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Original Research Article

Auto Transplantation of Thyroid in Patients with Total Thyroidectomy and Comparison of Thyroid Levels

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Abstract:

Background: Total thyroidectomy is increasingly used for treating bilateral benign thyroid diseases, but it requires ongoing levothyroxine replacement therapy to prevent hypothyroidism. Heterotopic thyroid auto transplantation was suggested to eliminate this need and preserve the body's thyroxin synthesis. However, limited data exists on this topic. Previous studies on animals have shown successful auto transplantations, but limited clinical trials have used cryopreserved thyroid autografts, with insufficient number of studies and patients, and inconsistent study procedures.

Aim and objectives: The purpose is to assess the positioning of thyroid tissue in the thigh muscle following total thyroidectomy for benign simple nodular goiter, with the goal of avoiding the need for lifetime thyroid hormone replacement medication and preserving the autoregulatory mechanism of thyroid hormone production.

Methods: We performed a case series analysis on a group of 30 patients who were diagnosed with multinodular goiter and were being considered for complete thyroidectomy. The patients were randomly assigned to two groups: group A (consisting of 15 patients) who were administered 5 g of healthy non-nodular thyroid tissue, and group B (also consisting of 15 patients) who were administered 10 g of the same tissue. The viability and efficacy of heterotopic auto transplanted thyroid tissue were evaluated using hormonal analysis and ultrasound imaging of the thigh (the location of the transplanted thyroid graft) at 2, 6, and 12 months after the surgery.

Results: The study found no significant difference in radioactive iodine uptake between group A and group B, but significant differences in free T3, T4, TSH levels, and pulse after the 2nd, 6th, and 12th months. The processing and injection time range for auto transplanted thyroid tissue was 18-20 minutes, with no immediate or delayed problems.

Conclusion: Thyroid auto transplantation involves injecting a suspension of thyroid tissue, resulting in increased thyroid hormone levels. Larger implants absorb isotopes more, but not hormone levels. The process is safe, effective, and efficient, with superior outcomes in younger individuals. The process improves over time.

Keywords: Thyroidectomy, autotransplantations, non-nodular thyroid tissue, hormone, free T3, T4.

Introduction

The primary surgical method for treating patients with bilateral benign thyroid diseases is now total thyroidectomy (TT). Several publications have documented that TT may currently be conducted with a high level of safety, and that careful surgical technique can result in low rates of complications [1,2]. While surgery is an effective option for avoiding the need for long-term pharmaceutical use, patients will still need to undergo life-long levothyroxine (L-T4) replacement therapy. It is worth noting that this therapy has been linked to coronary heart diseases and disruptions in lipid metabolism [3,4].

Although postoperative management of hypothyroidism after total thyroidectomy (TT) through L-T4 replacement therapy may appear straightforward, it can be burdensome for patients to adhere to a daily L-T4 dose and attend regular follow-up visits at the hospital. This noncompliance may hinder the achievement of a euthyroid state through replacement therapy [5]. An additional obstacle to achieving a euthyroid state by replacement therapy is the potential for medication malabsorption caused by gastrointestinal disorders [6].

Autotransplantation of non-cancerous thyroid tissue after total thyroidectomy (TT) prevents the need for long-term thyroid hormone replacement treatment. Another benefit of heterotopic thyroid autotransplantation is the preservation of the autoregulatory mechanism of thyroxin production within the body based on its specific requirements [7].

Heterotopic thyroid autotransplantation was suggested as a means to prevent the need for further surgery in the neck area in cases where goiters or hyperthyroidism reoccur. This article aims to provide a comprehensive analysis of the history of thyroid transplantation, focusing on its experimental trials and therapeutic uses.

The objective of the study was to investigate and contrast the correlation between the volume of auto donated thyroid tissue and the achievement of a euthyroid condition in individuals who underwent total thyroidectomy. Long-term follow-up is necessary to allow sufficient time for the implant to establish its vascularity and function properly.

In the event of recurrence or malignant transformation, a thyroid scan can be performed to obtain precise information regarding the location, size, and potential malignancy of the nodule. This scan can differentiate between a cold nodule (indicating recurrence) and a warm nodule. Consequently, exploration of the thigh region would be a more convenient option compared to re-exploration of the neck.

