



TOTAL THYROIDECTOMY VS. LOBECTOMY IN DIFFERENTIATED THYROID CANCER: SYSTEMATIC REVIEW

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Abstract

Background: Because of the favorable prognosis of differentiated thyroid cancer (DTC), recommendations recommend total thyroidectomy (TT) or thyroid lobectomy (TL) as surgical therapy for DTC with a low to moderate risk of recurrence. There is still debate over the best risk-based surgical technique for differentiated thyroid carcinoma.

Objectives: To evaluate total thyroidectomy (TT) and thyroid lobectomy (TL) as surgical treatment for DTC with a low to moderate probability of recurrence over time.

Methodology: Adhering to the PRISMA guidelines, a comprehensive search was conducted in October 2022, primarily using PubMed. The search focused on studies published in English that investigated the comparison between total thyroidectomy (TT) and thyroid lobectomy (TL). Specific inclusion and exclusion criteria were established to ensure the relevance and quality of the studies.

Results: The review encompassed diverse studies from various geographical locations, with a predominant focus on middle-aged participants. A consistent trend emerged, highlighting a significant proportion of DTC patients undergoing thyroidectomy and lobectomy surgeries.

Conclusion: The severity of DTC is evident across different populations and settings. Factors such as severity of risk and timing of diagnosis can determine which type of surgeries is most benefit in such patients. Thyroidectomy and lobectomy surgeries are crucial for optimal health outcomes.

Keywords: " Thyroidectomy," " Lobectomy," "Surgery," "Between" and " Differentiated Thyroid Cancer".

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Introduction:

Thyroid cancer is the most prevalent endocrine cancer [1], a diverse illness originating from two distinct kinds of epithelial cells. Follicular cells are the source of the majority of thyroid malignancies, including anaplastic thyroid carcinoma (ATC), papillary thyroid carcinoma (PTC), Hurthle cell carcinoma, and follicular thyroid carcinoma (FTC). PTC and FTC are included together as differentiated thyroid carcinoma (DTC). Up to 90% of thyroid cancer cases are caused by DTC [1,2].

Differentiated thyroid cancer is typically asymptomatic for lengthy periods of time and manifests as a solitary thyroid nodule. Approximately half of all malignant nodules are discovered during standard physical examinations, with the remainder discovered by the patient. Malignant nodules often do not cause any symptoms, but if they are hard, fastened to nearby tissues, induce vocal cord paralysis, develop quickly, or invade neck structures, there is a seven-fold increased risk of malignancy [3].

Ages under 15 or over 60, gender, a history of head and neck radiation, a family history of thyroid cancer, the presence of familial syndromes linked to thyroid cancer, nodule sizes larger than 4 cm, and the presence of suspicious ultrasound-detected features like hypo-echogenicity, irregular borders, or micro-calcifications are additional factors that raise the risk of suspicion of thyroid cancer [4].

Depending, DTC is an uncommon illness with a generally good prognosis. It happens in 7-15% of thyroid surgery patients. In 2014, over 63,000 new instances of DTC were identified in the United States, compared to only 31,200 new cases in 2009. Every year, around 6000 new cases of DTC are diagnosed in Germany. The increased use of diagnostic technologies, such as ultrasonography of the neck, is causing a rise in the incidence of thyroid cancer and a shift in tumor diagnosis to smaller tumors. According to one study, papillary thyroid carcinoma would be the third most costly malignancy in women in the United States [5]. Additionally, Thyroid cancer is expected to cause 44,280 new cases and 2200 deaths in the United States in 2021 [6].

To provide best long-term treatment quality, DTC should be treated with suitable way. Surgical, endocrinology, pathology, and nuclear medicine specialists should be accessible. The therapy strategy is tailoring to the patient's specific needs and risks. The two major surgical treatments for DTC with a low to moderate risk of recurrence are thyroid lobectomies (TL) and total

thyroidectomies (TT) [7]. Typically, the first risk assessment is conducted at the time of surgery, and if there is no involvement of lymph nodes, the kind of intervention might vary from partial thyroidectomy (TT) to thyroid lobectomies (TL). However, perspectives differ on the scope of surgery, particularly in low-risk individuals [8]. Therefore, Health-related quality of life is becoming more well recognized as an important clinical concern in thyroid cancer. Individuals' perceptions of their situation in life in respect to their objectives, aspirations, standards, and worries are classified as health-related quality of life.

