most patients with NPC are in the locally advanced stage when diagnosed, at which point intensity-modulated radiotherapy (IMRT) with concurrent chemoradiotherapy (CCRT) is the standard treatment[2, 3]. IMRT can increase the survival of patients and decrease the damage to normal tissues[4–7]. The quality of life (QoL) and late toxicities have attracted more and more attention, along with the improved survival.

As a result of the side effects of radiotherapy and chemotherapy, patients with locally advanced nasopharyngeal carcinoma (LA-NPC) commonly suffer from varying degrees of malnutrition and poor QoL during CCRT[8–10]. Several studies have demonstrated the link between poor nutritional status and a lower rate of survival among patients with NPC[11–13]. Moreover, nutritional status proved to be independently associated with QoL in cancer patients[14–16]. As a result, enteral nutritional support is an effective tool for patients with LA-NPC to preserve their nutritional status during treatment, thereby ensuring a smooth treatment progression.

The nasogastric tube, percutaneous endoscopic gastrostomy (PEG), and surgical gastrostomy are commonly used methods to provide enteral nutritional support. Nasogastric tubes are only appropriate for patients who are unable to eat by mouth for a brief period of time (less than 30 days) but need nutritional support, while PEG is appropriate for patients who need long-term (more than 30 days) nutritional support. PEG is less invasive, easier to handle, has fewer complications, and is less costly than surgical gastrostomy, making it more accessible to patients[17]. Our previous study found that prophylactic PEG prior to CCRT, as well as aggressive enteral nutritional support, maintained the nutritional status of patients with LA-NPC during CCRT and improved treatment completion rates[18]. And these advantages can be translated into survival advantages for N3 NPC patients.[19]. However, the role of PEG in patients' QoL is still controversial[20–29]. Prophylactic PEG before radiotherapy increases QoL in patients with head and neck cancer[21–24]. Some research, however, have indicated that prophylactic gastrostomy placement prior to radiotherapy for patients with head and neck cancer is associated with a higher incidence of dysphagia and a greater reliance on PEG nutritional support[25–29]. Moreover, studies on the impact of PEG on QoL in NPC patients are lacking. Hence, this study aims to investigate the impact of PEG on patients' long-term QoL.

Patients And Methods

Patients and Study Design

Patients with pathologically confirmed progressive stage of primary nasopharyngeal carcinoma admitted to Fujian Cancer Hospital between June 1, 2010 and June 30, 2014 were included in this retrospective study. 133 NPC patients who had received prophylactic PEG feeding at the discretion of their doctors before beginning CCRT and 133 non-PEG patients who was matched based on age, gender, and tumor, node, and metastases level were recruited firstly.[18]. Further exclusion criteria were as follows: 1) By June 30,

2020, patients who had died, had a recurrence, or had metastasis. 2) Patients under the age of 18 at the time of the initial consultation. 3) Patients who failed to complete the QOL questionnaires. As shown in Fig. 1, a total of 148 NPC patients were finally enrolled in this study. The research was approved by the Fujian Cancer Hospital's Ethics Review Committee, and all participants signed a written informed consent form.

Radiation Treatment and Chemotherapy

All patients received IMRT in combination with systemic chemotherapy. The radiotherapy was at a total dose of 68.8-81.75Gy (median, 70Gy) in 31–36 fractions (median, 33 fractions) for the primary tumor site. Except for three patients who received only two CCRT cycles, all patients were treated with cisplatin-based neoadjuvant chemotherapy (NACT) and CCRT. Detailed descriptions of IMRT and chemotherapy regimens have been published previously.[18]

PEG Placement

All patients were free of severe stomach and other gastrointestinal lesions, without any past history of aggressive liver disease, hepatic or kidney dysfunction, congestive heart failure, chronic malignancy, dementia, respiratory failure, and coma. The pull method was used to place all PEG tubes[30]. PEG tubes were placed before the start of radiotherapy and were removed only after the acute mucositis had disappeared and the patient was able to consume enough food orally. All patients and their families were fully informed of the potential side effects of radiotherapy, the efficacy of PEG and its expected advantages as well as possible risks before treatment.

