

# Effect of Modified Miccoli's Thyroidectomy on Post-Operative Stress Responses and Quality of Life in Patients with Differentiated Thyroid Cancer

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**AIM:** Differentiated thyroid cancer (DTC) is a type of thyroid cancer with rapid progression and poor prognosis, and effective clinical treatment is of great significance in safeguarding the prognostic health of patients. Therefore, we assessed the effect of modified Miccoli's thyroidectomy on stress responses and quality of life in DTC patients, aiming to provide a more comprehensive reference for future DTC treatment.

**METHODS:** This study retrospectively analyzed 100 DTC patients admitted to our hospital from January 2023 to December 2023. Study participants were divided into two groups: The research group (n = 57) receiving modified Miccoli's thyroidectomy and the control group (n = 43) receiving routine open thyroidectomy. Surgical indexes (incision length, operative time, intraoperative bleeding, and the number of lymph nodes dissected) and post-operative indexes (post-operative pain, drainage volume, and hospitalization time) were comparatively assessed between the two experimental groups. Furthermore, stress response-associated indexes and immune function were evaluated before and after surgery. Additionally, the post-operative quality of life was investigated in both experimental groups.

**RESULTS:** The research group showed higher operative time but smaller incision length, less intraoperative bleeding, lower post-operative pain scores, less drainage volume, and shorter hospitalization time than the control group ( $p < 0.05$ ). Furthermore, we observed reduced post-operative stress responses, better immune function, and higher quality of life scores in the research group compared to the control group ( $p < 0.05$ ).

**CONCLUSIONS:** Modified Miccoli's thyroidectomy can effectively alleviate post-operative stress responses in DTC patients and promote their post-operative rehabilitation and quality of life.

**Keywords:** differentiated thyroid cancer; modified Miccoli's thyroidectomy; stress response; quality of life; immune function

## Introduction

Thyroid cancer (TC) is the most common malignancy of the endocrine system, accounting for 1.1% of all systemic cancers. It originates from the thyroid follicular epithelium and often manifests as a painless neck mass or nodule [1]. The 2022 World Epidemiological Survey indicates that the incidence of TC ranges from 4.7 to 13.7/100,000, with an increasing trend over the years [2]. Pathologically, TC is divided into differentiated thyroid cancer (DTC) and undifferentiated TC. Among them, DTC is a tumor close to normal thyroid tissue with mild severity and is a common type of disease in clinical practice, accounting for about 60%–70% of all TC cases [3]. Compared to ordinary TC, DTC progresses more rapidly and has a worse prognosis, thus, timely treatment is required to protect the patient's life [4]. With the rapid development of minimally invasive techniques, the modified Miccoli's thyroidectomy has achieved significant attention for TC treatment. This procedure

which uses an energy system, allows for a conventional thyroidectomy through a 3 cm neck incision. It is recognized as an ideal surgical procedure, integrating surgical safety, radical tumor treatment, minimal invasiveness, and wound aesthetic benefits. This modified procedure offers the advantages of smaller incisions, less impact on aesthetics, shorter post-operative recovery time, and milder discomfort compared to conventional surgery [5]. However, due to its complexity and high requirements for clinicians and specialized equipment, this procedure has not been widely used in primary hospitals [6]. Additionally, clinical references are limited due to the scanty reports on the effectiveness of modified Miccoli's thyroidectomy for DTC.

Based on this, we investigated the impact of modified Miccoli's thyroidectomy on post-operative stress responses and quality of life in DTC patients, providing a more comprehensive reference for future clinical treatment of DTC and promoting the widespread use of the procedure in future TC treatment.

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## Materials and Methods

### Study Population

This retrospective study included 100 DTC patients admitted to our hospital from January 2023 to December 2023. The study participants were divided into the research group (n = 57) and the control group (n = 43). The patients in the research group underwent modified Miccoli's thyroidectomy, while those in the control group underwent routine open thyroidectomy. The study was conducted in strict compliance with the Declaration of Helsinki and has obtained approval from the Ethics Committee of The People's Hospital of Leshan (approval number: KY2021-07-06). Additionally, each study participant provided a signed informed consent form.

