The effects of radiofrequency ablation on lymphocytes, subsets and cytokines in patients with thyroid cancer: A meta-analysis

B. Miao, G. Ruan*, F. Meng, Q. Zhang, J. Pei, D. Li

Breast & Thyroid & Head and Neck Surgery, Affiliated Hospital of Shaoxing University, Shaoxing, 312000, China

▶ ***Original article***

****Corresponding author:***
Gangqiang Ruan,
E-mail:
ruangangqiang0711@126.com

Received: November 2023
Final revised: February 2024
Accepted: March 2024

Int. J. Radiat. Res., January 2025; 23(1): 1-12

DOI: 10.61186/ijrr.23.1.1

Keywords: *Thyroid cancer, Radiofrequency ablation, Lymphocytes and sub-populations, Cytokines, Meta-analysis.*

ABSTRACT

Background: To systematically evaluate the effects of radiofrequency ablation on lymphocytes, subsets, and cytokines in patients with thyroid cancer. ***Materials and Method:*** Radiofrequency ablation, thyroid cancer, lymphocytes, and other key terms are used to search for randomized controlled clinical trials (RCTs) related to them.The data analysis is conducted using RevMan 5.3 software. The relative risk (RR) is used to analyze the effect magnitude of binary variable data. The mean difference (MD) represents the continuous variable data results. The interval estimation is presented as 95% CI. ***Results:*** The standardized mean difference between the CD3+, CD4+, sub-population counts, and CD4+/CD8+ratios among the studies was 1.91 (95% CI0.91 ~ 2.91), 0.07(95% CI-0.07 ~ 0.22). The combined effect quantity indicated that radiofrequency ablation had a significant effect on improving lymphocytes and sub-populations in thyroid cancer patients.The heterogeneity test results among different studies were I2 = 99%, 99%, P < 0.01 and 0.32. The results indicated a high level of heterogeneity between the two groups. The standardized mean difference of cytokine levels such as IL-6 and TNF-a in different studies was -4.20 (95% CI-4.30 ~ -4.10), -6.40 (95% CI-7.07 ~ -5.77). The combined effect quantity indicated that radiofrequency ablation had a significant effect on reducing serum inflammatory cytokine levels in thyroid cancer patients.The heterogeneity test results between different studies were I2 = 100%, 97%, and P < 0.01. The results indicated a high level of heterogeneity between the two groups. The differences between groups are statistically significant (x2 = 4.48, P < 0.01). ***Conclusion:*** Compared with other surgeries, radiofrequency ablation can inhibit CD4+, promote CD8+lymphocyte proliferation, and reduce inflammatory factors in thyroid cancer patients.

INTRODUCTION

Thyroid cancer is one of the most common malignant tumors of endocrine system. The incidence rate is increasing year by year (1). According to the pathological characteristics, it can be classified into Papillary Thyroid Cancer (PTC) (2), Follicular Thyroid Cancer (FTC), Medullary Thyroid Cancer (MTC) (3), and Anaplastic Thyroid Cancer (4). In addition, there is also a type of Thyroid Follicular Epithelial Neoplasm. It includes FTC and Follicular Thyroid Adenoma (5). Pathological classification is crucial for determining treatment plans, predicting prognosis, and selecting appropriate treatment methods (6).

Among various pathological subtypes of thyroid cancer, Papillary Thyroid Cancer (PTC) usually has the best prognosis (7). In recent years, the incidence rate of Thyroid Micro-carcinoma (TMC) has been rising. Approximately 49% of new cases are TMC, of which 75% are Papillary Thyroid Micro-carcinoma (PTMC), which means PTC with a diameter of no more than 10 millimeters (8). Recent research shows that PTMC accounts for about 30.0%~60% of the incidence rate of PTC. Thyroid micro-carcinoma refers to thyroid cancer where the diameter of the lesion does not exceed 10 millimeters. This cancer usually has occult properties because the cancer lesion is small and difficult to detect through clinical palpation (9). Among them, PTMC refers to papillary carcinoma with a diameter of no more than 1 cm. It is also one of the most common pathological types (10).

PTMC is a special type of papillary carcinoma. The biological characteristics are similar to papillary carcinoma, with high tissue differentiation and relatively low malignancy. However, there is a higher risk of cervical lymph node metastasis (11). This cancer is more common among female patients (12). Most PTMCs are found in an asymptomatic state, which is not significantly different from normal healthy individuals (13). Research has shown that approximately 28% to 55% of PTMC are accompanied by cervical lymph node metastasis (14). Although PTMC usually has a good prognosis, treatment and follow-up are still crucial, especially

[DOI: 10.61186/ijrr.23.1.1]

for patients with lymph node metastasis [15]. The treatment and follow-up plan should be developed based on the specific situation of the patient to ensure the best treatment effect [16].

Radiofrequency ablation, as a local treatment method, has received widespread attention in the treatment of thyroid cancer in recent years [17]. Although radiofrequency ablation has achieved some success in eliminating thyroid cancer lesions, the impact on the immune system has not been fully elucidated [18]. Lymphocytes, their sub-populations, and cytokines play key roles in the immune response. However, the impact of radiofrequency ablation on these immune parameters remains controversial in thyroid cancer patients [19].

Lymphocytes, their sub-populations, and cytokines are one of the predictive indicators of treatment response and prognosis in thyroid cancer patients. There is a close relationship between immune monitoring, anti-tumor immunity, Treg cells, and immune regulation in thyroid cancer patients [20]. Cytokines play a role in tumor immune escape and drug resistance, thereby affecting treatment response and prognosis.

Radiofrequency ablation, as a minimally invasive method for treating thyroid cancer, has many unique features. Firstly, this method utilizes advanced ablation techniques that can quickly and accurately destroy diseased tissue, effectively reducing the volume of thyroid nodules, improving symptoms, and even potentially replacing surgical treatment [21]. Secondly, radiofrequency ablation uses microwave or high-power radiofrequency energy to damage cells within the lesion, which is a non-invasive therapy with advantages such as non-invasive, safe, rapid recovery, and less pain. In addition, this technology only requires local anesthesia or general anesthesia, which has little impact on the whole body and relatively low surgical risks [22].

To comprehensively learn the impact of radiofrequency ablation on the immune system of thyroid cancer patients, a meta-analysis is conducted. The aim is to systematically summarize and analyze existing literature, and evaluate the effects of radiofrequency ablation on lymphocyte count, sub-population distribution, and cytokine levels in thyroid cancer patients. By integrating multiple independent research data, it is expected to provide more convincing evidence to gain a deeper understanding for the potential impact of radiofrequency ablation on the immune status of thyroid cancer patients, providing scientific basis for clinical practice and treatment strategy development. The results of this study are expected to provide a new perspective for the treatment of thyroid cancer patients and provide guidance for the application of immune regulation in cancer treatment.

MATERIALS AND METHODS

General information

Inclusion criteria: The research types are clinical research, including randomized controlled trials, prospective research, cohort research, *etc* The subjects were thyroid cancer patients, regardless of age, gender, and duration of the disease. Intervention measures: Radiofrequency ablation is the main treatment method. Control group: including data comparison before and after treatment in the control group. Measurement indicators include the number of lymphocytes, proportion of lymphocyte sub-populations (such as CD4+, CD8+, *etc*.), and cytokine levels (such as IL-6, TNF-α, IL-10, *etc*.). Provide sufficient data: The research report provides sufficient data, including sample size, mean, standard deviation, etc. Thyroid cancer types: papillary thyroid carcinoma, undifferentiated thyroid carcinoma, follicular thyroid carcinoma, *etc*.

Exclusion criteria: Research type: retrospective studies, case reports, comments, edited articles, and other non-clinical studies Subjects: Non thyroid cancer patients or patients with other diseases ③Intervention measures: Other treatment interventions except for radiofrequency ablation Insufficient data: The data provided in the research report is insufficient for meta-analysis Language limitation: Research only includes specific languages.

Methods

Determine keywords: Firstly, a set of related keywords are identified, including terms and synonyms, to cover various aspects of the research topic. In this study, keywords can include "radiofrequency ablation", "thyroid cancer", "lymphocytes", "sub-populations", "cytokines", "immune system", etc. Retrieve the RCTs of the effects for radiofrequency ablation and conventional radiotherapy and chemotherapy on lymphocytes, sub -populations, and cytokines in thyroid cancer patients at home and abroad. Database selection: Select appropriate medical databases for retrieval, such as PubMed, Web of Science, Embase, *etc*. These databases contain a large amount of medical literature, covering a wide range of research fields. Search strategy: The search date is as of June 2023. The selected keywords are used to construct appropriate retrieval strategies. There is an example of a possible retrieval strategy, ("radiofrequency association") AND, ("thyroid cancer") AND, ("lymphocytes") AND, ("subgroup") AND, "cytokines") and ("immune system").

