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Original Article

Transoral endoscopic thyroidectomy vestibular approach for papillary thyroid microcarcinoma: an analysis of clinical outcomes

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Abstract: Objective: To analyze the influence of transoral endoscopic thyroidectomy vestibular approach (TOETVA) on the clinical outcomes of patients with papillary thyroid microcarcinoma (PTMC). Methods: The clinical data of PTMC patients (n=90) who visited the Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University from July 2019 to July 2021 were retrospectively analyzed. Patients who underwent endoscopic thyroidectomy via the transthoracic-areola approach were included in the control group (CG; n=42) and those with TOETVA were assigned to the observation group (OG; n=48). The operative time (OT), length of hospital stay (LOS), postoperative drainage volume, and complications were recorded. Besides, C-reactive protein (CRP), white blood cell count (WBC), erythrocyte sedimentation rate (ESR), as well as scores of the Visual Analogue Scale (VAS), Vancouver Scar Scale (VSS), postoperative patient satisfaction, and the Short-Form 36 Item Health Survey (SF-36) were compared between the two groups. Results: The data showed that the OT and LOS of the OG were not statistically different from those of the CG, and the postoperative drainage volume was less than that of the CG ($P<0.05$). The two cohorts of patients showed a similar incidence of complications such as postoperative hematoma, transient hoarseness, infection, temporary recurrent laryngeal nerve injury and transient hypothyroidism (all $P>0.05$). CRP, WBC and ESR increased in both groups after treatment but showing no evident difference between groups. The OG had statistically lower VAS and VSS scores at two days after surgery, a statistical higher satisfaction rate than the CG, and a statistically higher score of SF-36 at three months after surgery than in the CG (all $P<0.05$). Conclusions: While ensuring the therapeutic effect, TOETVA can significantly reduce the pain degree of patients and scarring, as well as provide better cosmetic effect, higher patient satisfaction, and better quality of life, which is worthy of clinical promotion.

Keywords: Endoscopy via oral vestibular approach, thyroidectomy, papillary thyroid microcarcinoma, clinical outcome

Introduction

Papillary thyroid carcinoma (PTC) is histologically the same as follicular thyroid carcinoma (FTC) and Hurthle cell carcinoma [1], which all develop from thyroid follicular cells and form well-differentiated tumors [2]. With an increasing incidence, PTC has become one of the most common endocrine malignancies [3]. While papillary thyroid microcarcinoma (PTMC) refers to a PTC with tumor a diameter of less than 1 cm, and which is less malignant in clinical manifestations [4]. At present, PTMC is commonly treated by surgery, with a very low mortality after proper surgical treatment [5, 6]. However, according to past clinical practice, patients who underwent open thyroidectomy were often left with significant scarring [7]. Therefore, this study aimed at finding a therapeutic method with both therapeutic and cosmetic effects from the perspective of surgical approach of PTMC.

Transoral endoscopic thyroidectomy vestibular approach (TOETVA) is an innovation in thyroid surgery. Unlike other approaches, it has the advantage of a concealed incision, which can avoid scarring on the patient's body surface [8]. A report on thyroidectomy by He et al. [9] suggested that transoral vestibulectomy is a viable

alternative for patients with cosmetic claims. Previous clinical practice has demonstrated that TOETVA has achieved remarkable results in the treatment of hyperthyroidism and benign thyroid tumors, with high patient satisfaction [10]. In a study by Nguyen et al. on the treatment of benign thyroid tumors [11], TOETVA showed higher satisfaction than open thyroidectomy among patients. Meanwhile, Grogan et al. confirmed the safety of TOETVA in their report on hyperparathyroidism [12].

Recent years have witnessed the constant progress made in minimally invasive techniques, but the clinical efficacy and safety of TOETVA in the treatment of early malignancies remain to be explored [13]. Accordingly, in this study, TOETVA was compared with endoscopic thyroidectomy via the transthoracic areola approach, mainly from the aspects of effectiveness, safety and scarring in the treatment of PTMC, aiming to provide new insights for surgical optimization of PTMC.