Thyroid autotransplantation has the potential to preserve the original thyroid function in a convenient location, such as the thigh, which eliminates the possibility of regrowth in the neck area. Additionally, it allows for a greater quantity of thyroid tissue to be implanted. In the event of recurrence, it would not happen in the neck, so preventing any compression on the trachea and eliminating the need for a risky reoperation in that area. Precautions have been implemented, encompassing both preoperative and operational procedures. Prior to the surgical procedure, those having a familial predisposition to thyroid cancer or a history of neck irradiation were not included. A comprehensive clinical evaluation, together with a neck ultrasound and fine-needle aspiration cytology, were performed to investigate any potentially concerning nodules.

Even the smallest indication of cancer made the patient ineligible for autotransplantation. During the operation, the most visually healthy internodular section of the removed goiter was selected for implantation. The chosen tissue was finely emulsified to ensure that no significant changes in appearance or texture were overlooked.

In theory, a goiter located in the thigh is less likely to be noticeable or to exert pressure on vital structures. The surgical procedure for treating this type of edema would be less severe compared to a subsequent operation in the neck [8].

Materials and Methods:

The present study carried out from August 2017 to June 2018.This a prospective randomized comparative analysis designed to evaluate the volume of thyroid tissue auto transplantation and its efficacy in achieving a euthyroid state postoperatively. The study encompasses a sample size of 30 patients who presented with thyroid swelling to the General Surgery Outpatient Department at Annapoorana Medical College & Hospitals, Salem. All patients underwent comprehensive preoperative evaluations and were planned for total thyroidectomy.

Patients were randomly allocated into two groups of 15 each, designated as Group A and Group B, using a lot method for randomization.

In Group A, patients received 5 grams of healthy, non-nodular thyroid tissue, while Group B patients received 10 grams of the same tissue type. The primary endpoints included survival and functional capacity of the transplanted thyroid tissue, assessed through thyroid profiles (FT3, FT4, and TSH levels) and ultrasound examinations at the site of transplantation. Follow-ups were scheduled at 2 months, 6 months, and 12 months postoperatively. Patients included in the study were adults over 18 years of age, diagnosed with simple nodular goiter, and in a euthyroid state. Exclusion criteria included patients younger than 18 years, those with malignant goiters, and those with recurrent goiters.

The sample size was determined using power analysis, calculated through the independent samples Student's t-test. With a power of 0.8 and an alpha error of 0.05, a minimum of 15 patients per group was deemed necessary, resulting in a total sample size of 30 patients. Random allocation to the study arms was performed using a balanced physical randomization method. Following total thyroidectomy, the excised thyroid tissue was examined grossly for healthy, non-nodular sections and subsequently sent for pathological examination. Frozen sections were utilized to rule out malignancy. The verified healthy non-nodular tissue was then weighed, mixed with normal saline, and injected into the lateral aspect of the thigh using a wide bore, blunt-tip transfer needle. Postoperatively, patients were prescribed 50 mcg of L-Thyroxine to support thyroid function until the autotransplanted tissue began functioning. Clinical assessments, thyroid function tests, and ultrasound scans of the transplantation site were conducted at 2, 6, and 12 months post-surgery to monitor the viability and function of the grafted tissue. All operations and transplant procedures were performed or supervised by senior surgeons, with resident surgeons actively participating.

This methodology aims to rigorously evaluate the effectiveness of thyroid tissue autotransplantation in maintaining a euthyroid state, providing valuable insights into the potential of this surgical intervention for patients undergoing total thyroidectomy.

The statistical analysis for the required sample size per group was carried out using Statistica version 9 (StatSoft, Inc, 1984-2009, USA). All other statistical analyses were performed using the Statistical Package for Social Sciences for Windows 8.0 software. The results are presented as means with their respective standard deviations. To make comparisons, analysis of variance (ANOVA) was employed, followed by The unpaired Student's t-test assessed statistical differences between quantitative variables, and the Chi-square test was utilized for qualitative variables. Pearson correlation analysis was used to calculate correlations between variables. The results were evaluated within a 95% confidence interval, and significance was determined with a probability level of less than 0.05.