[DOI: 10.61186/ijrr.23.1.1]

Data extraction

Research information: Basic information such as author, year of publication, and research location. Study design: Randomized controlled trials, prospective cohort studies, or other types of studies. Sample size: The number of subjects in the intervention group and control group. Intervention measures: Specific methods and procedures for radiofrequency ablation. Lymphocyte and sub-population data: The number and changes of lymphocytes before and after treatment, such as CD4+ and CD8+ before and after treatment. Cytokine data: Changes in cytokines before and after treatment, such as IL-6 and TNF-α IL-10, *etc*. Data processing: If the literature provides mean and standard deviation, these data are used directly. If the literature provides other forms of data (such as median and range), it can be converted as needed. When extracting data, it is recommended to use a data extraction table or tool to ensure that the data of each study can be accurately recorded and facilitate subsequent statistical analysis. Meanwhile, the data extraction process is transparent and replicable to enhance the reliability of meta-analysis.

Literature quality evaluation

Research design: Evaluate the research design of each study, such as the randomness of randomized controlled trials and the traceability of prospective cohort studies. A high-quality research design can increase the reliability of the study. Sample size: Consider whether the sample size of each study is large enough to support the statistical significance of the results. A larger sample size can reduce the impact of accidental errors. Data collection and analysis: Evaluate whether the data collection process for each study is rigorous, whether the data has undergone statistical analysis. Reasonable data collection and analysis methods can help reduce bias. Control variables: Pay attention to whether each study has adequately controlled for important variables that may affect the results to reduce the impact of confounding factors. Result report: Check whether the results of each study fully report the main observations, avoiding selective reporting of results. Method bias risk assessment: Use tools such as Cochrane Collaboration's Risk of Bias Tool to assess the methodological bias risk of each study, including randomization process, allocation concealment, blinding, *etc*. Publication bias assessment: Consider whether each study may be affected by publication bias, meaning that unpublished studies may not be easily accessible, thereby affecting the comprehensiveness of the results. Based on the above evaluation factors, a quality scoring tool can be used to comprehensively consider each factor and assign a quality score to each study. These evaluation factors help evaluate the credibility and applicability of the study for authoritative summary and analysis in meta-analysis. It should be noted that quality evaluation should be conducted independently by two researchers to reduce the impact of subjective bias. In literature quality assessment, the "Bias Risk Graph" and "Bias Risk Summary Graph" are used to measure the risk of various biases. These biases include selection bias, implementation bias, measurement bias, follow-up bias, reporting bias, and other biases. Each bias risk is divided into three levels: "low risk", "unknown risk", and "high risk".

When evaluating the risk level, the following criteria are adopted: "Low risk" refers to a multi-center randomized controlled trial. The researchers and/or subjects are blinded, and the evaluation method and outcome are blinded, with fewer lost contacts. "High risk" indicates a lack of blinding in retrospective studies. There are many people who are lost during the research process, or the research results report is incomplete. "Unknown risk" indicates insufficient information and cannot be clearly classified as the two risk levels mentioned above.

Through these evaluation methods, a more comprehensive understanding for the risk of each study can be obtained, ensuring that possible bias factors are considered in the meta-analysis, thereby improving the credibility and scientificity of the analysis results.

Statistical analysis

RevMan 5.3 software is used for meta-analysis. The data results extracted from the included literature are summarized and analyzed. For the results of binary variable data, Relative Risk (RR) is used as the effect measure indicator. For continuous variable data, the Mean Difference (MD) is used to represent the results. The interval estimation uses a 95% confidence interval (CI).

When conducting heterogeneity analysis, X^2-test is applied. Based on the P-value, the heterogeneity is determined. When $P \geq 0.1$, $F^2 \leq 50\%$, it is considered that the heterogeneity test results are not statistically significant, and a fixed effects model is chosen. When $P \leq 0.1$, $P \geq 50\%$, the heterogeneity test results have statistical significance, and a random effects model is used. In addition, if the number of included literature reaches or exceeds 10, a funnel plot will be drawn to analyze the publication bias of the included study.

RESULTS

Literature search and screening results

Related literature was searched and a total of 1121 articles were obtained. Except for duplicate articles and preliminary abstract screening, 75 articles remained. Literature that did not meet the inclusion criteria were excluded, resulting in 19 articles. The literature retrieval process is shown in figure 1.

[DOI: 10.61186/ijrr.23.1.1]

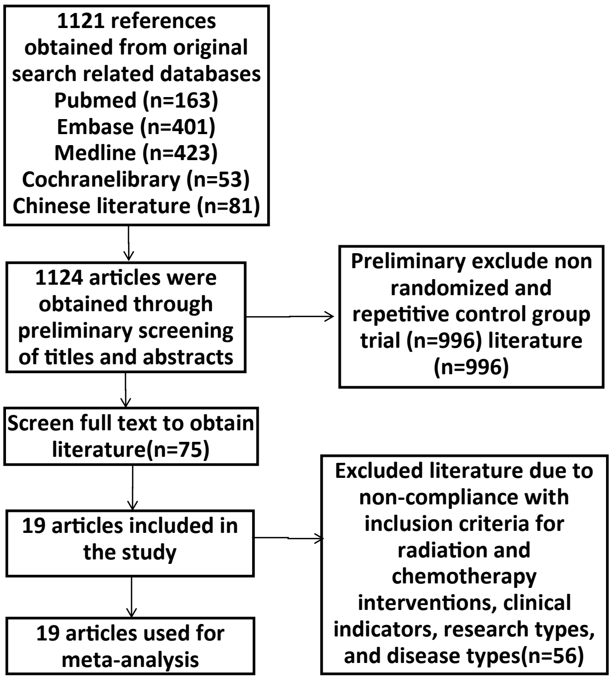


Figure 1. Literature retrieval process.

Basic features included in the literature

There were a total of 1726 study subjects, divided into a group of 880 patients who received radiofrequency ablation intervention and a control group of 846 patients. The specific information of the selected literature is shown in table 1.

Literature quality evaluation

After analyzing the research reports of 19 randomized controlled trials (RCTs), these reports have certain biases or deficiencies in several key aspects. The following elaborates on these shortcomings and evaluates them in detail. Firstly, regarding the concealment of random sequences, this is an important step in ensuring research fairness. However, in these reports, the concealment of random sequences is not sufficiently done. This may lead to potential biases affecting the research results, thereby reducing the external validity of the study. In order to improve the quality of research, future research should pay more attention to the concealment of random sequences. Secondly, in the

Table 1. Basic information of included literature.