Data and methods

General case data

In this retrospective study, 90 PTMC patients presented to the Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University from July 2019 and July 2021 and they were selected and divided into an observation group (OG) with 48 cases and a control group (CG) with 42 cases. Patients in the CG received endoscopic thyroidectomy via the transthoracic areola approach, while patients in the OG were treated with TOETVA. The CG was composed of 11 males and 31 females, aged 19 to 44 with an average of (32.14±6.54) years and a mean disease course of (3.52±0.51) years; tumor location: the tumor was found on the left side in 20 cases and on the right side in 22 cases; tumor diameter: (0.72±0.17) cm. The OG was composed of 8 males and 40 females who were aged between 18 and 46 with a mean age of (34.56±7.06) years and an average disease course of (3.58±0.77) years; 26 cases had the tumor located on the left side and 22 on the right side, with a tumor diameter of (0.75±0.20) cm. The Ethics Committee of the Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University gave their approval for conducting this research.

Eligibility criteria

The eligible patients (age: 18-50) were all diagnosed as having PTMC by CT scan and puncture cytology in the Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University and were operated on for the first time, with no related drugs used for intervention within one month before surgery. All of them signed informed consent and actively cooperated with the treatment.

Cases with maximum tumor diameter >1 cm, hyperthyroidism, thyroiditis, coagulation disorders, intolerance to surgery, severe mental diseases, or non-compliance with the above inclusion criteria were excluded. Besides, those who were unwilling to cooperate with the treatments or with incomplete data that affected the efficacy judgment were ruled out.

Treatment methods

CG (transthoracic areola endoscopic thyroidectomy group): The patients were treated by endoscopic thyroidectomy via the transthoracic areola approach that was performed by the same group of doctors. The patient was placed in a supine position with neck and shoulder slightly elevated. Routine skin preparation and draping were conducted after general anesthesia. First, a 0.5 cm arc-shaped incision was made at the areola, the flap was dissociated to the superior margin of thyroid cartilage, and the thyroid gland was exposed along the linea alba cervicalis. After tumor resection, the wound was cleaned, and the incision was sutured after placing a catheter.

OG (TOETVA group): The patients received TOETVA. Broad-spectrum antibiotics were administered to patients preoperatively to prevent infection. The patient was placed in a supine position with the neck raised and the head tilted back. Nasotracheal anesthesia was performed, after which, disinfection and draping the same as in the CG were carried out. Then, a 1.2 cm incision was made in the patient's anterior mucosa of the posterior teeth of the oral vestibule, and a 1 cm Trocar puncture was used as the viewing port. The main and auxiliary operation ports were punctured on both sides of the oral vestibule mucosa, through which the endoscope and operation

instruments were inserted. After opening the cervical linea alba, the thyroid gland was exposed, and the lesion was resected. After that, the catheter was indwelled and the incision was closed.

Observation indices

(1) Surgical indicators. The efficacy evaluation criteria have been described as above, where the total effective rate = (the patients with marked response + the patients with response)/ the total number of patients × 100%.

(2) Complication rate. Complications that occurred in both groups during treatment, including hematoma, transient hoarseness, infection, temporary recurrent laryngeal nerve injury, transient hypothyroidism, were observed.

(3) Serum indices. Venous blood was collected from subjects and serum was extracted to measure changes in C-reactive protein (CRP), white blood cell count (WBC) and erythrocyte sedimentation rate (ESR) before and 2 days after treatment with related kits and measuring instruments. The operation steps strictly followed the instructions of human CRP kit (Shanghai Enzyme-linked Biotech, EK-H12249), WBC kit (WBC Biocoen Biotech, 340502) and ESR tester (Beijing Perlong New Technology, PUC-2068B).