Data Collection

The late adverse effects of radiotherapy were evaluated in accordance with CTCAE 4.0. To assess the QoL of patients, we used the validated and internationally accepted European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Version 3 (EORTC QLQ-C30)[31]. The questionnaire comprises 30 questions, and is divided into 15 domains. There are five multi-item functional scales (bodily, cognitive, emotional, social and role functions), as well as three multi-item symptom scales (fatigue, pain, and nausea/emesis) and general QoL. Six single-item scales concerning dyspnea, insomnia, appetite loss, constipation, diarrhea and financial difficulties are also included. The items were graded on a 1–4 scale, with the exception of the general QoL issue, which was scored on a 1–7 scale. The mean score for each scale was calculated and transformed into a value between 0 and 100. Higher scores for functioning and general QoL suggest better functioning and general QoL, whereas higher scores for symptoms indicate worse outcomes. To optimize the response rate, questionnaires were evaluated by telephone interviews conducted by the same professional training investigator.

Statistical Analyses

The baseline characteristics of subjects were analyzed using the *t* test for normal continuous variables and Nonparametric Kruskal-Wallis test for non-normal continuous variables. The Chi-Square test or Fisher exact probability method was used to analyze qualitative data. SPSS, version 19.0.0.1 (IBM SPSS, 2010, Chicago, IL, USA) was used for statistical analyses. All *P* values were two-tailed, and *P* values of 0.05 were considered statistically important.

Results

Baseline Characteristics of the Study Population

A total of 148 NPC patients (78 in the PEG group and 70 in the non-PEG group) were included in the study, based on the inclusion criteria. The male patients accounted for 107 (72.3%) of the total. The entire cohort's mean age at initial diagnosis was 43.27±11.34 years. In terms of gender, age, educational level, pathological type, clinical stage, T stage, N stage, and chemotherapy regimen, there were no statistically significant differences between the two groups (each *P*>0.05). All details are provided in Table 1.

Table 1

Baseline characteristics of the study population

Variable	Non-PEG	PEG	<i>P</i> value
Gender, n (%)			0.714
Male	52(74.3)	55(70.5)	
Female	18(25.7)	23(29.5)	
Age, mean±SD	42.34±12.08	44.10±10.65	0.310
Educational level, n (%)			0.193
primary school and less than	18(25.7)	21(26.9)	
junior middle and high school	37(52.9)	31(39.7)	
junior college or above	15(21.4)	26(33.3)	
Pathology subtype, n (%)			0.599
Keratinising squamous	2(2.9)	2(2.6)	
Non-keratinising Undifferentiated squamous	64(91.4)	68(87.2)	
Non-keratinising differentiated squamous	4(5.7)	8(10.3)	
Clinical stage, n (%)			0.612
III	42(60.0)	41(52.6)	
IVA	18(25.7)	22(28.2)	
IVB	10(14.3)	15(19.2)	
T stage, n (%)			0.632
T1	4(5.7)	8(10.3)	
T2	13(18.6)	16(20.5)	
T3	33(47.1)	30(38.5)	
T4	20(28.6)	24(30.8)	
N stage, n (%)			0.431
N0	1(1.4)	4(5.1)	
N1	18(25.7)	15(19.2)	
N2	41(58.6)	44(56.4)	
N3	10(14.3)	15(19.2)	
Regimens of CCRT			0.137
Single agent	67(95.7)	69(88.5)	
Two drugs	3(4.3)	9(11.5)	
PEG, percutaneous endoscopic gastrostomy; CCRT, concurrent chemoradiotherapy.			

Comparison of Late Toxicities between Non-PEG and PEG Groups

As shown in Table 2, the PEG group had a higher incidence of xerostomia than the non-PEG group (51.7% vs. 50%), and the difference was statistically significant ($P=0.044$). There were no statistically meaningful variations between the two groups of patients in terms of other distant adverse effects (all $P>0.05$). Incidence of neck fibrosis, xerostomia, hearing loss, tinnitus, and dysphagia were 41.9%, 50.7%, 68.9%, 42.6%, and 31.1%, respectively.