Literature	Cases T(Male/Female)	Cases C(Male/Female)	Age (years) T	Age (years) C	Intervention measures T	Intervention measures C	Outcome indicators (Subgroup count, cytokines, complications)
Hou Li 2018 [23]	32/18	32/18	30-71 (52.4±2.4)	30-71 (52.3±2.3)	Radiofrequency ablation	Hepatic artery chemoembolization method	Peripheral blood immune cell sub-populations (CD3+, CD4+, CD4+ /CD8+) Cytokines level (IL-6, TNF-α)
Shi Kaiyuan 2018 [24]	7/21	5/19	19-78 (35.51±14.70)	18-68 (34.59±13.32)	Radiofrequency ablation	Surgical resection	Complications
Yang Xiaohong 2022 [25]	16/23	14/25	20-69 (58.34±13.79)	19-71 (59.32±15.13)	Ultrasound guided radiofrequency ablation	Ultrasound guided microwave ablation	IL-6、TNF-a
Lu Yanyan 2021 [26]	13/22	12/23	26-68 (41.35±1.05)	25-67 (41.34±1.06)	Ultrasound guided radiofrequency ablation	Minimally invasive surgery under endoscopy	TNF-α, IL-6, complications
Du Zhuofeng 2021 [27]	13/24	11/26	31-59 (45.42±6.12)	32-57 (44.62±5.97)	Radiofrequency ablation	Resection	IL -6, TNF-α, Serum thyroid hormone levels (FT_3, FT_4, TSH), complications
Sun Ping 2018 [28]	20-27	18/21	29-61 (42.66±4.19)	27-63 (43.09±5.14)	Radiofrequency ablation	Ultrasound guided microwave ablation	IL-6, TNF-a
Wang Heng 2021 [29]	12/22）	12/23	29-40 (35.70±1.03)	30-41 (35.63±1.01)	Radiofrequency ablation	Traditional thyroidectomy	FT_3, FT_4, TSH, complication
Ma Deqing 2020 [30]	5/47	6/44	20-50 (38.24±5.32)	20-50 (36.25±6.37)	Radiofrequency ablation	Traditional Resection surgery	FT_3, FT_4, TSH, complications
Zhao Xiaoyong 2017 [31]	23/15	25/13	25-70 (54.23±5.48)	25-70 (54.77±5.12)	Radiofrequency ablation	Subtotal thyroidectomy	TSH, FT_3, FT_4
Wan Yufeng 2023 [32]	17/25	20/22	27-65 (43.80±4.55)	30-63 (43.16±5.12)	Radiofrequency ablation	Routine surgical resection	FT_3, FT_4, TSH,TNF-a, IL-6, complications
Zhao Xiaoli 2022 [33]	10/41	11/40	27-67 (47.35±7.65)	26-66 (46.14±7.35)	Radiofrequency ablation	Surgical resection	FT_3, FT_4, TSH, TNF-a, IL-6, complication
Gong Hai 2019 [34]	23/52	26/53	32-64 (49.67±7.39)	31-62 (49.32±7.48)	Radiofrequency ablation	Ultrasound guided microwave ablation	TSH, FT_3, FT_4, TNF-a, IL-6, complications
Zhu Bo 2015 [35]	10/36	12/34	19-52 (36.25±1.42)	19-52 (35.44±1.56)	Radiofrequency ablation	Ultrasound guided microwave ablation	IL-6, TNF-a
Bao Xiaoyao 2021 [36]	11/29	13/27	41-78 (53.45±3.16)	42-78 (53.47±3.19)	Radiofrequency ablation	Ultrasound guided microwave ablation	Complications
Zhang Xinying 2020 [37]	29/31	27/33	32-68 (48.30±5.70)	32-65 (47.80±5.40)	Radiofrequency ablation	Ultrasound guided microwave ablation	Complications
Zhang Wenjie 2022 [38]	12/29	14/27	21-68 (46.82±6.33)	23-66 (46.65±6.25)	Radiofrequency ablation	Surgical resection	TSH, FT_3, FT_4, complications
Zhou Huisheng 2020 [39]	11/40	14/36	20-62 (42.16±10.28)	19-67 (44.72±9.94)	Radiofrequency ablation	Surgical resection	Complications
Shao Chunmei 2011 [40]	24/50	13/27	26-56 (40.20±4.20)	26-55 (41.20±4.7)	Radiofrequency ablation	Conventional therapy	CD3+, CD4+, CD4+ /CD8+
hang Lidan 2018 [41]	18/32	16/34	25-79 (52.73±12.25)	25-77 (51.38±12.35)	Radiofrequency ablation	Conventional therapy	CD3+, CD4+, CD4+ /CD8+

Note: CD3+: Cluster of Differentiation 3 positive cells; CD4+: Cluster of Differentiation 4 positive cells; CD4+ /CD8+: Cluster of Differentiation 4 positive cells/ Cluster of Differentiation 8 positive cells; IL-6: Interleukin-6; TNF-α: Tumor necrosisfactor-α; CRP: C-reaction protein; TSH: Thyroid stimulating hormone; FT_3: Free triiodothyronine; FT_4: Free thyroxine; T: Radiofrequency ablation intervention; C: Routine intervention.

[DOI: 10.61186/ijrr.23.1.1]

description of random methods, some reports did not provide detailed descriptions, which made the research process less transparent. Improving transparency helps ensure research quality. Therefore, future research should focus on elaborating the process of the random method in detail. In addition, some reports also have certain shortcomings in the blinding of outcome indicator evaluators. Blindness is an important means of evaluating the reliability of research results. If the evaluator does not conduct a blind evaluation, it may affect the reliability of the research results. Therefore, future research should strengthen the implementation of evaluator blinding. In terms of bias risk assessment, existing research reports are not yet clear. To better evaluate the bias risk, each stage of the research process should be thoroughly analyzed to ensure the reliability of the research results. The number of high-quality literature selected for research is relatively small. This phenomenon has affected the overall quality of the article. Therefore, it is recommended that future research pay more attention to quality control, improving the overall quality of research in the literature screening process. The detailed content is shown in figure 2.

Meta-analysis results

The effect of radiofrequency ablation on lymphocyte and subgroup counts

In the current study, a total of 19 references were included. The aim is to explore the effects of radiofrequency ablation on lymphocytes and subsets in patients with thyroid cancer. Among the 19 articles, 3 articles included "lymphocytes and sub-populations". Radiofrequency ablation has a significant effect on improving lymphocytes and subsets in patients with thyroid cancer. The standardized mean differences between researches for CD4+, subgroup count, and CD4+/CD8+ ratio were 1.91 (95% CI 0.91-2.91) and 0.07 (95% CI -0.07 -0.22), respectively. The intergroup effect is statistically significant (Z = 3.75, 0.99, P = 0.001, 0.32). The combined effect quantity indicated that radiofrequency ablation had a significant effect on improving lymphocytes and sub-populations in thyroid cancer patients. However, there is high heterogeneity among various studies. The heterogeneity test results were I^2=99%, 99%, P<0.01, 0.32. This indicates that although radiofrequency ablation has a significant effect on improving lymphocytes and subsets in thyroid cancer patients, there are still some differences in the results among different studies. To present the results of these studies more intuitively, figures 3 and 4 are drawn.

The effect of radiofrequency ablation on cytokine levels in patients with thyroid cancer

In the current study, a total of 9 relevant literatures are included to explore the impact of radiofrequency ablation on cytokine levels in patients with thyroid cancer. To ensure the reliability of the research results, the "cytokine levels" in these literature is used as the main observation indicators for in-depth analysis. In analyzing various studies, attention is paid to cytokines such as IL-6 and TNF-a. After standardization, the mean differences between the studies were -4.20 (95% CI -4.30 ~ -4.10) and -6.40 (95% CI -7.07 ~ -5.77). This indicates that radiofrequency ablation has a significant effect in reducing serum inflammatory cytokine levels in patients with thyroid cancer. At the same time, statistical tests are conducted on the intergroup effect. The effect was significant (Z = 80.69, 19.42, P < 0.01). However, high heterogeneity was observed in various studies. The heterogeneity test results showed that the I^2 values were 100% and 97%, with P < 0.01. This indicates that there is high heterogeneity among studies in the effectiveness of radiofrequency ablation in reducing serum inflammatory cytokine levels in thyroid cancer patients. To illustrate this phenomenon more intuitively, figures 5 and 6 show in detail the heterogeneity between the studies.

Interventional effects of radiofrequency ablation and other therapies on complications

In the current study, a total of 11 relevant literatures are analyzed. The literature considers the incidence of postoperative complications as the main observation indicator. The incidence rate ratio of postoperative complications (OR) is 0.39 (95% CI 0.26 - 0.59). The difference between groups was statistically significant (x^2 = 4.48, P < 0.01). The heterogeneity test between different studies showed I^2 = 34%, P = 0.13. This result indicates significant differences among the studies. The incidence of postoperative complications has significantly decreased, indicating that the intervention measures adopted have to some extent improved the safety of surgery. Secondly, heterogeneity testing shows differences between studies, which helps to further explore the factors that affect the postoperative complications. This is to provide more accurate diagnosis and treatment recommendations for clinical doctors. To present this result more intuitively, a detailed forest map is drawn, as shown in figure 7.

The effect of radiofrequency ablation on serum thyroid hormone levels in patients with thyroid cancer

In the current study, 19 relevant literatures are focused on to explore the role of serum thyroid hormone levels in various diseases. For comparative analysis, 9 articles are selected. The research results of these literature are interpreted in detail. There was statistical heterogeneity among the studies

[DOI: 10.61186/ijrr.23.1.1]

(P=0.62, 1.85 and -1.44, I^2 = 75%, 99% and 100%). This indicates that the data distribution among studies is not completely consistent. This may be influenced by factors such as research methods, sample size, etc. Further analysis revealed a statistically significant difference (P<0.05) between the two groups, indicating that serum thyroid hormone levels may differ significantly in different disease states. To present this result more intuitively, figures 8, 9, and 10 are plotted, respectively, showing the data distribution and statistical analysis results in each study.