### Inclusion and Exclusion Criteria

The predetermined inclusion criteria included: (1) The confirmed diagnosis of DTC through pathological examination, (2) eligibility for modified Miccoli's thyroidectomy or open surgery [7], (3) patients aged >18 years, (4) patients with a single lesion, (5) patients with clinical stages I-II, (6) those with no surgical contraindications, (7) tolerance to anesthesia, and (8) those with no autoimmune deficiencies. Exclusion criteria include: (1) Those with a history of radiotherapy or chemotherapy, (2) vital organ lesions, (3) hematologic diseases, (4) coagulation dysfunction, (5) history of neck trauma, and (6) psychiatric disorders.

### Surgical Procedures

Surgical procedure for the research group: Under general anesthesia with tracheal intubation (induced with midazolam 0.05 mg/kg + atracurium cis-benzenesulfonate 0.2 mg/kg + sufentanil 0.3 µg/kg + propofol 1.2 mg/kg, followed by successful conventional tracheal intubation, and maintained with propofol 1–3 mg/kg intraoperatively), the patients were placed in a supine position with the shoulders raised, head tilted back, and neck extended to fully expose the neck. After routine skin preparation and draping, a 2 cm transverse incision was made 1.5 cm above the suprasternal notch, followed by sequential skin and subcutaneous tissue cutting. A portion of the subcutaneous fat was then removed, the platysma was incised and carefully dissociated, and the skin flap was retracted. The linea alba cervicalis was opened, and the anterior cervical muscle group was retracted using an automatic retractor. The operation space was established under the endoscope using the suspension method. The thyroid isthmus was then cut with an ultrasonic scalpel with the assistance of the endoscope. The affected gland lobe was slightly retracted to the opposite side, and the middle, superior, and inferior arterial veins of the thyroid gland were severed with the ultrasonic scalpel. After this, the affected lobe was removed. The central lymph nodes were dissected, and bleeding was stopped to complete thyroid lobectomy. The recurrent laryngeal nerves and parathyroid glands were protected dur-

ing the procedure. After ensuring thorough hemostasis, a catheter was placed for drainage, and the wound was sutured layer by layer. Lastly, routine anti-infection treatment was performed post-operatively.

Surgical procedure for the control group: A routine open thyroidectomy under general endotracheal anesthesia was performed, with the patient's position similar to that of the research group. After routine skin preparation and draping, a transverse arc incision of about 5–8 cm in length was made along the transverse lines of the neck. The skin, subcutaneous tissue, and platysma were incised layer by layer. The flap was freed and retracted, the linea alba cervicalis was opened, and the anterior cervical muscles were pulled with a retractor. Subsequently, the isthmus of the thyroid gland was cut off by the ultrasonic scalpel and bluntly dissociated, revealing the affected thyroid gland lobe. Following the routine resection of the affected lobe, central lymph node dissection was performed. After thorough hemostasis, an indwelling drainage tube was placed, and the wound was sutured layer by layer. Patients received routine anti-infective therapy after surgery.

### Blood Sample Collection and Analysis

Venous blood was collected into pro-coagulation tubes before and 12 hours after surgery. The blood sample was centrifuged, and the resultant serum was divided into two parts: One part was assessed for anti-thyroglobulin antibodies (TGAb) and anti-thyroid peroxidase antibody (TPOAb) using an automatic electrochemiluminescence analyzer. In contrast, the other part was analyzed for superoxide dismutase (SOD) (SBJ-H0249), glutathione peroxidase (GSH-Px) (SBJ-H0208), malondialdehyde (MDA) (SBJ-H0336), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) (SBJ-H0132), and interleukin-6 (IL-6) (SBJ-H0465) using corresponding enzyme-linked immunosorbent assay (ELISA) kits. These kits were purchased from Nanjing Sembega Biotechnology Co., Ltd. (Nanjing, China), and the procedures followed the manufacturer's instructions.