Table 2

Comparison of late toxicities between non-PEG and PEG groups

Variables	All, n(%)	Non-PEG				PEG				P value ^a
		Grade 0, n(%)	Grade 1, n(%)	Grade 2, n(%)	Grade 3, n(%)	Grade 0, n(%)	Grade 1, n(%)	Grade 2, n(%)	Grade 3, n(%)	
Neck fibrosis, n(%)	62(41.9)	47(67.1)	19(27.1)	4(5.7)	0(0)	39(50.0)	35(44.9)	2(2.6)	2(2.6)	0.052
Xerostomia, n(%)	75(50.7)	35(50.0)	22(31.4)	13(18.6)	0(0)	38(48.7)	32(41.0)	5(6.4)	3(3.8)	0.044
Worst hearing, n(%)	102(68.9)	19(27.1)	42(60.0)	4(5.7)	5(7.1)	27(34.6)	42(53.8)	5(6.4)	4(5.1)	0.757
Tinnitus, n(%)	63(42.6)	40(57.1)	21(30.0)	6(8.6)	3(4.3)	45(57.7)	22(28.2)	11(14.1)	0(0)	0.224
Trismus, n(%)	10(6.8)	64(91.4)	5(7.1)	0(0)	1(1.4)	74(94.9)	4(5.1)	0(0)	0(0)	0.495
Dysphagia, n(%)	46(31.1)	50(71.4)	14(20.0)	6(8.6)	0(0)	52(66.7)	22(28.2)	3(3.8)	1(1.3)	0.335
Dysarthria, n(%)	11(7.4)	65(92.9)	3(4.3)	0(0)	2(2.9)	72(92.3)	5(6.4)	1(1.3)	0(0)	0.329
Chewing, n(%)	22(14.9)	62(88.6)	1(1.4)	7(10.0)	0(0)	64(82.1)	2(2.6)	8(10.3)	4(5.1)	0.260
Hoarseness, n(%)	9(6.1)	68(97.1)	1(1.4)	0(0)	1(1.4)	71(91.0)	3(3.8)	1(1.3)	3(3.8)	0.451
Tongue dysfunction, n(%)	5(3.3)	67(95.7)	1(1.4)	1(1.4)	1(1.4)	76(97.4)	2(2.6)	0(0)	0(0)	0.480
^a Fisher exact probability method. PEG, percutaneous endoscopic gastrostomy.										

Results of the EORTC QLQ-C30

Data for the EORTC QLQ-C30 scales are presented in Table 3. The mean score of general QoL was 83.78±16.11. There were no significant differences between PEG and non-PEG group in the EORTC QLQ-C30 scales. Furthermore, after stratifying by age, no significant differences between the groups were observed (all $P>0.05$) (Figure 2 and Figure 3).

Table 3

Comparison of quality of life between non-PEG and PEG groups

Variables	Non-PEG, median (range)	PEG, median (range)	All, Mean±SD	P value
Global health status/QoL	83(8-100)	83(25-100)	83.78±16.11	0.826
Physical functioning	100(53-100)	100(53-100)	94.19±11.88	0.322
Role functioning	100(0-100)	100(0-100)	96.51±15.46	0.633
Emotional functioning	100(50-100)	100(25-100)	89.47±15.23	0.707
Cognitive functioning	83(0-100)	83(33-100)	83.00±19.49	0.178
Social functioning	100(0-100)	100(0-100)	90.14±21.17	0.739
Fatigue	0(0-33)	0(0-100)	14.86±21.71	0.169
Nausea and vomiting	0(0-100)	0(0-50)	0.90±5.42	0.144
Pain	0(0-100)	0(0-33)	2.25±10.41	0.249
Dyspnoea	0(0-67)	0(0-100)	4.50±15.38	0.859
Insomnia	0(0-100)	0(0-100)	13.96±25.50	0.242
Appetite loss	0(0-67)	0(0-100)	4.73±15.56	0.980
Constipation	0(0-100)	0(0-67)	5.86±16.37	0.727
Diarrhoea	0(0-67)	0(0-0)	3.83±14.30	0.868
Financial difficulties	0(0-67)	0(0-0)	9.91±21.46	0.683

PEG, percutaneous endoscopic gastrostomy; QoL, quality of life.

Comparison of Weight and Xerostomia Recovery between Non-PEG and PEG Groups

Compared with patients in the PEG group, more patients in the non-PEG group took more than a year to return to baseline weight and recover from xerostomia, but no statistically significant differences between groups was seen (all $P>0.05$) (Table 4).

Table 4

Comparison of weight and xerostomia recovery between non-PEG and PEG groups

Variables	Non-PEG	PEG	P value
Time to return to baseline weight			0.425
≤1 years	34(48.6)	43(55.1)	
>1 years	36(51.4)	35(44.9)	
Time of recovery from xerostomia			0.628
≤1 years	19(27.1)	24(30.8)	
>1 years	51(72.9)	54(69.2)	

PEG, percutaneous endoscopic gastrostomy.