(4) Pain relief degree. Patients' postoperative pain relief was assessed by the Visual Analogue Scale (VAS), a measurement with a total score of 10 points. Lower scores suggest milder pain [14].

(5) Scar evaluation. We compared and analyzed postoperative scarring between the two groups by the Vancouver Scar Scale (VSS). On a 15-point scale, higher scores are associated with severe scarring [15].

(6) Patient satisfaction. After the operation, patient satisfaction was surveyed by a 10-point self-made satisfaction scale. The higher the score, the better the patient's satisfaction.

(7) Quality of Life. Patients' quality of life at postoperative three months was assessed by the Short-Form 36 Item Health Survey (SF-36) from eight aspects, physical functioning (PF), role physical (RP), body pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH). With 100 points for each domain, the score is positively related to the patient's quality of life.

Statistical processing

SPSS 21.0 (SPSS, Inc., Chicago, IL, USA) was used for data analysis and GraphPad Prism 6 (GraphPad Software, San Diego, USA) was employed for data visualization. The number of cases/percentage (n/%) was utilized to denote categorical data, and χ^2 test was used for comparison of categorical data. For quantitative data (mean ± SEM), the inter-group and intra-group comparisons were performed by independent sample t-test and paired t-test, respectively. $P<0.05$ indicated a statistically significant difference.

Results

Comparison of baseline data between the two groups of patients

By analyzing 90 PTMC patients' general data (**Table 1**), we found that there were no statistical differences in sex, (mean) age, disease course, tumor site, tumor diameter, place of residence and drinking history between the OG and CG, indicating clinical comparability between two groups (all $P>0.05$).

Comparison of surgical indicators between the two groups of patients

We analyzed OT, LOS and postoperative drainage volume of both groups of patients (**Figure 1**), and the results showed longer OT but less LOS in the OG versus the CG, but with no statistical significance ($P>0.05$); while the postoperative drainage volume was statistically less in the OG ($P<0.05$).

Comparison of complications between the two groups of patients

By comparing and analyzing the incidence of complications in terms of hematoma, transient hoarseness, infection, temporary recurrent laryngeal nerve injury and transient hypothyroidism, we found that although there was no statistical difference ($P>0.05$), the overall complication rate was lower in the OG compared with the CG (12.49% *vs.* 21.42%, **Table 2**).

Table 1. Baseline data of PTMC patients [n (%), mean ± SEM]

Factors	n	Control group (n=42)	Observation group (n=48)	χ^2/t	P
Sex				1.220	0.265
Male	19	11 (26.19)	8 (16.67)		
Female	71	31 (73.81)	40 (83.33)		
Age (years old)				0.465	0.495
<30	31	16 (38.10)	15 (31.25)		
≥5	59	26 (61.90)	33 (68.75)		
Average age (years old)	90	32.14±6.54	34.56±7.06	1.679	0.097
Disease course (years)	90	3.52±0.51	3.58±0.77	0.429	0.669
Tumor site				0.384	0.535
Left	46	20 (47.62)	26 (54.17)		
Right	44	22 (52.38)	22 (45.83)		
Tumor diameter (cm)	90	0.72±0.17	0.75±0.20	0.710	0.476
Residence				0.809	0.369
Urban areas	69	34 (80.95)	35 (72.92)		
Rural areas	21	8 (19.05)	13 (27.08)		
Drinking history				0.864	0.353
No	34	18 (42.86)	16 (33.33)		
Yes	56	24 (57.14)	32 (66.67)		

Note: PTMC, Papillary Thyroid Microcarcinoma.