Results:

Table 1: Demographic characteristics among the study population

Demographic	N (%)
Gender	
Male	3 (10)
Female	27 (90)
Age (years)	
Mean ± SD	41.7 ± 4.5
Median (IQR)	41.2 (37-46.5)
Range (minimum-maximum)	30-50

The table 1 shows demographic data of the study participants indicates that the majority were female, accounting for 90% (27 out of 30), while males comprised only 10% (3 out of 30). The age of participants ranged from 30 to 50 years, with a mean age of 41.7 years (± 4.5). The median age was 41.2 years, with an interquartile range (IQR) of 37 to 46.5 years.

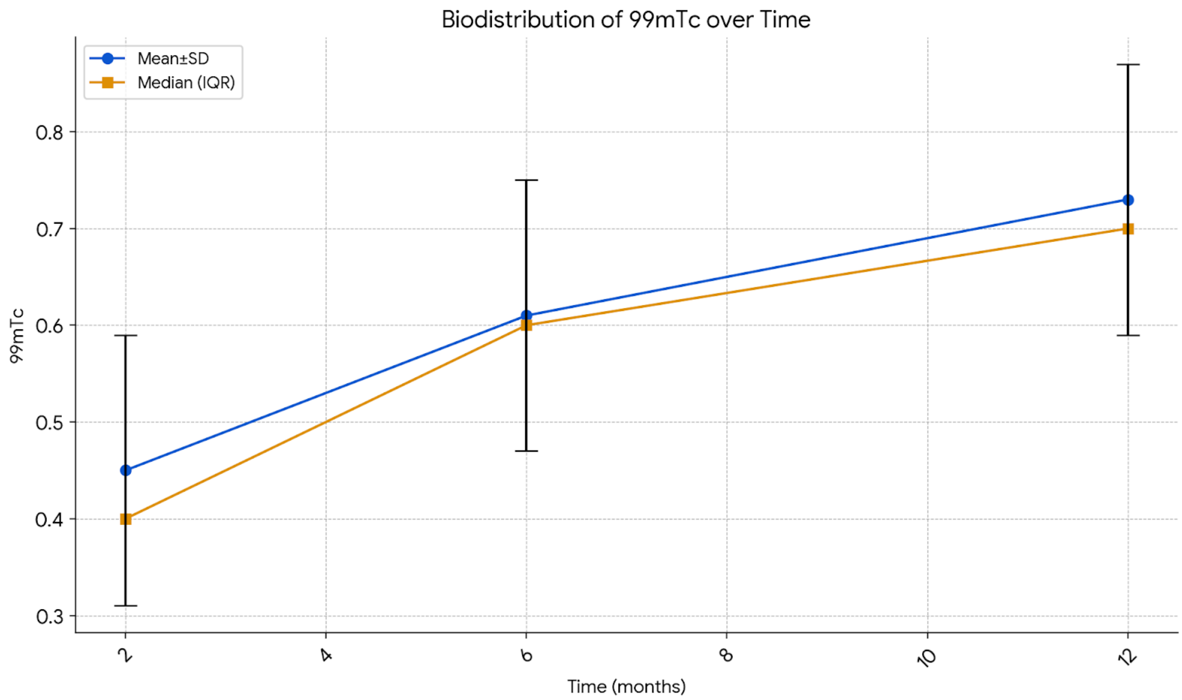

Figure 1: Postoperative thyroid scan (99m tc) uptake by implant among the study population follow-up

The figure 1 illustrates the biodistribution of 99mTc over time, measured at intervals of 2, 6, and 12 months. Two statistical measures are presented: the mean with standard deviation (Mean±SD) and the median with interquartile range (Median (IQR)).

At the 2-month mark, the mean level of 99mTc is approximately 0.5 with a notable standard deviation, indicating a wide spread of values among patients. The median level at this time is slightly lower, around 0.4, with a smaller interquartile range, suggesting a more consistent distribution among the middle 50% of patients. By the 6-month mark, both the mean and median levels of 99mTc have increased to around 0.6.

The error bars for both measures at this point indicate a reduction in the spread of values for the mean, while the interquartile range for the median remains relatively small, showing consistent growth in 99mTc levels among patients. At 12 months, the mean level of 99mTc rises further to about 0.7, with an increase in standard deviation, indicating more variability in the values.

The median level also increases to approximately 0.65, maintaining a consistent trend with a relatively small interquartile range. This suggests that most patients have similar increases in 99mTc levels over time, though individual variations are more pronounced by the end of the study period.