### Endpoint Observations

Endpoint observations were determined as follows:

Surgical treatment: The incision length, procedure duration, intraoperative bleeding, and number of lymph nodes dissected were documented.

Post-operative indicators: Post-operative pain was assessed using the Visual Analogy Scale (VAS) [8]. Post-operative drainage volume and hospitalization time were also recorded.

Stress responses: The levels of SOD, GSH-Px, MDA, TNF- $\alpha$ , and IL-6 were evaluated before and after the procedure.

Immune function: TGAb and TPOAb levels were assessed before and after the operation.

Quality of life: One month after surgery, the quality of life of patients was examined using the European Organization for Research and Treatment of Core Quality of Life Ques-

**Table 1. Comparison of baseline characteristics between the two experimental groups.**

Variables	Control group (n = 43)	Research group (n = 57)	$\chi^2$ or <i>t</i>	<i>p</i> -value
Age (years)	47.2 ± 5.7	47.8 ± 5.7	0.521	0.603
Diameter of tumor (cm)	1.55 ± 0.45	1.60 ± 0.43	0.564	0.574
Sex			0.162	0.687
Male	16 (37.21%)	19 (33.33%)		
Female	27 (62.79%)	38 (66.67%)		
Type of tumor			0.912	0.340
Papillary	39 (90.70%)	48 (84.21%)		
Follicular	4 (9.30%)	9 (15.79%)		
Place of residence			0.070	0.792
Urban	23 (53.49%)	32 (56.14%)		
Rural	20 (46.51%)	25 (43.86%)		

tionnaire (QLQ-C30) [9]. This questionnaire includes five domains: Physical, role, social, cognitive, and emotional functioning, with higher scores indicating better outcomes.

#### Statistical Analysis

The data were statistically analyzed using SPSS 24.0 (IBM, Armonk, NY, USA), with statistical significance determined by a *p*-value < 0.05. Count data were expressed as [n (%)] and analyzed using a chi-square test to compare between groups. The Shapiro-Wilk test of normality was used for continuous data, and all continuous data in the text obeyed a normal distribution. Measurement data were presented as mean ± standard deviation ( $\bar{x} \pm s$ ) and analyzed using independent sample *t*-test for between-group comparison and paired *t*-test for within-group comparison.

## Results

#### Comparison of Baseline Characteristics between the Two Groups

There were no significant differences in age, gender, tumor type, and tumor diameter between the two experimental groups (*p* > 0.05, Table 1).

#### Comparison of Surgical Indexes between the Two Experimental Groups

There was no significant difference in the number of lymph nodes dissected (*p* > 0.05) between the two experimental groups. Furthermore, the research group showed longer operative time but had a smaller incision length and less intraoperative bleeding than the control group (*p* < 0.05, Fig. 1).

#### Comparison of Post-Operative Indexes between the Two Experimental Groups

We observed that the post-operative VAS score, post-operative drainage volume, and hospitalization time were significantly reduced in the research group compared to the control group (*p* < 0.05, Fig. 2).

#### Comparison of Stress Responses between the Two Experimental Groups

No significant differences were found between groups in the levels of SOD, GSH-Px, MDA, TNF- $\alpha$ , and IL-6 before surgery (*p* > 0.05). However, SOD and GSH-Px levels were significantly alleviated in both groups after surgery, with higher levels in the research group compared to the control group. In contrast, MDA, TNF- $\alpha$ , and IL-6 were increased in both groups, with substantially lower levels in the research group (*p* < 0.05, Fig. 3).