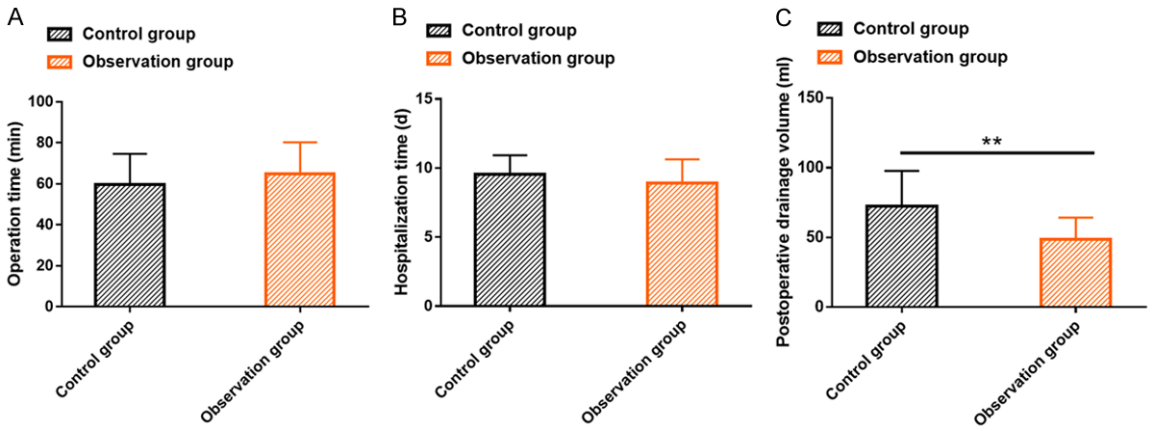

Figure 1. Comparison of surgical indicators between the two groups of patients. A. Operation time of the control group and observation group. B. Hospitalization time of the control group and observation group. C. Postoperative drainage volume of the control group and observation group. Note: **P<0.01.

Comparison of serum CRP, WBC and ESR between the two groups of patients

Serum CRP, WBC and ESR levels were measured before and 2 days after surgery (**Figure 2**). The data showed no significant difference before treatment between groups (P>0.05). Postoperatively, their levels elevated significantly in both groups (P<0.05), but the postoperative improvement degree was not significantly different between the OG and the CG (P>0.05).

Comparison of VAS, VSS and satisfaction scores between the two groups of patients

VAS, VSS, and satisfaction scores were measured 2d postoperatively (**Figure 3**). The OG showed more significant postoperative pain relief and less scarring than the CG (P<0.05).

Table 2. Complications in PTMC patients [n (%)]

Categories	Control group (n=42)	Observation group (n=48)	χ^2 value	*P* value
Haematoma	1 (2.38)	1 (2.08)	-	-
Transient hoarseness	2 (4.76)	1 (2.08)	-	-
Infection	2 (4.76)	3 (6.25)	-	-
Temporary recurrent laryngeal nerve injury	1 (2.38)	0 (0)		
Transient hypothyroidism	3 (7.14)	1 (2.08)		
Total incidence	9 (21.42)	6 (12.49)	1.286	0.257

Note: PTMC, Papillary Thyroid Microcarcinoma.