Historically, the justification for a total thyroidectomy has been on the thorough removal and destruction of every thyroid tissue. Thyroid gland removal facilitates the use of thyroglobulin as a cancer marker for interval follow-up and facilitates the use of ultrasonography to identify recurrences in the neck. Modern advancements in high-resolution ultrasound and sensitive thyroglobulin tests challenge long-held beliefs by enabling the early diagnosis of recurrences with a single thyroid lobe in situ. Another advantage of complete thyroidectomy is the opportunity to do postoperative radioactive iodine ablation for residual ablation and adjuvant treatment [9].

Lobectomy provides several advantages as a surgical treatment for low-risk thyroid carcinoma. Thyroid surgery has two major problems that are reduced with lobectomy. First, a damage to the recurrent laryngeal nerve, which innervates the vocal chord, can cause stridor and hoarseness. A tracheostomy would be necessary for a bilateral damage, which is only doable with bilateral surgery such as a complete thyroidectomy. Furthermore, the possibility of hypo-calcemia following surgery is eliminated when a unilateral neck exploration technique like lobectomy is employed, as it only involves the damage of two of the four parathyroid glands [9]. Due to the many features of the two types of surgeries, there is still debate over the best surgical strategy.

Patients with DTC had a 92% 10-year overall survival rate, a 99% disease-specific survival rate, and a 98% recurrence-free survival rate. On the other hand, some research finds no statistically significant variations in overall survival or disease-free survival [10]. Because most differentiated thyroid cancer survivors have a lengthy life expectancy, it is critical to understand which surgery responses on the variances in clinical, pathologic, and therapeutic factors change their survival risk profiles.

The influence of surgery extent on survival rates is a topic of dispute in the surgical literature.

There haven't been any significant long-term randomized controlled studies for this illness, which is why the debate continues. Many retrospective studies have attempted to answer this topic, but the findings have been equivocal and contradictory[11]. The best way to handle DTC has become a topic of more debate in recent times. Wherefore, this review longitudinally compare between DTC patients who undergoing TT and TL surgeries.

Methodology

For this systematic review, the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta- Analyses) standards were used.

Study Design and Duration

This was a systematic review conducted in October 2022.

Search strategy

To retrieve the relevant research, a thorough search was conducted across major databases, Using PubMed Mainly as a search engine for studies. We only searched in English. The following keywords were converted into PubMed Mesh terms and used to find studies that were related; " Thyroidectomy," " Lobectomy," "Differentiated Thyroid Cancer," "Tumor" and " Thyroid". The Boolean operators "OR" and "AND" matched the required keywords. Among the search results were publications in full English language, freely available articles, and human trials.

Selection criteria

We considered the following criteria for inclusion in this review:

- Studies that investigate the comparison between Thyroidectomy and Lobectomy in Differentiated Thyroid Cancer.
- Clinical Trials were included.
- Observational Studies were included.
- Free accessible articles.

Exclusion criteria

- We excluded systemic reviews.
- We excluded studies that focused only on papillary thyroid cancer
- We excluded article reviews.
- We excluded meta-analysis.
- We excluded studies older than 10 years.

- We excluded studies that focused only on specific populations
- Case reports, letters to the editors, and replies to conflicts were excluded.
- Non-English language.

Data extraction

Duplicates in the search strategy output were found using Rayyan (QCRI) [12]. To determine the titles' and abstract relevance, the researchers used a set of inclusion/exclusion criteria to filter the combined search results. The reviewers carefully read each paper that matches the requirements for inclusion. The authors provided other methods of resolving disputes with some thought. The authors extracted data about the study titles, authors, study year, country, patients, gender, surgical approach , main outcomes, and conclusion.