#### Comparison of Immune Function between the Two Experimental Groups

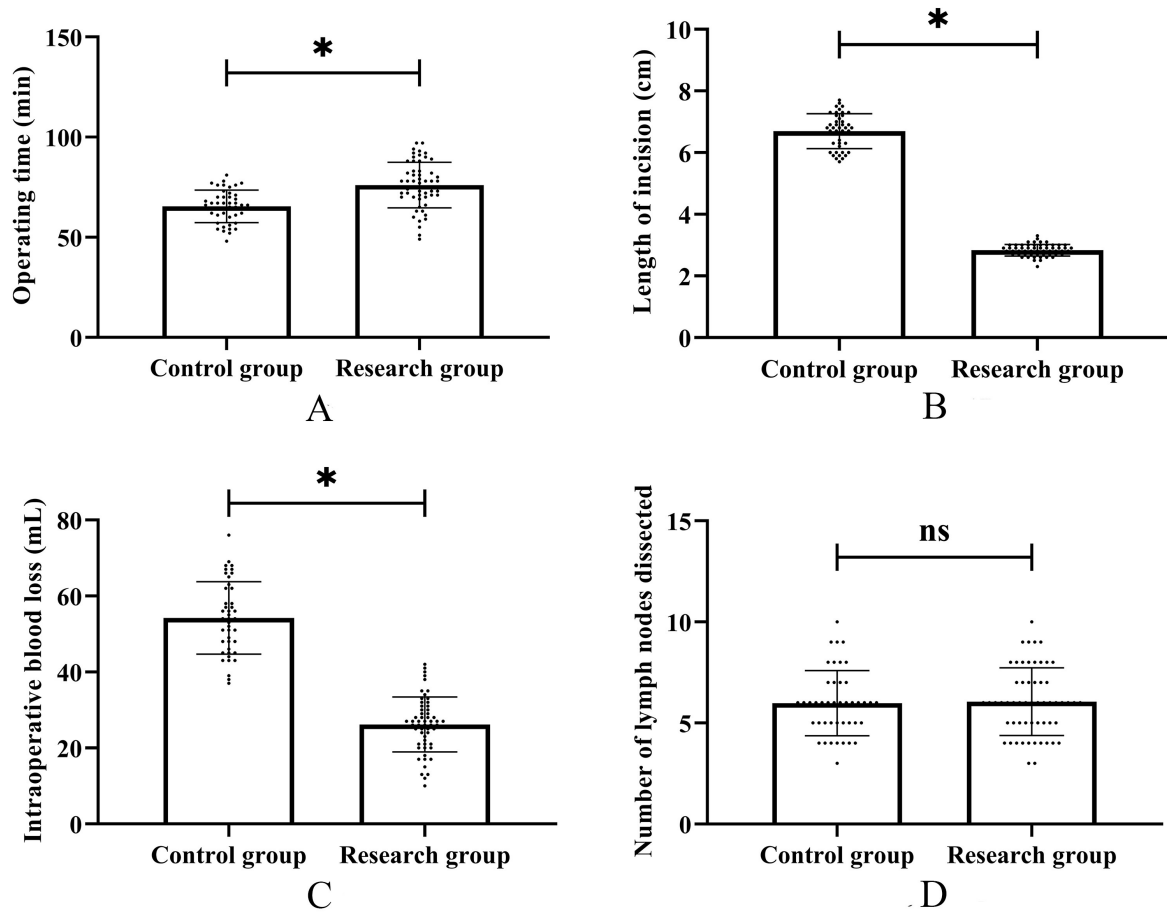
The preoperative TGAb and TPOAb levels were similar between the two groups (*p* > 0.05). However, after surgery, TGAb and TPOAb levels in both groups increased, with considerably lower in the research group compared to the control group (*p* < 0.05, Fig. 4).