Discussion

Patients who underwent prophylactic PEG experienced significant improvements in nutritional status and QoL while also showing increased treatment adherence during radiotherapy. Nonetheless, among patients with head and neck cancer, the role of PEG in

terms of long-term QoL and adverse effects is debatable. In this study, xerostomia was more common in the PEG group than in the non-PEG group. The frequency of other adverse effects such as dysphagia did not vary statistically significantly between the two groups. There was no statistically significant difference between the two groups in terms of QoL. However, the patients' high general QoL scores showed that both groups of patients had a decent general QoL. To our knowledge, this is the first research that examines the impact of prophylactic PEG on long-term QoL and adverse effects in NPC patients. PEG does not appear to have a detrimental effect on long-term QoL, including swallowing function, according to our findings.

Similar results were observed in several head and neck cancer studies[22–24]. Axelsson et al[22] used a EORTC QLQ-head and neck 35 scale and a 5-level oral intake scale to test swallowing outcomes in a randomized study that included patients with head and neck cancer who were randomly assigned to one of two groups: prophylactic PEG or nutritional support according to clinical practice. The patients' capacity to swallow foods did not vary between the groups, according to the findings. Prestwich et al.[23] retrospectively included 56 patients with head and neck cancer in two matched groups who received either a prophylactic gastrostomy tube (GT) or a nasogastric tube as required and used the MD Anderson Dysphagia Inventory questionnaire to assess swallowing outcomes. In line with our findings, there was no significant difference in long-term swallowing function between the groups. Another study conducted by Prestwich et al.[24] showed the same results, as well.

However, some studies indicated that prophylactic PEG increases the risk of long-term dysphagia[25–28]. Patients who received prophylactic GT before treatment had a higher incidence of GT dependence and stricture diagnosis than those who did not. The authors hypothesized that the high incidence of long-term GT dependency in patients may be due to atrophy of the muscles that control the swallowing process[25]. Oozeer et al.[26] performed another analysis that yielded the same findings. Prophylactic PEG tubes were independent predictors of PEG tube dependency at least 1 year after treatment in patients with head and neck cancer who received definitive chemoradiation, according to a retrospective review[27]. A retrospective study[28] supports the hypothesis that patients treated with PEG feeding have higher severe late dysphagia than patients treated with R-NG feeding. The convenience of PEG placement, according to the authors, can deter patients from working hard to become nutritionally independent after therapy is completed. The opposite was found in our research. There was no significant difference between PEG and non-PEG groups in terms of long-term QoL, including dysphagia. Unlike the studies above, only NPC patients were included in our study. During radiotherapy, we encouraged patients in PEG groups to do swallowing exercises like drinking. In addition, the PEG tube was removed after the acute mucositis has resolved, allowing for adequate food intake orally (approximately 4–6 weeks after the end of radical radiotherapy). Moreover, to avoid interference with recurrence and metastasis, only patients without progression were included in our analysis.

Using the EORTC QLQ-C30 scale to assess the QoL of NPC patients who survived more than two years, a study included 216 NPC survivors found that these patients had a slightly high incidence of dry mouth, fatigue, hearing loss, depression and anxiety, but had a good QoL [32]. Another randomized controlled trial[33] showed that the observation group (nutritional support) had a lower incidence of adverse effects and had better short-term outcomes and QoL than the control group, which was likely due to the patients' improved nutritional status. Of the 148 patients in our study, 102 (68.9%) had hearing loss and 75 (50.7%) were troubled by xerostomia. Patients, however, had higher mean scores for overall QoL as well as the five major functions of somatic, social, task, emotional, and cognitive functioning, and lower scores for the remaining symptoms. The fact that all of our study participants received intensity-modulated radiotherapy may have contributed to their high QoL. Intensity-modulated radiotherapy, as compared to traditional radiotherapy, helps protect normal tissues, reduce the occurrence of long-term side effects, and increase patients' long-term QoL[34–37]. The other possible reason may be that final analysis included only patients without progression. The presence of xerostomia was significantly higher in the PEG group compared to the non-PEG group (51.7% vs. 50%, $P=0.044$). However, there was no significant difference in Grade ≥ 2 xerostomia between groups.