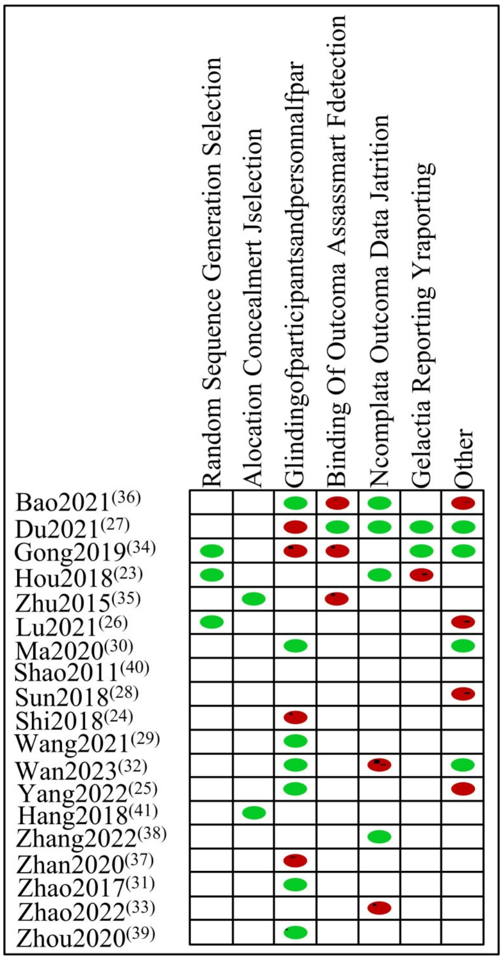


Figure 2. Bias risk assessment of in selected randomized controlled trials. "●" represents data points or regions with high bias risk. It refers to points that have a significant impact on the overall data or analysis results, or deviate from the expected range, indicating anomalies, errors, or uncertainties in the data that require special attention and further investigation. "●": represents data points or regions with low bias risk. It refers to points that are consistent with the overall data or analysis results, or within the expected range. This is considered to be a relatively reliable and trustworthy data, with little impact on the overall results. The figure shows that in the included RCTs, some studies do not adequately describe the blinding implementation, which may lead to measurement bias. There is a bias risk in data collection and processing in some studies. Data collection and processing are crucial steps in the experimental results, ensuring the integrity and accuracy of the data. During the data collection process, researchers need to follow standardized operating procedures and take effective quality control measures. There is a bias risk in the interpretation and conclusion for some studies. The interpretation and conclusion of the results are based on inference from experimental data. It is necessary to ensure its objectivity and impartiality. When interpreting the results, researchers need to consider various possible bias risks and make appropriate interpretations and inferences about the results.

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV.Fixed.95%CI
Bao2021(36)	40.3	9.2	50	31.5	5.1	50	11.7%	8.80[5.09,11.72]
Shao2011(40)	34.1	3.1	74	38.1	3.8	40	50.8%	-4.00[-5.40,-2.50]
Hang2018(41)	43.35	4.12	50	35.57	4.2	50	37.5%	7.78[6.15,9.41]
Tolal(95% CI)			**174**			**140**	**100.00%**	**1.91[0.91,2.91]**

Heterogenity.Chi^2=139.69,df=2(P<0.001);I^2=99%

Test For Overall Efect Z=375(P=0.0002)

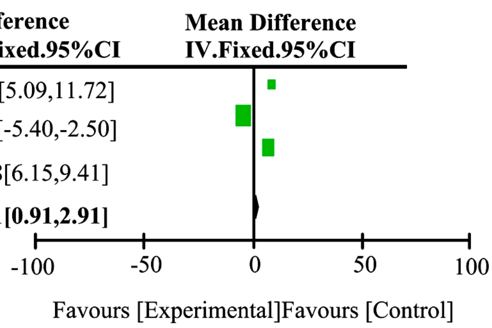
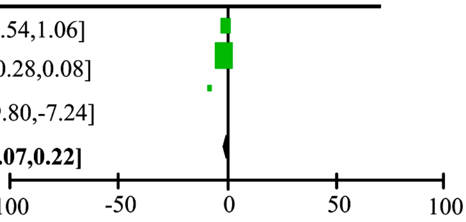


Figure 3. Intervention effect of radiofrequency ablation and other therapies on CD4+. This figure shows the standardized mean difference of CD4+ subgroup counts. From the figure, radiofrequency ablation has a significant effect on improving lymphocytes and subsets in thyroid cancer patients.

[DOI: 10.61186/ijrr.23.1.1]

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV.Fixed.95%CI
Bao2021[36]	1.9	0.8	50	1.1	0.5	50	31.7%	0.80[0.54,1.06]
Shao2011[40]	1.3	0.4	74	1.4	0.5	40	67.0%	-0.10[-0.28,0.08]
Hang2018[41]	21.17	3.02	50	29.69	3.5	50	1.3%	-8.52[-9.80,-7.24]
Tolal(95% CI)			**174**			**140**	**100.00%**	**0.07[-0.07,0.22]**

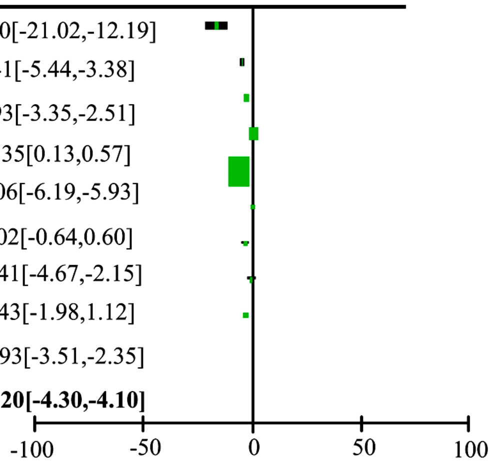


Heterogenity.Chi^2=206.01,df=2(P<0.001);I^2=99%

Test For Overall Efect Z=0.99(P=0.32)

Figure 4. Forest map of the intervention effect of radiofrequency ablation and other therapies on CD4+/CD8+. This figure shows the standardized mean difference of CD4+/CD8+ ratio and the heterogeneity testing results. In the figure, the I2 value is as high as 99%, indicating high heterogeneity among the studies. In addition, the P-value is less than 0.01, which indicates that the heterogeneity test results are statistically significant.

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV.Fixed.95%CI
Bao2021[36]	39.9	9.6	50	56.5	12.7	50	0.1%	-16.60[-21.02,-12.19]
Du2021[27]	7.92	2	37	12.33	2.48	37	1.0%	-4.41[-5.44,-3.38]
Gong2019[34]	4.41	1.32	75	7.34	1.34	79	5.9%	-2.93[-3.35,-2.51]
Zhu2015[35]	3.18	0.35	46	2.83	0.68	46	21.3%	0.35[0.13,0.57]
Lu2021[26]	4.07	0.26	35	10.13	0.28	35	64.9%	-6.06[-6.19,-5.93]
Sun2018[28]	4.36	1.26	47	4.38	1.61	39	2.7%	-0.02[-0.64,0.60]
Wan2023[32]	11.23	2.89	42	14.64	3.02	42	0.7%	-3.41[-4.67,-2.15]
Yang2022[25]	11.78	3.38	39	12.21	3.6	39	0.4%	-0.43[-1.98,1.12]
Zhou2020[39]	4.4	1.64	51	7.33	1.33	51	3.1%	-2.93[-3.51,-2.35]
Tolal(95% CI)			**422**			**418**	**100.00%**	**-4.20[-4.30,-4.10]**

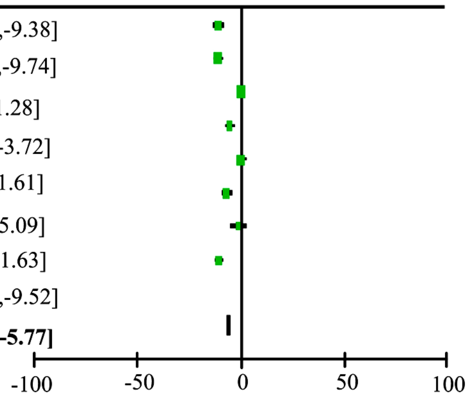


Heterogenity.Chi^2=2740.09,df=2(P<0.001);I^2=100%

Test For Overall Efect Z=80.69(P<0.001)

Figure 5. Forest map of the intervention effect of radiofrequency ablation and other therapies on IL-6. The horizontal axis represents the effect size of each study, and the vertical axis represents the study name. Each rectangle represents a study. The length represents the range of the 95% confidence interval. Radiofrequency ablation may have a more significant effect in reducing IL-6 compared to other therapies.