#### Comparison of Quality of Life between the Two Experimental Groups

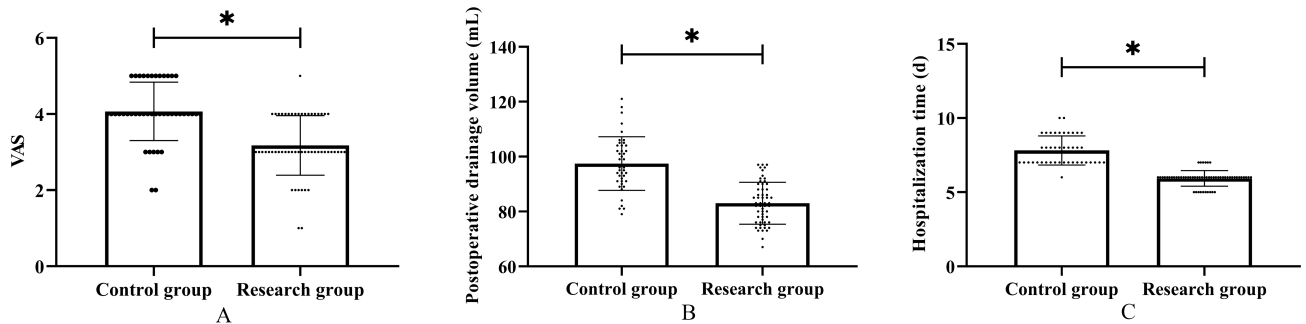
The QLQ-C30 survey revealed that the research group had substantially higher physical, role, emotional, cognitive, and social functioning scores than the control group (*p* < 0.05, Fig. 5).

## Discussion

In this study, the modified Miccoli's procedure effectively alleviated stress responses and improved quality of life in DTC patients, indicating its significant clinical value. Initially, we compared the surgical outcomes between the experimental groups of patients. The number of lymph nodes dissected was found to be consistent between the two groups. Although the operative time of the research group was longer compared to the control group, the incision length was smaller and the intraoperative bleeding was less, indicating significantly lower surgical trauma in the research group compared to the control group. Conventional thyroidectomy requires a large incision approximately two fingers above the suprasternal fossa, offering a clear surgi-



**Fig. 1. Comparison of surgical indexes between the two groups.** (A) Operative time, (B) incision length, (C) intraoperative blood loss, (D) number of lymph nodes dissected. \* $p < 0.05$ , <sup>ns</sup> $p > 0.05$ .