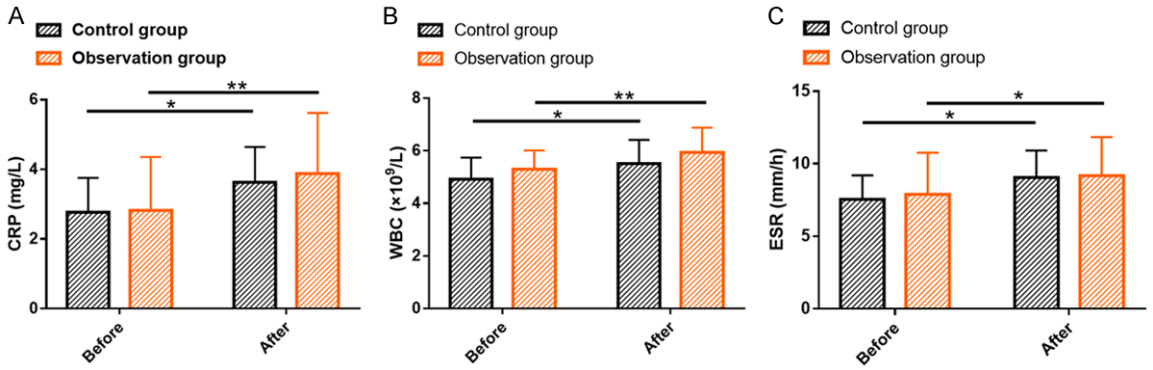

Figure 2. Comparison of serum indices between the two groups of pateints. A. CRP of the two groups of patients. B. WBC of the two groups of patients. C. ESR of two groups of patients. Note: *P<0.05; **P<0.01. CRP, C-Reactive Protein; WBC, White Blood Cell Count; ESR, Erythrocyte Sedimentation Rate.

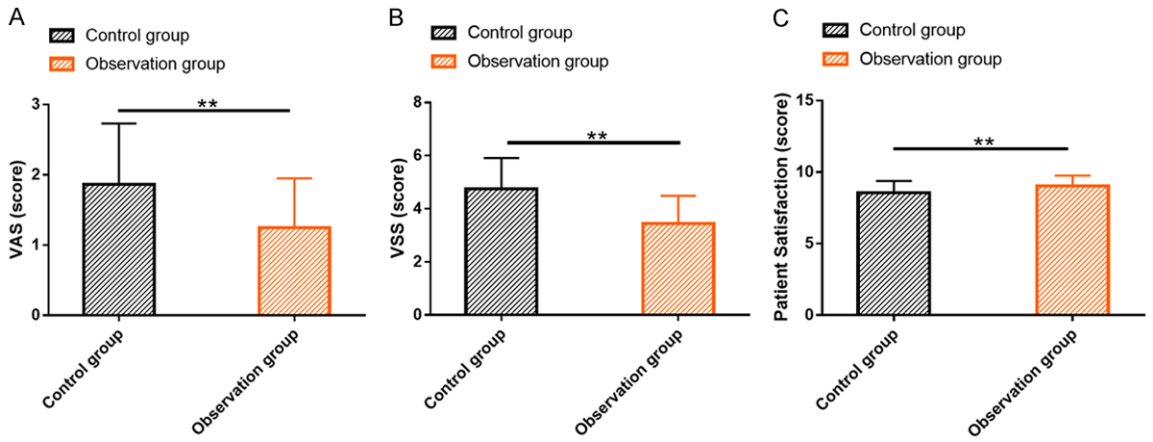

Figure 3. Comparison of VAS, VSS and satisfaction scores between the two groups of patients. A. VAS scores of patients 2 days after operation. B. VSS scores of patients 2 days after operation. C. Postoperative satisfaction scores of patients. Note: **P<0.01. VAS, Visual Analogue Scale; VSS, Vancouver Scar Scale.

Besides, patients in the OG were more satisfied with the treatment they received (P<0.05).

Comparison of SF-36 score between the two groups of patients

The SF-36 score was assessed 3 months postoperatively (**Figure 4**). The data showed that after treatment, the eight-dimensional scores of PF, RP, BP, GH, VT, SF, RE, and MH in the OG were significantly higher than those in the CG (P<0.05).

Discussion

Recent years have witnessed the growing global incidence of thyroid cancer, with the majority being PTC [16]. Of the increased PTC cases,