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV.Fixed.95%CI
Du2021[27]	38.44	4.45	37	49.8	4.26	37	10.7%	-11.36[-13.34,-9.38]
Gong2019[34]	34.18	4.03	75	45.43	5.48	79	18.3%	-11.25[-12.76,-9.74]
Zhu2015[35]	19.82	3.21	46	20.1	4.32	46	17.4%	-0.28[-1.84,1.28]
Lu2021[26]	39.42	4.27	35	45.14	4.26	35	10.5%	-5.72[-7.72,-3.72]
Sun2018[28]	34.11	3.98	47	34.25	4.25	39	13.7%	-0.14[-1.89,1.61]
Wan2023[32]	49.22	5.12	42	56.33	4.3	42	10.3%	-7.11[-9.13,-5.09]
Yang2022[25]	49.71	7.35	39	51.26	6.97	39	4.2%	-1.55[-4.73,1.63]
Zhao2017[31]	34.24	4.3	51	45.43	4.3	51	15.1%	-11.19[-12.86,-9.52]
Tolal(95% CI)			**372**			**368**	**100.00%**	**-6.42[-7.07,-5.77]**



Heterogenity.Chi^2=2740.09,df=2(P<0.001);I^2=100%

Test For Overall Efect Z=80.69(P<0.001)

Figure 6. Forest map of the intervention effect of radiofrequency ablation and other therapies on TNF-α. From the graph, radiofrequency ablation has a significant advantage in reducing TNF-α. Compared with other therapies, the intervention effect of radiofrequency ablation is numerically lower. This indicates that it can effectively control the TNF-α. In addition, the standard deviation of the intervention effect for radiofrequency ablation is relatively small, indicating that its results are relatively stable and reliable.

[DOI: 10.61186/ijrr.23.1.1]

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H.Fixed.95%CI
Bao2021(36)	15	40	17	40	13.6%	0.81[0.33,1.99]
Du2021(27)	6	37	7	37	7.5%	0.83[0.25,2.76]
Gong2019(34)	1	75	9	79	11.0%	0.11[0.01,0.85]
Lu2021(26)	1	35	9	35	11.2%	0.08[0.01,0.71]
Ma2020(30)	1	52	6	50	7.7%	0.14[0.02,1.24]
Shi2018(24)	3	28	5	24	6.1%	0.46[0.10,2.15]
Wang2021(29)	4	24	6	35	5.2%	0.97[0.24,3.87]
Wan2023(32)	3	42	7	42	8.3%	0.38[0.09,1.60]
Zhang2022(38)	4	41	4	41	4.6%	1.00[0.23,4.30]
Zhao2017(31)	1	51	13	51	16.3%	0.06[0.01,0.47]
Zhao2020(39)	2	51	7	50	8.7%	0.25[0.05,1.27]
Tolal(95% CI)		**476**		**484**	**100.00%**	**0.39[0.26,0.59]**
Tolal events	41		90			

Heterogenity.Chi^2=15.14,,df=10(P=0.13);I^2=34%

Test For Overall Efect Z=4.48(P<0.00001)

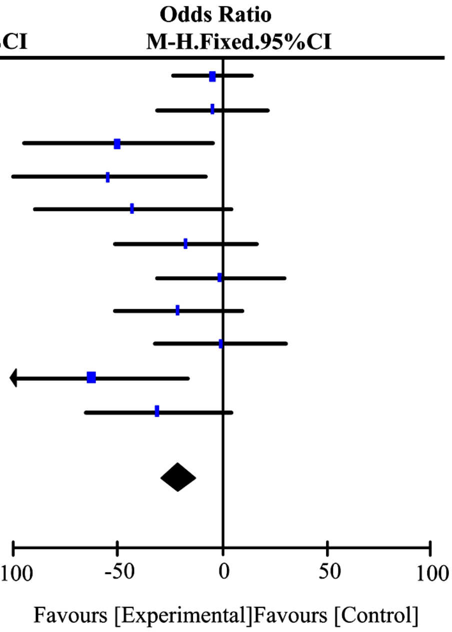


Figure 7. Forest map of the intervention effect of radiofrequency ablation and other therapies on complications. "◇" (representing radiofrequency ablation) is more inclined towards the lower right corner compared to other "●" (representing other therapies), indicating that radiofrequency ablation has better effects in reducing the incidence of complications.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV.Fixed.95%CI
Du2021(27)	4.64	0.6	37	3.86	0.66	37	8.1%	0.78[0.49,1.07]
Gong2019(34)	4.23	0.51	75	3.77	0.48	79	27.4%	0.46[0.30,0.62]
Ma2020(30)	5.1	0.62	52	4.69	0.72	50	9.8%	0.41[0.15,0.67]
Wang2021(29)	4.69	1.11	24	4.29	1.05	35	2.1%	0.40[-0.16,0.96]
Wan2023(32)	4.28	0.4	42	3.41	0.26	42	32.3%	0.87[0.73,1.01]
Zhang2022(38)	13.22	2.63	41	11.85	2.51	41	0.5%	1.37[0.26,2.48]
Zhao2022(33)	4.23	0.48	51	3.76	0.47	51	19.8%	0.47[0.29,0.65]
Tolal(95% CI)			**322**			**335**	**100.00%**	**0.62[0.54,0.70]**

Heterogenity.Chi^2=24.09,df=6(P=0.0005);I^2=75%

Test For Overall Efect Z=14.81(P<0.00001)

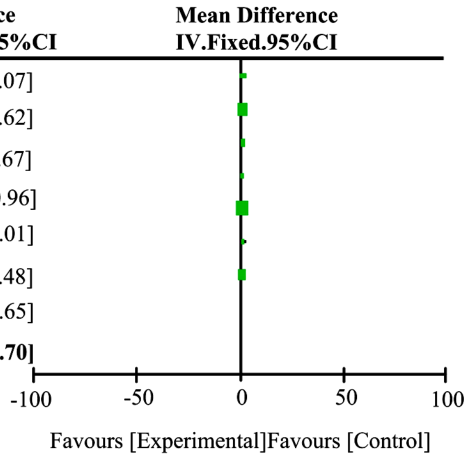


Figure 8. Forest map of the intervention effect of radiofrequency ablation and other therapies on FT_3. The horizontal axis represents radiofrequency ablation and other therapies. The vertical axis represents the change in FT_3. Each box represents the effect of a study or treatment method. The size of the box is proportional to the weight or sample size of the study. The horizontal line represents the 95% confidence interval (CI) of the effect magnitude. The central vertical line represents the average effect size of all studies. The vertical error line connects the effect magnitude and 95% CI of each study. From the graph, compared with other therapies, radiofrequency ablation has a more significant intervention effect on FT_3, with a higher effect magnitude than other therapies. The 95% CI of the effect magnitude of radiofrequency ablation is relatively narrow, indicating that the results of this study are more accurate. The intervention effects of other therapies on FT_3 vary greatly, with some showing significant effects and others not. The central vertical line leans towards radiofrequency ablation, indicating that radiofrequency ablation has the best average intervention effect on FT_3 among all studies.

[DOI: 10.61186/ijrr.23.1.1]

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV.Fixed.95%CI
Du2021[27]	12.37	1.78	37	10.5	2.12	37	3.9%	1.87[0.98,2.76]
Gong2019[34]	13	2.03	75	10.05	1.15	79	11.1%	2.95[2.43,3.47]
Ma2020[30]	15.09	0.91	52	13.8	0.86	50	26.0%	1.29[0.95,1.63]
Wang2021[29]	13.02	2.11	24	12.96	2.08	35	2.6%	0.06[-1.03,1.15]
Wan2023[32]	18.9	1.95	42	10.01	1.11	42	6.7%	8.89[8.21,9.57]
Zhang2022[38]	4.33	0.65	41	3.85	0.65	41	38.7%	0.48[0.20,0.76]
Zhao2017[31]	18.24	2.44	38	15.03	2.01	38	3.0%	3.21[2.20,4.22]
Zhao2022[33]	12.96	1.94	51	10.04	1.14	51	8.0%	2.92[2.30,3.54]
Tolal(95% CI)			**360**			**373**	**100.00%**	**1.85[1.67,2.02]**

Heterogenity.Chi²=560.54,df=7(P<0.00001);I²=99%

Test For Overall Efect Z=20.68(P<0.00001)