There are several limitations to the current study. First, there was selection bias in this study since it was not a prospective randomized controlled trial and the decision to conduct PEG was based on the patients' wishes. Second, investigators gathered information on patients' QoL mostly through telephone follow-up inquiries, resulting in information bias. Bias may be minimized to some extent in this study because the questionnaire was filled out by the same professionally qualified investigator after interviewing the patients, item by item via telephone follow-up.

Conclusions

During concurrent chemoradiotherapy, prophylactic PEG enhanced the nutritional status of patients with LA-NPC, without any adverse consequences for long-term QOL, including swallowing function. It remains an active and effective nutritional intervention for patients with LA-NPC who are deficient in nutrition and are unable to successfully complete the treatment. Prospective studies are also required for further evidence.

Abbreviations

NPC, nasopharyngeal carcinoma; IMRT, intensity-modulated radiotherapy; CCRT, concurrent chemoradiotherapy; QoL, quality of life; LA-NPC, locally advanced nasopharyngeal carcinoma; PEG, percutaneous endoscopic gastrostomy; NACT, neoadjuvant chemotherapy; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Version 3; GT, gastrostomy tube

Declarations

Acknowledgements

The authors would like to express their gratitude to all participants for their cooperation and to all staffs for recruiting subjects and their technical assistance.

Fundings

This work was supported by the Natural Science Foundation of Fujian Province (grant no. 2018J01275, by Jingfeng Zong), the Natural Science Foundation of Fujian Province (grant no. 2019Y0061, by Yun Xu), the Training project of young talents in health system of Fujian Province (grant no. 2020GGB013, by Yun Xu) and the Training project of young talents in health system of Fujian Province (grant no. 2020GGA014, by Qiaojuan Guo).

Conflict of interest

All the authors declare that there are no financial or other relationships that might lead to a conflict of interest of the present article.

Availability of data

The datasets used can be available from the corresponding author on reasonable request.

Code availability

None.

Authors' contributions

Conceptualization: Yun Xu and Shaojun Lin; *Methodology:* Hwei Peng and Xian-E Peng; *Formal analysis and investigation:* Yun Xu, Hwei Peng, Qiaojuan Guo, Lanyan Guo, Jingfeng Zong, Bijuan Chen and Hanchuan Xu; *Writing—original draft preparation:* Yun Xu and Hwei Peng; *Writing—review and editing:* Jianji Pan, Xian-E Peng and Shaojun Lin; *Funding acquisition:* Yun Xu, Qiaojuan Guo and Jingfeng Zong; *Supervision:* Xian-E Peng and Shaojun Lin.

Ethics approval

The research was carried out in compliance with the Declaration of Helsinki and approved by the Fujian Cancer Hospital's Ethics Review Committee.

Consent to participate

Informed consent was obtained from all subjects involved in the study.

Consent for publication

Written informed consent has been obtained from the patients to publish this paper.