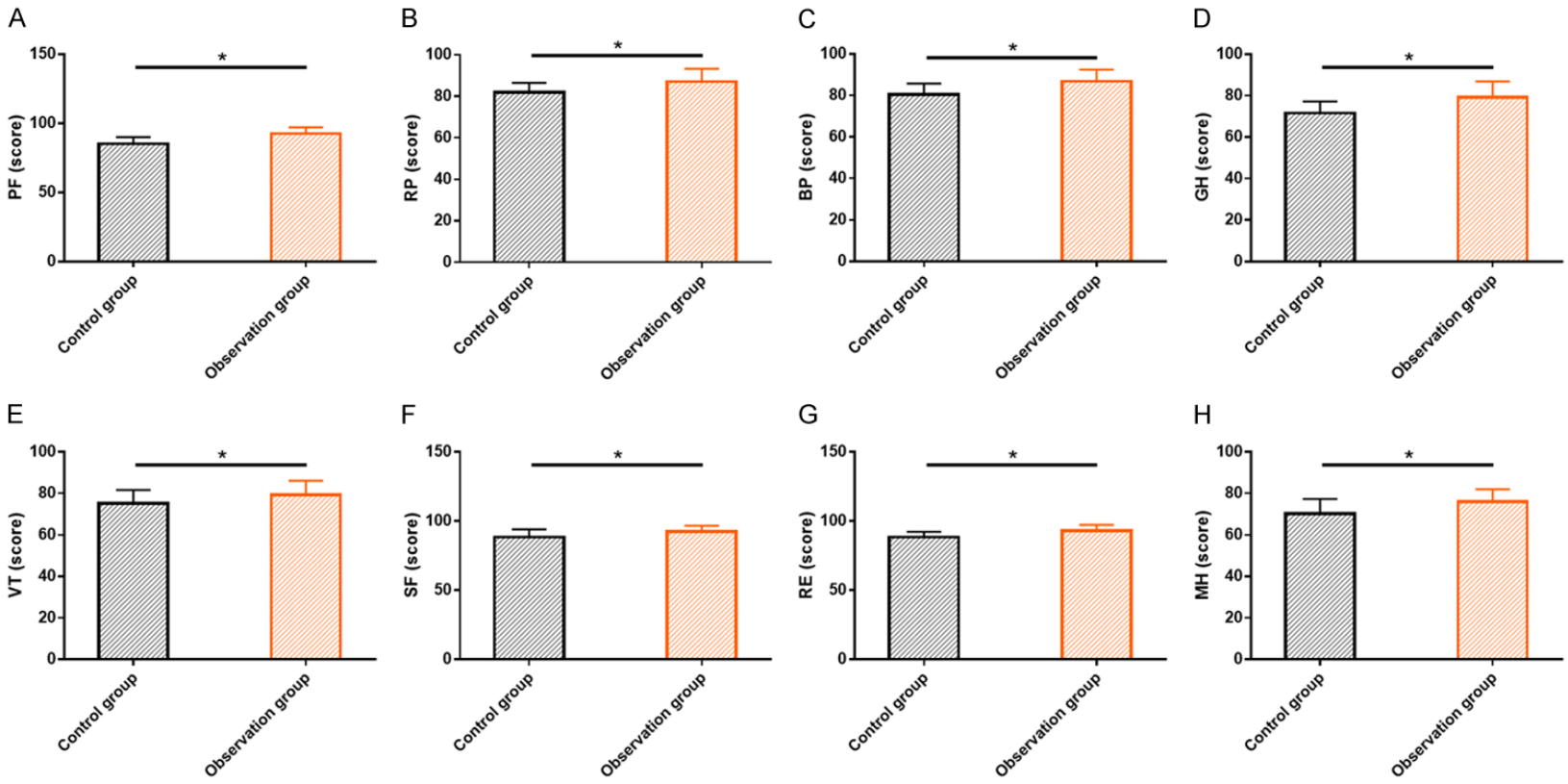

Figure 4. Comparison of SF-36 scores between the two groups of patients. A. PF scores of patients 3 months after operation. B. RP scores of patients 3 months after operation. C. BP scores of patients 3 months after operation. D. GH scores of patients 3 months after operation. E. VT scores of patients 3 months after operation. F. SF scores of patients 3 months after operation. G. RE scores of patients 3 months after operation. H. MH scores of patients 3 months after operation. Note: *P<0.05. PF, Physical Functioning; RP, Role Physical; BP, Bodily Pain; GH, General Health; VT, Vitality; SF, Social Functioning; RE, Role Emotional; MH, Mental Health.