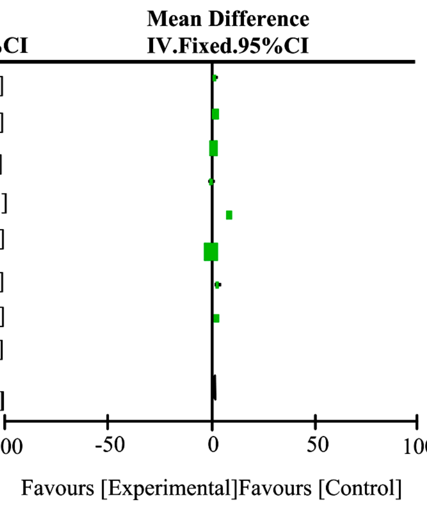


Figure 9. Forest map of the intervention effect of radiofrequency ablation and other therapies on FT_4.The horizontal axis represents the treatment method. The vertical axis represents the horizontal variation of FT_4. The bar chart corresponding to each treatment method shows its effectiveness in reducing FT_4. The height of the bar chart represents the FT_4reduction degree. The figure includes different treatment methods such as radiofrequency ablation, drug therapy, and dietary therapy. Each treatment method corresponds to a 95% confidence interval. From the forest plot, radiofrequency ablation has shown a good effect in reducing FT_4 levels, with the highest corresponding bar chart indicating the most significant effect in reducing FT_4. The bar charts corresponding to other treatment methods such as drug therapy and dietary therapy are lower, indicating that their effect in reducing FT_4 is not as good as radiofrequency ablation. In addition, each bar chart in the forest chart has a diagonal line, which represents the comparison results between different treatment methods. If there is no diagonal connection between the bar charts corresponding to two treatment methods, it indicates that there is no direct comparison result between these two treatment methods. From the graph, there are more comparison results between radiofrequency ablation and other treatment methods, indicating that its effect in reducing FT_4 has been supported by more research.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV.Fixed.95%CI
Du2021[27]	2.12	1.17	37	14.01	2.63	37	0.8%	-11.89[-12.82,-10.96]
Gong2019[34]	1.45	0.58	75	13.25	3.4	79	1.2%	-11.80[-12.56,-11.04]
Ma2020[30]	2.43	0.8	52	3.75	1.2	50	4.3%	-1.32[-1.72,-0.92]
Wang2021[29]	2.18	0.43	24	2.23	0.44	35	13.2%	-0.05[-0.28,0.18]
Wan2023[32]	2.04	0.22	42	3.23	0.22	42	76.0%	-1.19[-1.28,-1.10]
Zhang2022[38]	1.5	0.72	41	6.11	2.85	41	0.8%	-4.61[-5.51,-3.71]
Zhao2017[31]	2	1.25	38	3.51	1.2	38	2.2%	-1.51[-2.06,-0.96]
Zhao2022[33]	2.01	0.2	51	13.24	2.4	51	1.5%	-11.23[-11.89,-10.57]
Tolal(95% CI)			**360**			**373**	**100.00%**	**-1.44[-1.52,-1.36]**

Heterogenity.Chi²=2263.26,df=7(P<0.00001);I²=100%

Test For Overall Efect Z=34.45(P<0.00001)

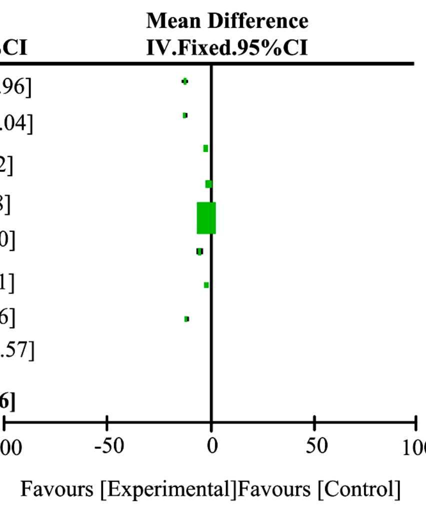


Figure 10. Forest map of the intervention effect of radiofrequency ablation and other therapies on TSH. The horizontal axis represents different treatment methods. The vertical axis represents changes in TSH levels. Each rectangular box represents a study, with its center position representing the effect value of the study and its length representing the confidence interval of the effect value. The color depth of the rectangular box indicates the size of the effect value. Dark color indicates a large effect value. From the graph, radiofrequency ablation has a significant advantage in intervening in TSH compared to other therapies. The effect value of radiofrequency ablation is the highest and its confidence interval is the narrowest, indicating that this method has the most stable and reliable intervention effect on TSH. In contrast, the effectiveness of other therapies such as drug therapy and surgical treatment is relatively limited. Their confidence intervals are wide. It indicates that there is significant uncertainty in the effectiveness for these methods.

Publication bias analysis

In medical research, complications are often important indicators for measuring treatment effectiveness and safety. To comprehensively evaluate the advantages and disadvantages of various treatment methods in preventing and treating complications, relevant literature is comprehensively analyzed. In this process, scatter plots are an effective method to visually compare the incidence of complications with treatment methods. However, publication bias in literature may affect the accuracy of scatter plots. Therefore, publication bias is detected. Publication bias refers to the uneven distribution of research results due to certain factors

[DOI: 10.61186/ijrr.23.1.1]

affecting their publication. In this case, the scatter plot may appear as an inverted funnel shape with asymmetry on both sides. This asymmetry indicates that some research results have not been published, which may lead to biased conclusions. Therefore, when conducting scatter plot analysis, attention should be paid to the shape of the funnel plot to determine whether there is publication bias. Figure 11 shows this process more intuitively.

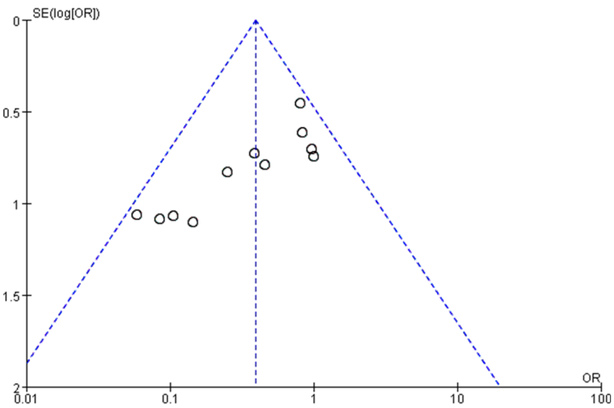


Figure 11. Publication bias of inclusion studies in funnel monitoring. There is a clear centerline in the figure, representing the ideal symmetry line. All data points should be as close to this line as possible to represent the symmetry and unbiased nature of the data. The data points in the figure represent the various studies included in the study. Under normal circumstances, these points should be evenly distributed on both sides of the centerline; From the graph, some data points clearly deviate from the centerline, indicating that there may be publication bias in these studies. The direction deviating from the centerline may indicate the direction of bias, such as bias towards positive or negative results. The left side represents the incidence of complications, while the right side represents the effectiveness of different treatment methods in preventing and treating complications. The inverted funnel plot shows an asymmetric phenomenon on both sides. It is important to be cautious of publication bias.

DISCUSSION

Radiofrequency ablation may affect the immune status of thyroid cancer patients, thereby affecting tumor development. Specifically, radiofrequency ablation may increase the proportion of CD3+, CD4+, and CD8+ lymphocytes by activating the immune response in the body. This is consistent with the study by Shen Ruichao *et al.* [42] that radiofrequency ablation can accelerate lesion coagulation, clear various inhibitory factors in the body, and improve the patient's immune response level. Lymphocytes and their subpopulations play an important role in immune monitoring, tumor development, and treatment response, which have significant clinical significance. Immune monitoring and anti-tumor immune response: Lymphocytes were the main component of the immune system. It could identify and attack abnormal cells, including cancer cells. In thyroid cancer patients, lymphocytes play an immune monitoring role by identifying and eliminating malignant thyroid cells, helping to suppress tumor growth and spread. CD4+and CD8+T cells: CD4+T cells played a crucial role in regulating immune responses. It could activate other immune cells, such as B cells and CD8+T cells, thereby enhancing the immune response. CD8+T cells were cytotoxic T cells that could directly recognize and kill tumor cells [43]. In thyroid cancer patients, the appropriate number and function of CD4+and CD8+T cells were crucial for controlling tumor growth [44]. Immunotherapy strategy: Lymphocytes had a potential role in immunotherapy for thyroid cancer. By activating the immune system, such as anti-PD-1/PD-L1 drugs, the anti-tumor activity of lymphocytes could be enhanced, improving the treatment effectiveness [45]. Prognostic assessment: The number and status of lymphocytes and their subpopulations could serve as important prognostic indicators for thyroid cancer patients. Some studies showed that high levels of CD8+T cell infiltration were associated with better prognosis, which reflected stronger immune response and tumor control capabilities [46]. In summary, lymphocytes and their subpopulations play important immune monitoring and regulatory roles in thyroid cancer patients, affecting tumor development and treatment response. Therefore, it is of great significance to deeply understand the immunological role of lymphocytes and their clinical application, which helps optimize treatment strategies and improve patient prognosis [47].