Strategy for data synthesis

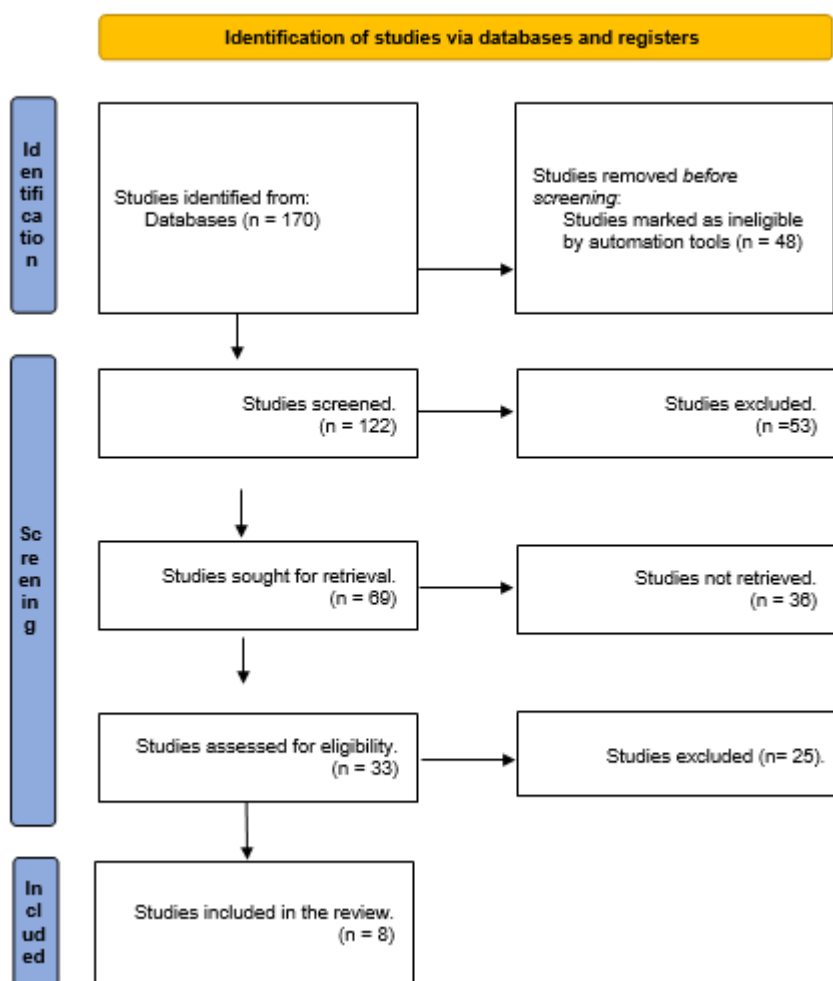
To provide a qualitative overview of the outcomes and study components, summary tables were developed utilizing information from relevant research. The most successful technique for using data from the included study articles was chosen after data extraction for the systematic review.

Risk of bias assessment

Using the ROBINS-I risk of bias assessment approach for non-randomized trials of therapies, the included studies' quality was assessed [13]. The seven themes that were assessed were confounding, participant selection for the study, classification of interventions, deviations from intended interventions, missing data, assessment of outcomes, and choosing of the reported result.

Results

Search results A total of 170 study articles resulted from the systematic search, and 48 were automatically removed. Title and abstract screening were conducted on 122 studies, and 53 studies were excluded. 69 studies were sought for retrieval, and only 36 articles were retrieved. Finally, 33 studies were screened for full-text assessment; 25 Studies were excluded for either having inappropriate study methodology or results. 8 eligible study articles were included in this systematic review. A summary of the study selection process is presented in **Figure 1**.



Characteristics of the included studies

Table 1: Socio-demographic Characteristics of Participants

Table (1) illustrates the socio-demographic details of participants from eight different studies, encapsulating a massive participant count of 3791 from references [14-20], with exception of study [16] the number of the participants wasn't reported. The geographical breadth of these studies is expansive, encompassing countries such as China, Australia, Italy, Brazil, Turkey, Spain and South Korea.

Regarding the representation of gender, *Chen W, Li J, Peng S, et al.* 2022 [14] exhibited the highest female percentage at 78.1%, similar to *Giuffrida, Dario et al.* 2019 [17] study which recorded a female percentage of 82% and *Vaisman, Fernanda et al.* 2013 [18], *Díez, Juan J et al.* 2021 [20] studies in which the percentage of female patients are higher than males recorded 94.3%, 78.8% and 128 females, respectively.