Overall, the graph demonstrates a steady increase in the biodistribution of 99mTc over the 12-month period, with both mean and median values showing upward trends and the variability among patients becoming more noticeable over time.

Table 2: Postoperative thyroid function follow up (free T3–free T4–thyroid-stimulating hormone)

Time	Free T3	Free T4	TSH
2 months follow up	2.1±0.61	0.68±0.14	46.3±16.8
6 months follow up	2.62±0.41	0.7±0.17	37.3±14.5
12 months follow up	3.95±1.2	1.06±0.20	22.7±9.72

Table 2 presents the postoperative thyroid function follow-up data, detailing levels of free T3, free T4, and thyroid-stimulating hormone (TSH) at intervals of 2, 6, and 12 months.

At the 2-month follow-up, the mean free T3 level was 2.1 ± 0.61, free T4 was 0.68 ± 0.14, and TSH was 46.3 ± 16.8. By the 6-month follow-up, free T3 increased to 2.62 ± 0.41, free T4 remained relatively stable at 0.7 ± 0.17, and TSH decreased to 37.3 ± 14.5. At the 12-month mark, significant changes were observed with free T3 rising to 3.95 ± 1.2, free T4 increasing to 1.06 ± 0.20, and TSH further decreasing to 22.7 ± 9.72.

These trends indicate an overall improvement in thyroid function over the course of the year following the thyroid tissue autotransplantation.

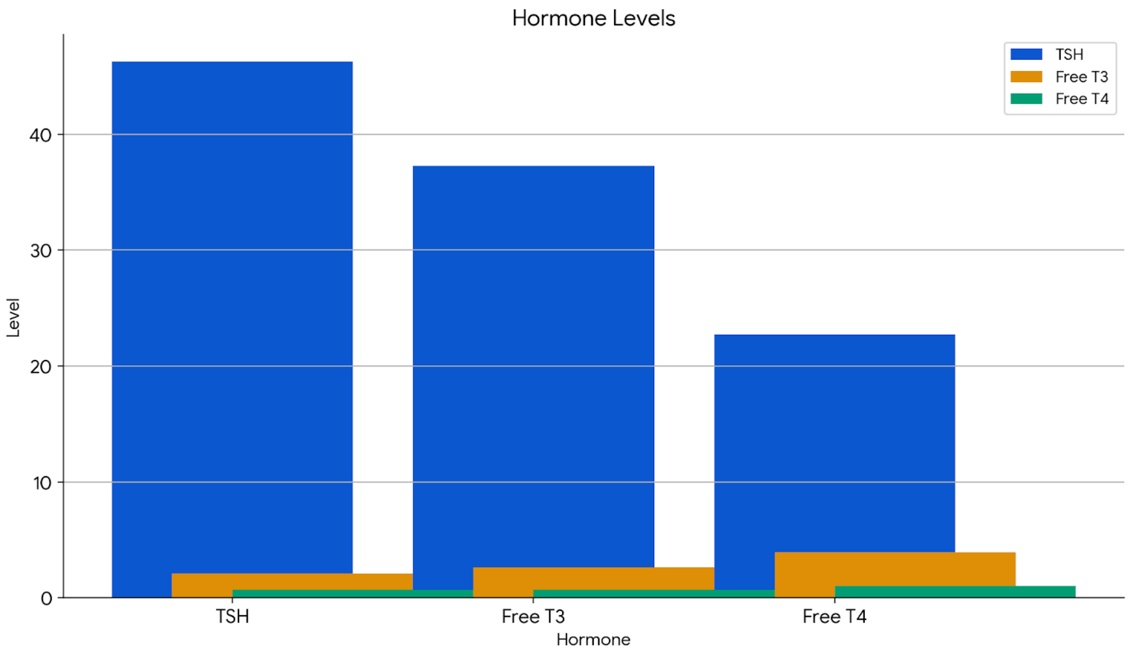

Figure 2: Postoperative thyroid function follow up (free T3–free T4–thyroid-stimulating hormone)

The table 3 presents correlations between various preoperative and demographic variables with postoperative outcomes at 12 months, including 99mTc uptake by the implant, TSH levels, free T3 levels, and free T4 levels. Age did not show significant correlations with any of the postoperative outcomes ($p > 0.18$ for all). Preoperative TSH levels had significant correlations with all outcomes: a negative correlation with 99mTc uptake ($r = -0.27$, $p = 0.0091$), and positive correlations with TSH ($r = 0.21$, $p = 0.018$), free T3 ($r = 0.4$, $p = 0.0062$), and free T4 levels ($r = 0.19$, $p = 0.035$). Preoperative FT3 levels were significantly positively correlated with 99mTc uptake ($r = 0.4$, $p = 0.00713$) but showed no significant correlation with TSH, free T3, or free T4 levels ($p > 0.47$ for all).