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Figures

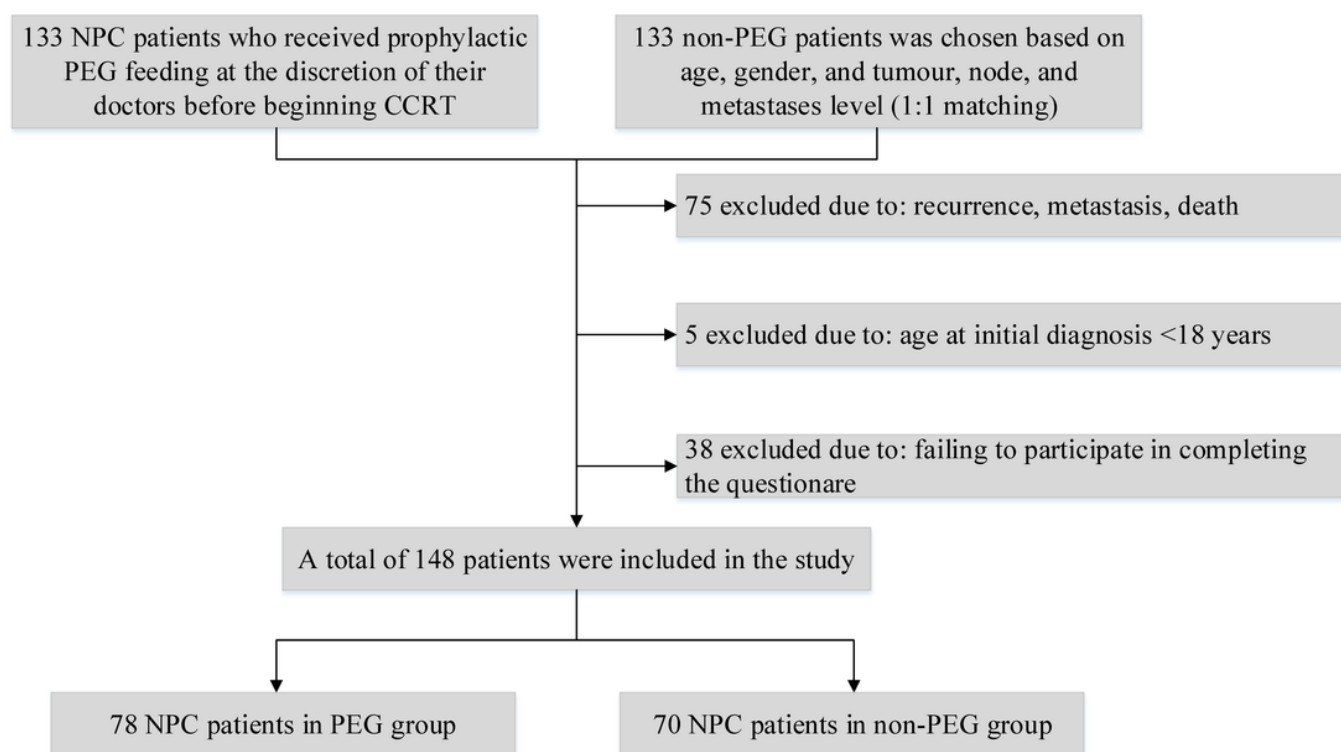


Figure 1

Flowchart of the study population. NPC, nasopharyngeal carcinoma; PEG, percutaneous endoscopic gastrostomy; CCRT, concurrent chemoradiotherapy.