Cytokines play an important role in thyroid cancer patients, involving multiple aspects such as immune regulation, inflammatory response, tumor development, and treatment response. The following are the roles and significance of cytokines in thyroid cancer patients. Immunoregulation: It could activate immune cells and promote anti-tumor immune response [48]. In thyroid cancer patients, appropriate immune regulation may enhance the body's immune attack against tumors and inhibit tumor growth [49]. Inflammatory response: Some cytokines, such as tumor necrosis factor-α (TNF-α), Interleukin-6 (IL-6) and other cytokines were involved in regulating inflammatory responses. In thyroid cancer patients, abnormal inflammatory reactions may be associated with tumor development and progression, as the inflammatory environment may provide favorable growth conditions for the tumor [50]. Tumor microenvironment: Cytokines could shape the tumor microenvironment and affect the interaction between tumor cells and immune cells. The excessive secretion of certain cytokines might lead to immune suppression, allowing tumors to evade immune attacks, thereby promoting the development and spread of tumors [51]. Prognostic evaluation: The cytokines could be one of the important prognostic

[DOI: 10.61186/ijrr.23.1.1]

indicators for thyroid cancer patients. High levels of certain immune activated cytokines were associated with better prognosis, reflecting stronger immune response and tumor control capabilities. Treatment response evaluation: Cytokine levels could be used to evaluate the effectiveness of treatment. The changes in cytokine levels after treatment might reflect changes in tumor sensitivity to treatment and immune response [52]. Overall, cytokines have multiple roles in thyroid cancer patients, involving immune regulation, inflammatory response, tumor microenvironment, and treatment response.

Radiofrequency ablation might affect the number and subpopulation distribution of lymphocytes in patients. The specific impact might include changes in the number of CD4+and CD8+T cells. These changes might affect the patient's immune status and response ability, having impacts on tumor control and prognosis [53]. Radiofrequency ablation affects the interaction between tumors and immune cells by altering the immune microenvironment of thyroid cancer patients. This may have a significant impact on the immune escape, drug resistance, and treatment response of tumors. It can also lead to changes in certain cytokines in the patient's body, including immune activating factors and inflammatory factors. This affects the intensity and nature of the immune response, thereby affecting the development and treatment response of tumors [54].

In summary, radiofrequency ablation may have a series of complex effects on lymphocytes, subsets, and cytokines in thyroid cancer patients. It also involves the regulation of the immune system and changes in the tumor microenvironment. Deeply studying these impacts is of great significance for optimizing treatment strategies, predicting prognosis, and developing personalized treatment plans. Although radiofrequency ablation has achieved certain results in the treatment of thyroid cancer, its impact on patient lymphocytes, subsets, and cytokines still needs further research. Future research should focus on the impact of radiofrequency ablation on the immune function of thyroid cancer patients, and explore its association with tumor progression and prognosis. In addition, attention should also be paid to the impact of different treatment methods on the immune function of thyroid cancer patients, providing a more comprehensive basis for clinical treatment.

ACKNOWLEDGMENT

The research thanks the support from Affiliated Hospital of Shaoxing University.

Funding: None

Conflict of interests: The authors declare no conflict of interests.

Ethical Compliance: Research experiments conducted in this article with animals or humans were approved by the Ethical Committee and responsible authorities of our research organization (s) following all guidelines, regulations, legal, and ethical standards as required for humans or animals.

Authors Contribution: B.M. put forward the research experiment: Radiofrequency ablation, thyroid cancer, lymphocytes, and other key terms are used to search for randomized controlled clinical trials (RCTs) related to them. G.R., F.M. and Q.Z. analyzed the data and J-f.P., D.L. helped with the constructive discussion. All authors made great contributions to manuscript preparation.

REFERENCES

1. Filetti S, Durante C, Hartl D, *et al.* (2019) Electronic address: clinicalguidelines@esmo.org. Thyroid cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. *Ann Oncol, **30 (12):** 1856-1883.*
2. Nabhan F, Dedhia PH, Ringel MD (2021) Thyroid cancer, recent advances in diagnosis and therapy. *Int J Cancer, **149(5):** 984-992.*
3. Coca-Pelaz A, Shah JP, Hernandez-Prera JC, *et al.* (2020) Papillary Thyroid Cancer-Aggressive Variants and Impact on Management: A Narrative Review. *Adv Ther, **37(7):** 3112-3128.*
4. Bauer AJ (2020) Pediatric Thyroid Cancer: Genetics, Therapeutics and Outcome. *Endocrinol Metab Clin North Am, **49(4):** 589-611.*
5. Maniakas A, Zafereo M, Cabanillas ME (2022) Anaplastic Thyroid Cancer: New Horizons and Challenges. *Endocrinol Metab Clin North Am, **51(2):** 391-401.*
6. Ciarallo A, Rivera J (2020) Radioactive Iodine Therapy in Differentiated Thyroid Cancer: 2020 Update. *AJR Am J Roentgenol, **215(2):** 285-291.*
7. Angell TE, Alexander EK (2019) Thyroid Nodules and Thyroid Cancer in the Pregnant Woman. *Endocrinol Metab Clin North Am, **48 (3):** 557-567.*
8. Grani G, Lamartina L, Durante C, *et al.* (2018) Follicular thyroid cancer and Hürthle cell carcinoma: challenges in diagnosis, treatment, and clinical management. *Lancet Diabetes Endocrinol, **6(6):** 500-514.*
9. Vinh D, Zafereo M (2021) Surgical Considerations in Thyroid Cancer: What the Radiologist Needs to Know. *Neuroimaging Clin N Am, **31(3):** 327-335.*
10. Nagayama Y (2018) Thyroid Autoimmunity and Thyroid Cancer - The Pathogenic Connection: A 2018 Update. *Horm Metab Res, **50 (12):** 922-931.*
11. Perri F, Giordano A, Pisconti S, *et al.* (2018) Thyroid cancer management: from a suspicious nodule to targeted therapy. *Anticancer Drugs, **29(6):** 483-490.*
12. Ham J, Wang B, Po JW, *et al.* (2021) Cancer-associated fibroblasts (CAFs) in thyroid papillary carcinoma: molecular networks and interactions. *J Clin Pathol, **74(12):** 759-765.*
13. Rajabi S, Shakib H, Dastmalchi R, *et al.* (2020) Metastatic propagation of thyroid cancer; organ tropism and major modulators. *Future Oncol, **16(18):** 1301-1319.*
14. Li L, Wang Z, Guo H, *et al.* (2023) Nanomaterials: a promising multimodal theranostics platform for thyroid cancer. *J Mater Chem B，**11(32):** 7544-7566.*
15. Li J, Vasilyeva E, Wiseman SM (2019) Beyond immunohistochemistry and immunocytochemistry: a current perspective on galectin-3 and thyroid cancer. *Expert Rev Anticancer Ther, **19(12):** 1017-1027.*
16. McDow AD, Pitt SC (2019) Extent of Surgery for Low-Risk Differentiated Thyroid Cancer. *Surg Clin North Am, **99(4):** 599-610.*
17. Rajan N, Khanal T, Ringel MD (2020) Progression and dormancy in metastatic thyroid cancer: concepts and clinical implications. *Endocrine, **70(1):** 24-35.*
18. van Velsen EFS, Leung AM, Korevaar TIM (2022) Diagnostic and Treatment Considerations for Thyroid Cancer in Women of Reproductive Age and the Perinatal Period. *Endocrinol Metab Clin North Am, **51(2):** 403-416.*
19. Zhang K, Li C, Liu J, *et al.* (2019) DNA methylation alterations as therapeutic prospects in thyroid cancer. *J Endocrinol Invest, **42(4):** 363-370.*
20. Lam D, Davies L, Sawka AM (2022) Women and thyroid cancer