In terms of participant age, while the age range was predominantly centered more than 18-year mark, there were variations. Specifically, *Chen W, Li J, Peng S, et al.* 2022 [14], *Vaisman, Fernanda et al.* 2013 [18] reported an age range

with a mean of 35 ± 5.0 years. *Colombo, Carla et al.* 2021 [16] solely indicated their participants' age to be over 18. *Díez, Juan J et al.* 2021 [20] highlighted a mean age of 50.8 years.

Conclusively, the overall tendency of all research alludes to a major focus on middle-aged participants, with the mean age hovering around the 30-50-year level in the socio-demographic investigations shown in Table (1).

Table (2) Clinical Characteristics and objectives of the Included Studies:

Table (2) depicts the surgical procedures performed in each research. *Chen W, Li J, Peng S, et al.* 2022 [14], *Barbaro, Daniele et al.* 2021 [15], and *Colombo, Carla et al.* 2021 [16] research compared TT with TL, as some patients had TT surgery and others had TL surgery. *Choi, Soon Min, et al.* 2022 [19] studied TL surgery as a main operation, followed by TT surgery as a secondary surgery.

The aims of each investigation were also described in the table (2). The studies by *Barbaro, Daniele et al.* 2021 [15] and *Colombo, Carla et al.* 2021 [16] sought to assess the health-related quality of life of DTC patients undergoing

thyroid/lobectomy. The research *Giuffrida, Dario et al.* 2019 [17] attempted to state the preference for thyroidectomy and describe the follow-up procedure. The clinical results of DTC patients treated with TL were emphasised by *Vaisman, Fernanda et al.* 2013 [18] and *Dez, Juan J et al.* 2021 [20].

Table (3) Outcomes of the Included Studies:

According to *Chen W, Li J, Peng S, et al.* 2022 [14] and *Barbaro, Daniele et al.* 2021 [15], lobectomy surgery was superior than

thyroidectomy in terms of quality of life in the short run. *Carla et al.* 2021 [16] and *Vaisman, Fernanda et al.* 2013 [18], all found that the frequency of problems following surgery was greater in TT patients. There were no changes in recurrence rates, disease-related death rates, or 10-year recurrence-free survival rates, according to the findings of the *Choi, Soon Min et al.* 2022 [19] research. *Dez, Juan J et al.* 2021 [20] confirmed that treating DTC patients with lobectomy is more beneficial.

Table (1): Socio-demographic characteristics of the included participants.

Study	Location	Study design	Total no of Patients	Age	Gender
<i>Chen W, Li J, Peng S, et al.</i> 2022 [14]	China	prospective observational longitudinal cohort study	1060	Median age :38 years	438 women under went lobectomy 390 women under went thyroidectomy
<i>Barbaro, Daniele et al.</i> 2021 [15]	Australia	A systematic review	NA	NA	NA
<i>Colombo, Carla et al.</i> 2021 [16]	Italy	Literature Review	370	18 years of age or older	NA
<i>Giuffrida, Dario et al.</i> 2019 [17]	NA	randomized, prospective data	359	176 older than 45 years	64 men 295 women
<i>Vaisman, Fernanda et al.</i> 2013 [18]	Brazil	Retrospective review	70	Median age : 35.5 years	94.3% females
<i>Choi, Soon Min et al.</i> 2022 [19]	South Korea	retrospective review	1,702	NA	NA
<i>Díez, Juan J et al.</i> 2021 [20]	Spain	Retrospective review	164	Mean age 50.8 years	128 women

Table (2): Clinical characteristics of the included studies.

Study	Surgical approach	No of patients undergoing thyroidectomy	No of patients undergoing lobectomy	Objectives
<i>Chen W, Li J, Peng S, et al.</i> 2022 [14]	Lobectomy vs. thyroidectomy	497	563	The health-related quality of life of DTC patients undergoing lobectomy/thyroidectomy was compared.
<i>Barbaro, Daniele et al.</i> 2021 [15]	Lobectomy vs. thyroidectomy	NA	NA	Evaluating DTC Individuals having thyroid/lobectomy in terms of their health-related quality of life
<i>Colombo, Carla et al.</i> 2021 [16]	Lobectomy vs. thyroidectomy	NA	NA	Provide post-surgery follow-up results.
<i>Giuffrida, Dario et al.</i> 2019 [17]	Thyroidectomy	100%	NA	Stating the preferability of thyroidectomy
<i>Vaisman, Fernanda et al.</i> 2013 [18]	Lobectomy	NA	100%	present clinical results in a group of thyroid cancer patients with low and intermediate risk who had thyroid lobectomy
<i>Choi, Soon Min et al.</i> 2022 [19]	Lobectomy then thyroidectomy	NA	NA	the need for and timing of complete thyroidectomy after thyroid lobectomy
<i>Díez, Juan J et al.</i> 2021 [20]	Lobectomy	NA	100%	Investigate the clinical outcomes of DTC patients treated with TL