Age <45 years

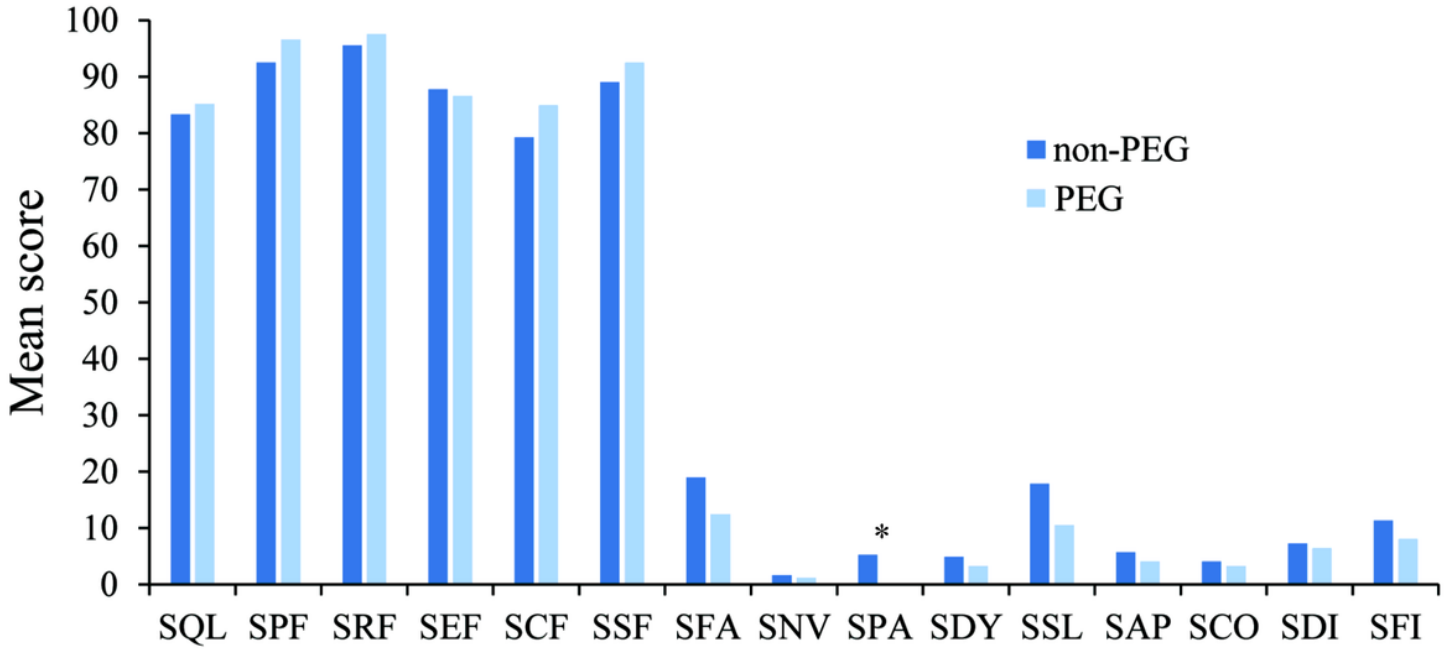


Figure 2

Comparison of quality of life in patients aged <45 years between non-PEG and PEG groups.

Age ≥45 years

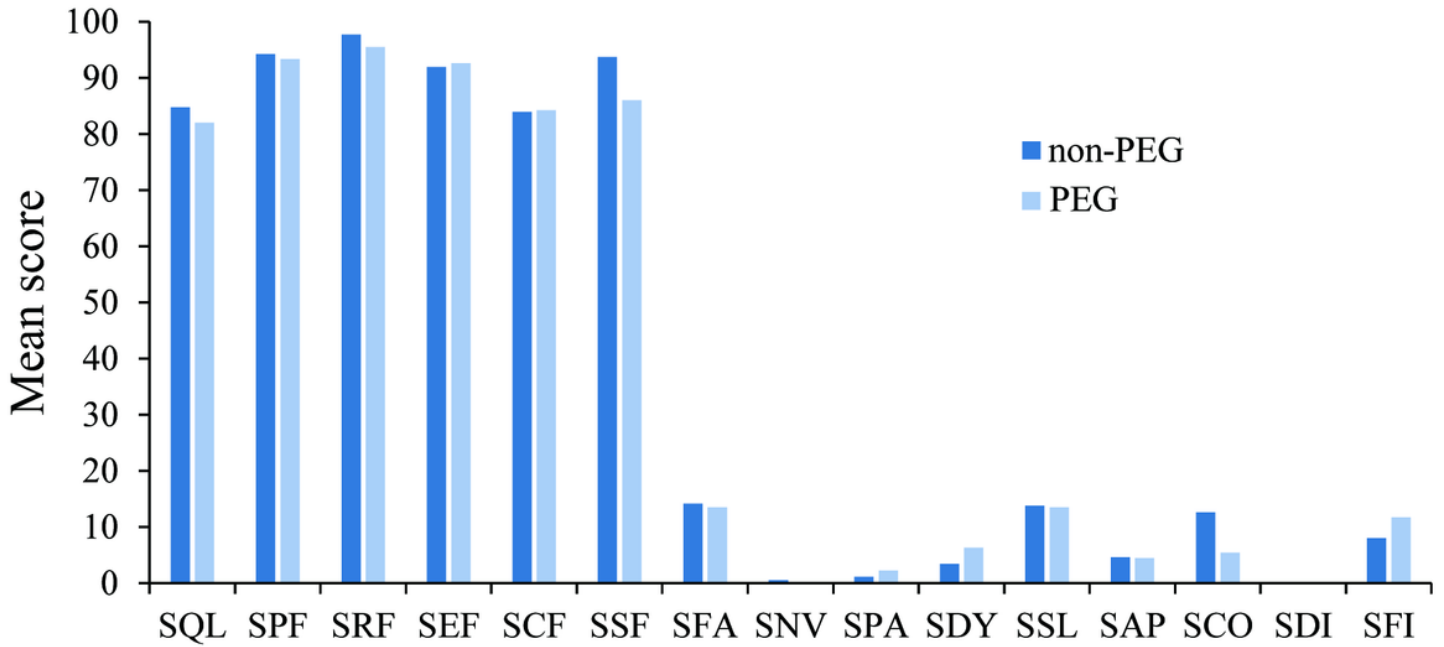


Figure 3

Comparison of quality of life in patients aged ≥45 years between non-PEG and PEG groups.