PTMC patients are reported to account for 32.1%, which is associated with the advancement of detection technology [17]. At present, most guidelines recommend thyroidectomy for treatment regardless of PTMC staging, but routine thyroidectomy often has problems such as significant pain or scarring, so optimizing PTMC treatment is of great significance [18]. This study mainly analyzed the serum levels, complications, VAS, VSS scores and other clinical indicators of PTMC patients, hoping to find effective, safe and aesthetic surgical methods for PTMC.

In our study, the OT and LOS of OG that were treated by TOETVA were similar to those of the CG that were treated by endoscopic thyroidectomy via the transthoracic areola approach, but the postoperative drainage volume was significantly lower in the OG, indicating that TOETVA can significantly reduce the postoperative drainage volume, which may be related to the relatively small wound surface and flap separation area of the procedure. In addition, we recorded the complications that occurred during treatment. The results identified that although insignificantly, the complication rate was lower in the OG than in the CG (12.49% *vs.* 21.42%), suggesting that changing the approach did not affect the safety, which was consistent with the results reported by Akritidou et al. [19] on the complications of TOETVA. We also measured pre- and post-operative serum CRP, WBC and ESR levels. It was found that postoperatively, the three indices increased markedly but showed no distinct difference between groups. It suggests that the two surgical approaches have similar effects on stress response. In PTC patients, higher ESR levels were suggested to be associated with poorer overall survival, elevated CPR levels were shown to be related to recurrence, and significant increases in WBC which were often in response to trauma, infection, and inflammation, etc. [20-22]. In our research, the three indexes increased significantly after operation. Karakas et al. [23] reported that WBC, CRP and other indexes increased markedly after oral operation, but most of them returned to normal levels within days.

It is noteworthy that there was a significant difference in the VAS score between groups, indicating that TOETVA can significantly reduce postoperative pain. Previous studies suggest that the reason for the decline of VAS score is that TOETVA has a smaller incision than other surgical methods, which allows for effective hemostasis and postoperative pain relief [24]. While ensuring the treatment effect and safety, we recorded the VSS score of patients and found a statistically lower VSS score in the OG, which means less scarring in patients undergoing TOETVA. This is because the OG was treated by an oral vestibular approach, with no body surface scars after surgery. Moreover, compared with transthoracic areola surgery, the separation area under TOETVA procedure is small, which will not affect oral function. So TOETVA has a significant advantage in the patient satisfaction survey. The results of SF-36 score showed that the OG had statistically better quality of life in all aspects than the CG. Similarly, Kasemsiri et al. [25] mentioned in their study on transoral thyroidectomy that TOETVA can improve patients' quality of life, which also leads to significantly higher overall satisfaction of patients.

The novelty of this study lies in the comparative evaluation of the clinical effects of TOETVA and endoscopic thyroidectomy via the transthoracic areola approach on PTMC patients in terms of surgical indicators, complications, serum indicators, as well as VAS, VSS, postoperative patient satisfaction and SF-36 scores. Although this work confirmed that TOETVA for PTMC patients can help improve serum indices, relieve pain, enhance aesthetic effects, postoperative satisfaction, and quality of life, there is still room for improvement. First of all, only 90 patients were included, so the number of subjects needs to be expanded to improve the accuracy of the study results. Second, this study is a single-center study, which is prone to information bias. The future research will be improved based on the above two points.

In summary, while being as effective and safe as endoscopic thyroidectomy via the transthoracic areola approach for PTMC, TOETVA can more significantly reduce the pain of patients and improve their quality of life without leaving scars, which is more popular among patients in clinical application and thus is worthy of clinical popularization.

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Disclosure of conflict of interest

None.

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