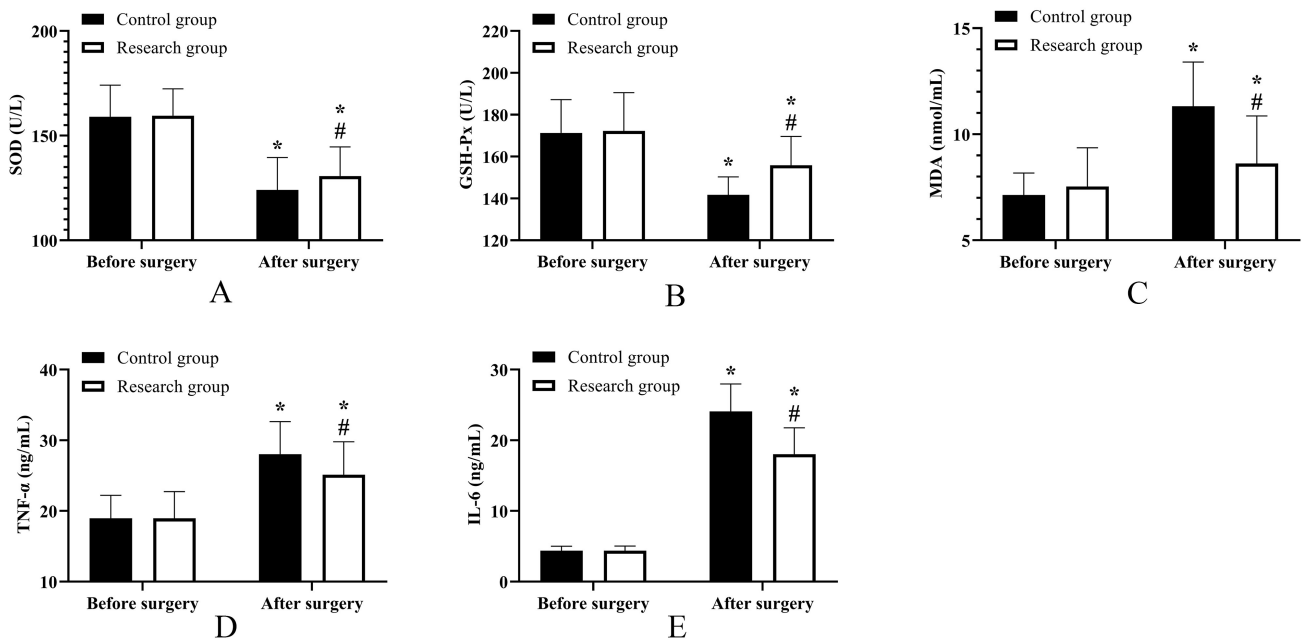


**Fig. 2. Comparison of post-operative indexes between the two groups.** (A) VAS, (B) post-operative drainage volume, (C) hospitalization time. \* $p < 0.05$ . VAS, Visual Analogy Scale.

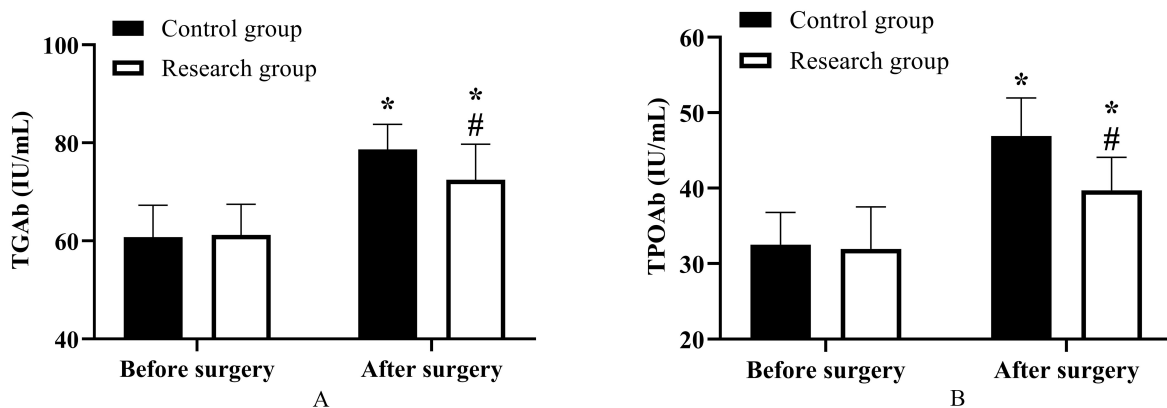
cal field to directly access and remove the affected thyroid gland lobe and isthmus. Although this technique allows for a direct approach, it involves a relatively larger incision which can impact the appearance of the patient.

Additionally, separating the skin flap under the platysma muscle during the procedure can result in substantial bleeding and increased trauma [10]. The modified Miccoli's thyroidectomy method can fully expose the surgical field by creating a cavity in the patient's neck and inserting a

5 mm endoscope. This method allows surgeons to accurately assess the size and position of the tumor, resulting in a smaller incision, alleviated bleeding, and improved clinical outcomes than conventional surgery [11, 12]. The cavity construction technique utilized in Miccoli's procedure provides a stable and adjustable working chamber, ensuring smooth surgical progress and leveraging the advantages of the minimally invasive approach. This approach ensures effective surgical intervention while minimizing the risk of



**Fig. 3. Comparison of stress responses between the two groups.** (A) SOD, (B) GSH-Px, (C) MDA, (D) TNF- $\alpha$ , (E) IL-6. \* $p < 0.05$  vs before surgery, # $p < 0.05$  vs control group. SOD, superoxide dismutase; GSH-Px, glutathione peroxidase; MDA, malondialdehyde; TNF- $\alpha$ , tumor necrosis factor- $\alpha$ ; IL-6, interleukin-6.