[DOI: 10.61186/ijrr.23.1.1]

incidence: overdiagnosis versus biological risk. *Curr Opin Endocrinol Diabetes Obes, **29(5):** 492-496.*
21. Mahmoudian-Sani MR, Jalali A, Jamshidi M, *et al.* (2019) Long Non-Coding RNAs in Thyroid Cancer: Implications for Pathogenesis, Diagnosis, and Therapy. *Oncol Res Treat, **42(3):** 136-142.*
22. Crenshaw ML, Goldenberg D, Bann DV (2022) Incidental Papillary Thyroid Cancer Identified During Parathyroidectomy. *Ear Nose Throat J, **101(10):** 657-659.*
23. Hou L, Song X (2018) "Effects of Radiofrequency Ablation on Peripheral Blood Lymphocyte Subpopulations and Cytokine Levels in Patients with Primary Liver Cancer.*"[J] China Medical Equipment, **15(12):** 101-105.*
24. Shi K, Xu D, Zheng C, *et al.* (2018) "Comparison of Radiofrequency Ablation and Surgical Resection in the Removal of Excessive Residual Thyroid Tissue before 131I Therapy for Differentiated Thyroid Cancer.*"[J] Chinese Journal of Medical Ultrasound (Electronic Edition), **15(4):** 281-286.*
25. Yang X, He Y (2022) "Observation of the Therapeutic Effect and Impact of Ultrasound-Guided Thyroid Radiofrequency Ablation on Patients with Thyroid Cancer.*" Clinical General Surgery Electronic Journal, **10(3):** 37-40.*
26. Lu Y, Gu G (2021) "Application of Ultrasound-Guided Radiofrequency Ablation in Thyroid Nodules.*"[J] Imaging Research and Medical Application, **5(24):** 216-218.*
27. Du Z, Dong G (2021) "Clinical Efficacy and Safety of Ultrasound-Guided Radiofrequency Ablation in the Treatment of Microscopic Papillary Thyroid Carcinoma." *O[J]ncology: Basic and Clinical, **34 (5):** 378-381.*
28. Sun P, Liang D (2018) "Efficacy of Ultrasound-Guided Radiofrequency Ablation for Microscopic Papillary Thyroid Carcinoma and Its Effects on Postoperative Stress.*" [J]Advances in Modern General Surgery in China, **21(3):** 217-219, 222.*
29. Wang H, Wu J (2021)"Effects of Radiofrequency Ablation on Thyroid Function and HSP70 Protein Expression in Patients with Benign Thyroid Nodules.*"[J] Practical Oncology Journal, **36(8):** 1281-1284, 1304.*
30. Ma D, Xi L, Zhang H (2020)"Influence of Radiofrequency Ablation on Thyroid Function in Patients with Solid Thyroid Nodules.*"[J] Baotou Medical College Journal, **36(6):** 34-35, 73.*
31. Zhao X, Shao L, Xue W, *et al.* (2017) "Effects of Percutaneous Microwave Ablation under Ultrasound Guidance on the Treatment of Benign Thyroid Tumors and Thyroid Hormone Levels.*" [J] Modern Diagnosis & Treatment, **28(21):** 4054-4055.*
32. Wan Y (2023) "Efficacy of Ultrasound-Guided Radiofrequency Ablation for Microscopic Papillary Thyroid Carcinoma and Its Impact on Postoperative Stress.*" [J]Medical Information, **36(8):** 112-115.*
33. Zhao X, Song M (2022) "Effects of Ultrasound-Guided Radiofrequency Ablation and Surgical Resection on the Treatment of Microscopic Papillary Thyroid Carcinoma and the Incidence of Complications.*" [J]Clinical Medical Research and Practice, **7(17):** 105-107.*
34. Gong H, Liu W, Yao Z (2019) "Observation of the Therapeutic Efficacy of Microwave Ablation and Radiofrequency Ablation under Ultrasound Guidance and Surgical Resection in the Treatment of Microscopic Papillary Thyroid Carcinoma.*" [J]China Cancer Clinical Rehabilitation, **26(7):** 781-784.*
35. Zhu B (2015)"Comparison of the Effects of Percutaneous Microwave Treatment and Radiofrequency Ablation under Ultrasound Guidance on Postoperative Stress Response in the Treatment of Microscopic Papillary Thyroid Carcinoma.*" [J]China Health Industry, **(20):** 168-169.*
36. Bao Xiaoyao (2021)"Analysis of the Safety and Long-Term Follow-Up Results of Ultrasound-Guided Radiofrequency Ablation in the Treatment of Thyroid Papillary Carcinoma.*"[J] China Medical Engineering, **29(11):** 128-130.*
37. Zhang X (2020) "Analysis of the Efficacy of Ultrasound-Guided Radiofrequency Ablation in the Treatment of Cervical Lymph Node Metastasis of Papillary Thyroid Carcinoma.*" [J]China Medical Device Information, **26(3):** 120-122.*
38. Zhang W (2022)"Clinical Effects of Ultrasound-Guided Percutaneous Microwave Ablation and Surgical Resection in the Treatment of Microscopic Papillary Thyroid Carcinoma Patients.*"[J] World Journal of Integrated Traditional and Western Medicine, **8(2):** 146-149.*
39. Zhou H, Li G, Chen Y (2020) "Treatment of Microscopic Papillary Thyroid Carcinoma with Ultrasound-Guided Percutaneous Microwave Ablation.*"[J] Modern Medicine, **48(3):** 373-378.*
40. Shao C (2011) "Changes in Peripheral Blood T Lymphocyte Subpopulations and Serum Immunoglobulins during the Perioperative Period in Patients with Thyroid Cancer." *[J]Chinese Primary Health Care, **18(21):** 2895-2896.*
41. Zhang L, Xi Y, You L, *et al.* (2018) "Effects of TSH Suppressive Therapy on Serum Tg, VEGF, TSGF, CD44V6, sIL-2R, and T Lymphocyte Subpopulation Levels in Differentiated Thyroid Cancer Patients after Surgery[J]." *Journal of Hainan Medical University, **24(2):** 242-245.*
42. Shen R, Xiong G, Hou M, *et al.* (2021) Effect of hepatic arterial chemoembolization combined with radiofrequency ablation in the treatment of hepatocellular carcinoma and its effect on serum T lymphocyte subpopulations and transforming growth factor β_1 levels [J]. *Chinese Journal of Contemporary Medicine, **28(26):** 130-133.*
43. Xu B, Ghossein RA (2020) Noninvasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features (NIFTP): An Update. *Head Neck Pathol, **14(2):** 303-310.*
44. Lorusso L, Cappagli V, Valerio L, *et al.* (2021) Thyroid Cancers: From Surgery to Current and Future Systemic Therapies through Their Molecular Identities. *Int J Mol Sci, **22(6):** 3117.*
45. Wang J, Zhanghuang C, Jin L, *et al.* (2022) Development and validation of a nomogram to predict cancer-specific survival in elderly patients with papillary thyroid carcinoma: a population-based study. *BMC Geriatr, **22(1):** 736.*
46. Al-Qurayshi Z, Foggia MJ, Pagedar N, *et al.* (2020) Thyroid cancer histological subtypes based on tumor size: National perspective. *Head Neck, **42(9):** 2257-2266.*
47. Estorch M, Mitjavila M, Muros MA, *et al.* (2019) Radioiodine treatment of differentiated thyroid cancer related to guidelines and scientific literature. *Rev Esp Med Nucl Imagen Mol (Engl Ed)9, **38 (3):**195-203.*
48. Schuster-Bruce J, Sargent P, Madden B, *et al.* (2022) A systematic review of endotracheal stenting in patients with locally advanced thyroid cancer. *Clin Otolaryngol, **47(3):** 414-423.*
49. Mahmoudian-Sani MR, Alghasi A, Saeedi-Boroujeni A, *et al.* (2019) Survivin as a diagnostic and therapeutic marker for thyroid cancer. *Pathol Res Pract, **215(4):** 619-625.*
50. Shafabakhsh R, Asemi Z, Mansournia MA, *et al.* (2023) CircRNAs: A Novel Strategy in Diagnosis and Treatment of Thyroid Cancer. *Curr Mol Med, **23(8):** 737-747.*
51. Vaisman F, Tuttle RM (2019) Clinical Assessment and Risk Stratification in Differentiated Thyroid Cancer. *Endocrinol Metab Clin North Am, **48(1):** 99-108.*
52. Hernandez-Prera JC (2020) The evolving concept of aggressive histological variants of differentiated thyroid cancer. *Semin Diagn Pathol，**37(5):** 228-233.*
53. Nishino M (2020) Thyroid pathology: Controversies and best practices. *Semin Diagn Pathol，**37(5):** 211-212.*
54. Boukheris H, Bachir Bouiadjra N (2022) Thyroid cancer incidence and trends by demographic and tumor characteristics in Oran, Algeria: 1993-2013, a population-based analysis. *Eur J Cancer Prev, **31(3):** 301-308.*

[DOI: 10.61186/ijrr.23.1.1]