Table (3): Methods and outcomes of the included participants.

Study	Methods	Outcomes
Chen W, Li J, Peng S, et al. 2022 [14]	DTC patients completed preoperative surveys and were classified as TT or TL based on the procedure they experienced.	In the short term, the TL group had greater health-related quality of life than the TT group.
Barbaro, Daniele et al. 2021 [15]	NA	Addressing postoperative health-related quality of life with patients when considering therapy alternatives is an essential element of patient-centered care and informed shared decision-making, and it should be treated holistically, taking into consideration its physical, psychological, and social aspects.
Colombo, Carla et al. 2021 [16]	DTC Patients with low- or intermediate-risk had (LT) or (TT) and were monitored.	Post-surgical problems were more common in individuals who had TT than in those who received LT.
Giuffrida, Dario et al. 2019 [17]	NA	In 23.7% of individuals, differentiated thyroid carcinoma was discovered. Nodal metastases were discovered in 128 individuals (35.7%), whereas distant metastases were discovered in 26 (7.2%) patients.
Vaisman, Fernanda et al. 2013 [18]	DTC patients underwent lobectomy	5 individuals had recurrences and 5 had completions for benign lesions, while 86% remained under observation with no signs of disease recurrence.
Choi, Soon Min et al. 2022 [19]	After surgery, DTC patients who underwent TL were divided into two groups: Group A with low risk and Group B with intermediate risk.	There was no statistically significant difference between the two groups in recurrence rates, disease-related death rates, or 10-year recurrence-free survival rates.
Díez, Juan Jet al. 2021 [20]	DTC Patients who had TL, were followed up on for a year. demographic, clinical, and histopathological information were gathered.	At 12 months, 71.6% of patients were in remission, and 74.4% were still alive at the end of the study. At the time, 34 patients (20.7%) had an unclear response, six (3.7%) had a biochemical incomplete response, and two (1.2%) had a structural incomplete response.

Discussion

Regarding the scope of thyroid surgery performed during the operation for differentiated thyroid cancer, there is a great deal of disagreement. The lack of randomized, prospective data to guide the selection of the best surgical method complicates matters. Since the prognosis is generally favorable, treatment guidelines and surgical techniques are regularly reviewed to prevent needless procedures and patient injury.

Thyroid cancer is now the most frequent endocrine malignant illness, and its prevalence is increasing, most likely due to greater identification [22]. Thyroid cancer is currently the most frequent malignant condition in South Korea, where institutional screening is in place. The majority of malignant thyroid tumors are well-differentiated thyroid cancers that are deemed low risk. The prognosis is good, with a 90%-95% 20-year survival rate [23].

It has long been recommended that individuals with well-differentiated thyroid cancer (nodules larger than 1 cm) receive a complete thyroidectomy [24]. This advice was based mostly on data from 52 173 people with papillary thyroid carcinoma in the United States' National carcinoma Database. According to our study, patients who had complete thyroidectomy had a

higher survival rate than those who got lobectomy. However, there is mounting evidence that a significant proportion of thyroid cancer patients are being over-treated [25]. A recent reassessment of information from the National Comprehensive Cancer Database, which comprised 61 775 individuals with thyroid cancer, revealed that for a subset of low-risk patients, lobectomy was superior than complete thyroidectomy [26]. This led to the most significant modification to the 2015 guideline: patients with well-differentiated thyroid carcinoma up to 4 cm can now get a thyroid lobectomy if they do not have certain high-risk characteristics [25].