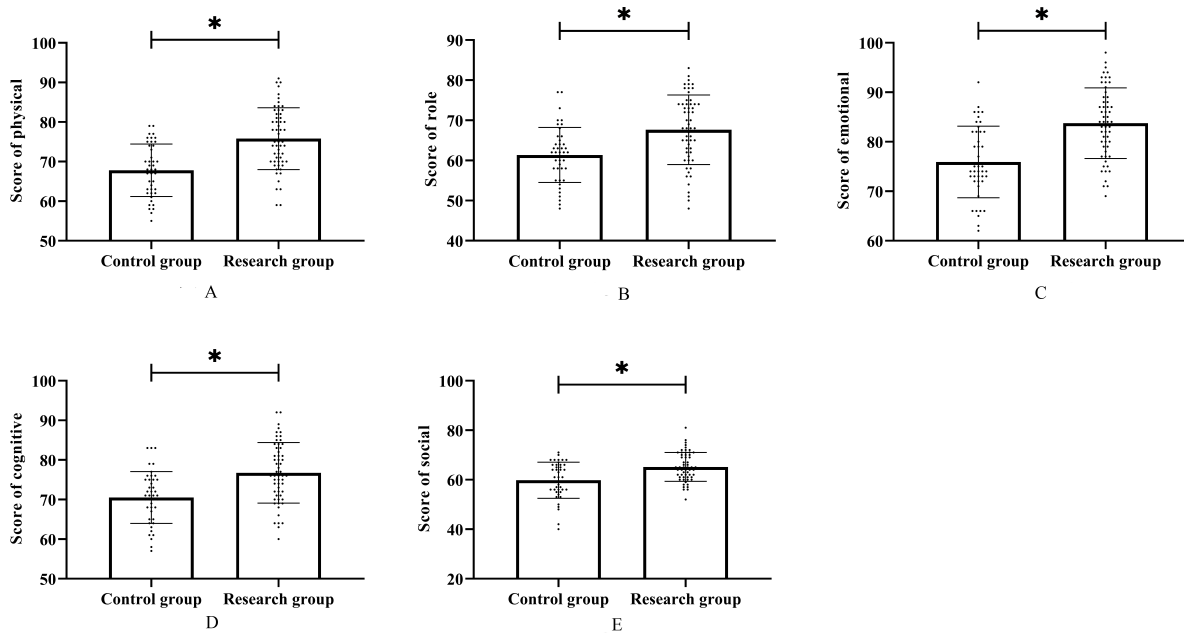


**Fig. 4. Comparison of immune function between the two groups.** (A) TGAb, (B) TPOAb. \* $p < 0.05$  vs before surgery, # $p < 0.05$  vs control group. TGAb, anti-thyroglobulin antibodies; TPOAb, anti-thyroid peroxidase antibody.

excessive intraoperative bleeding and large incisions. Consequently, the post-operative indexes in the research group were lower than those of the control group, suggesting that modified Miccoli's thyroidectomy positively influences the reduction of the post-operative rehabilitation process for DTC patients.

In comparing stress responses, the research group exhibited considerably lower post-operative levels of MDA, TNF- $\alpha$ , and IL-6 and higher levels of SOD and GSH-Px compared to the control group. These observations suggest that modified Miccoli's thyroidectomy leads to less stress damage to patients. This is because the incision under the modified Miccoli's procedure is located low in position and small in size (2.0 cm), with no need for extensive free flaps. Moreover, the lens of the endoscope and the illumination of the

light source can obviously enlarge the surgical field on the monitor screen, which is conducive to precise operations and comparison of adjacent nerves and blood vessels, as well as identification and protection of important tissues during surgery. Consequently, the modified Miccoli's procedure can reduce surgical trauma and inflammatory responses, thus accelerating post-operative recovery [13, 14]. Similarly, Yu H *et al.* [7] reported the excellent therapeutic outcomes of modified Miccoli's thyroidectomy in treating thyroid diseases, which aligns with our findings. In the subsequent comparison of immune function, TGAb and TPOAb in the research group were also lower compared to the control group, suggesting that modified Miccoli's thyroidectomy is more conducive to maintaining the stability of immune function in patients. The study by Miccoli P and



**Fig. 5. Comparison of quality of life between the two groups.** (A) Score of physical, (B) score of roles, (C) score of emotional, (D) score of cognitive, (E) score of social. \* $p < 0.05$ .

Bakkar S [15] observed that the modified Miccoli's procedure uses an ultrasonic scalpel to remove the lesion, which helps to vaporize tissue fluid and disintegrate cells. Therefore, modified Miccoli's thyroidectomy does not require sutures or ligation to cut the relevant vascular tissues, thus reducing the levels of TGAb and TPOAb. Additionally, Shen X *et al.* [16] in early 2013 proposed that modified Miccoli's thyroidectomy enhances safety and stabilizes patients' immune function post-operatively compared to conventional thyroid cancer surgeries, supporting our observation.

Finally, in investigating the quality of life, the research group scored higher than the control group, indicating a better prognosis for patients in this group. This improvement is due to the modified Miccoli's procedure, which offers enhanced safety and effective clinical outcomes, thus reducing stress damage and immune disorders in post-surgical patients and providing a more reliable guarantee for their post-operative rehabilitation and prognostic health. The findings of our study align with those of Miccoli P *et al.* [17] and Rossi L *et al.* [18], further supporting our viewpoint.

However, in the future clinical treatment of DTC with modified Miccoli's thyroidectomy, strict attention must be given to the following issues: (1) It is necessary to strictly adhere to the indications for the modified Miccoli's procedure and standardize the surgical operation. (2) The recurrent laryngeal nerves must be exposed throughout the operation to prevent permanent damage. When managing the superior and inferior thyroid arteries, it is necessary to approach the gland closely and ligate each branch individually to protect the blood supply to the parathyroid gland. For tissues that

cannot be identified as parathyroid glands, an intraoperative frozen section examination should be performed. (3) It is recommended to use intraoperative nerve detection technology and parathyroid protection measures to minimize the risk of intraoperative damage to the recurrent laryngeal nerves and parathyroid glands. (4) Calcium supplements and vitamin D should be administered after surgery to prevent transient hypocalcemia caused by temporary hypothyroidism.

Additionally, due to the small sample size in this study, there may be incidental findings. We plan to increase the number of cases for confirmation analysis. Meanwhile, we need to extend the follow-up period to evaluate the impact of modified Miccoli's thyroidectomy on the long-term prognosis of DTC patients. In the future, more in-depth and comprehensive research and analysis will be conducted on the clinical application of the modified Miccoli's procedure, providing more reliable references and guidance for clinical practice.

## Conclusions

Modified Miccoli's thyroidectomy is highly effective in treating DTC and is recommended as the first choice for TC treatment, as it can effectively relieve patients' post-operative stress responses, maintain immune function stability, promote post-operative rehabilitation, and improve quality of life.

## Availability of Data and Materials

The data used and/or analyzed during the current study are available from the corresponding author.

## Author Contributions

LH was responsible for conceptualizing the study, developing the methodology, supervising the work, and reviewing and editing the manuscript. XZ was responsible for data curation, formal analysis, conducting the investigation, and writing the original draft of the manuscript. YL was responsible for validating the results, providing resources, data visualization, and writing the original draft of the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Ethics Approval and Consent to Participate

The study was conducted in strict compliance with the Declaration of Helsinki and approved by Ethics Committee of The People's Hospital of Leshan (KY2021-07-06). Additionally, each study participant provided a signed informed consent form.

## Acknowledgment

Not applicable.

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## Conflict of Interest

The authors declare no conflict of interest.

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