Individuals' perceptions of their situation in life in respect to their objectives, aspirations, standards, and worries are classified as health-related quality of life. Health-related quality of life has become more important because DTC patients undergoing TT and TL have an equally good prognosis. Previous studies did not consistently draw conclusions when comparing the health-related quality of life of DTC patients after various thyroid operations. According to a retrospective analysis, individuals with DTC receiving TT were more likely than those having TL to experience health-related quality of life problems. Another

prospective research with a limited sample size discovered that at the 1-year follow-up, surgical procedures had no effect on the health-related quality of life of patients with thyroid cancer [27]. Similar to the work of Chen W, Li J, Peng S, et al. [14]. These two studies did not track participants' health-related quality of life in real time.

In the short term, there were notable variations in health-related quality of life between the TT and TL groups, according to a prospective longitudinal cohort research with a limited sample size of patients with papillary thyroid cancer; however, the disparities vanished in the long-term follow-up. None of these three studies looked at the relationship between problems and postoperative thyrotropin levels and health-related quality of life or patient satisfaction with surgical procedures [28].

The majority of research on this subject shows no differences in the outcomes of the two surgical techniques, but in five sizable series among the biggest reported to far, comprising 4813 patients TT was linked to a superior result. The variations might be related to a variety of factors, including sample size, diagnostic techniques, illness persistence criteria, and potentially ethnicity [29]. The two greatest Italian trials indicated that TT was related with a better result than LT [16].

Unexpectedly, there aren't any published data on this subject from other European nations. This is probably because LT has a narrow therapeutic indication for abnormal cytology or thyroid carcinoma. In fact, TT is favored in Europe because of the more complexity involved in evaluating patient outcomes after LT treatment or the comparatively large pool of highly qualified endocrine surgeons in the region [30].

In DTC patients with original tumor sizes ≤ 1 cm, lobectomy is mostly chosen because to the high risks of surgical complications, laryngeal nerve damage, and hypo-para-thyroidism [31]. But under the care of a skilled thyroid surgeon, the risk of complications from a complete thyroidectomy can be as low as 2%, and the likelihood of developing recurrent laryngeal nerve palsy increases when patients need to have the surgery again due to contralateral lobe recurrences [32].

Unless there is a contraindication, most current recommendations advocate complete thyroidectomy as the initial surgical option for known papillary thyroid cancer if the main tumor is more than 1 cm. Thyroid lobectomy is deemed adequate in the absence of known metastatic illness or prior radiation history if the underlying tumor is less than 1 cm in size and intra-thyroidal. The National Comprehensive Cancer Network

(NCCN) guidelines, on the other hand, allow for a thyroid lobectomy as the initial surgical procedure in tumors up to 4 cm in diameter if the patients are between the ages of 15 and 45 and there is no history of prior radiation or evidence of distant metastasis, cervical lymph node metastases, or aggressive histologic variants [33].

Nonetheless, the efficacy of radioactive iodine treatment in individuals with intermediate-risk DTC is debatable. Orosco et al. reported that radioactive iodine treatment was not linked with disease-specific mortality in patients with intermediate-risk DTC [34]. Wang et al. proposed that radioactive iodine treatment

increases disease-specific survival in intermediate-risk DTC patients [35]. There is a dearth of large-scale randomized clinical trials and inconsistent results from many research on radioactive iodine therapy, hence there are no firm recommendations for treating individuals with intermediate-risk DTC with this treatment.

Finally, pre-surgical staging may have influenced the decision between LT and TT. This disadvantage, however, does not seem to have materialized because the tumors treated with LT were either similar in size (low-risk category) or significantly larger (low-risk category), and there was no histological difference observed between the tumors treated with LT and those treated with TT with regard to nodal metastases.

Conclusion

Differentiated thyroid cancer is an uncommon tumor form, although its prevalence has been steadily growing over the previous few decades. The surgical procedure might range from lobectomy to complete thyroidectomy. Our findings suggest that TL might be used to treat low-risk thyroid cancer. Because the evaluation of an event-free result for patients treated with TL requires a longer follow-up period than for patients treated with TT, a longer follow-up period is necessary for a credible characterization of the response to surgery. TT, on the other hand, should be preferred for intermediate-risk tumors. Furthermore, while deciding on surgery for DTC patients, health-related quality of life should be taken into account.

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