Table 3: Correlations between 12-month follow up 99mTc uptake by the implant, thyroid-stimulating hormone levels, free T3, free T4, and preoperative level

Correlations	**12 months follow-up 99mTc uptake by the implant**	**12 months follow-up TSH levels**	**12 months follow-up free T3 levels**	**12 months follow-up free T4 levels**
Age				
r	-0.017	0.011	-0.017	0.024
P value	0.186	0.515	0.286	0.182
Preoperative TSH levels				
r	-0.27*	0.21*	0.4*	0.19*
P value	0.0091	0.018	0.0062	0.035
Preoperative FT3 levels				
r	0.4*	-0.011	-0.007	0.009
P value	0.00713	0.47	0.614	0.57
Preoperative FT4 levels				
r	0.016	0.012	0.023	0.009
P value	0.301	0.339	0.141	0.543

Preoperative FT4 levels did not show significant correlations with any of the postoperative outcomes ($p > 0.14$ for all). These results suggest that preoperative TSH and FT3 levels are important predictors of postoperative thyroid function and 99mTc uptake by the implant.

The 12-month follow-up TSH levels and the preoperative TSH levels were significantly correlated. Preoperative TSH levels and 12-month follow-up free T4 levels were significantly correlated.

Discussion:

The study presents a comprehensive analysis of postoperative thyroid function following thyroid tissue autotransplantation, with a focus on the biodistribution of 99mTc, thyroid function markers (free T3, free T4, TSH), and their correlations with preoperative and demographic variables.

The study population predominantly consisted of females (90%), with a mean age of 41.7 years. The results of our study align with the findings of Sakr et al.[9], who reported that the average age of patients with benign thyroid diseases was 36.65±12.19 years, and the majority of cases were women (75%). Alawady et al.[10] found that the average age of persons with benign thyroid problems was 36.2 years, and the majority of cases were women (90%). These demographic characteristics may influence the generalizability of the results, as hormonal and thyroid function variations can differ by gender and age. The postoperative thyroid scan indicated a progressive increase in the biodistribution of 99mTc over 12 months. Initially, at the 2-month follow-up, the mean 99mTc uptake was approximately 0.5 with a notable spread, indicating variability among patients. By the 6-month follow-up, both the mean and median uptake increased to around 0.6, with a reduction in variability, suggesting more consistent improvement across the cohort. At 12 months, the mean uptake further increased to 0.7, accompanied by greater variability, reflecting individual differences in recovery and function post-autotransplantation. The upward trend in 99mTc uptake suggests successful integration and function of the transplanted thyroid tissue over time.

In our study, all individuals received total thyroidectomy with immediate implantation of thyroid tissue into the quadriceps femoris muscle. This is in contrast to those who cryopreserved thyroid tissue for eventual autotransplantation when the patient develops hypothyroidism. In certain investigations, such as the one conducted by Gamal et al.[11], thyroid tissue was implanted in the sternomastoid muscle using the same procedure as a total thyroidectomy (TT), without the need for additional incisions. However, this method still carries the danger of injuring important tissues in the neck in cases of recurrence.

Thyroid function markers (free T3, free T4, and TSH) showed significant changes over the 12-month follow-up. Free T3 levels increased from 2.1 ± 0.61 at 2 months to 3.95 ± 1.2 at 12 months, indicating a significant improvement in thyroid hormone production. Free T4 levels also showed a gradual increase, while TSH levels decreased substantially from 46.3 ± 16.8 to 22.7 ± 9.72 over the same period. The decrease in TSH levels suggests a negative feedback mechanism in response to increasing thyroid hormone levels, indicating improved thyroid function.

The study conducted by Alawady et al.[10] showed that the level of TSH increased significantly one month after the operation, and then steadily reduced after 3, 6, and 12 months postoperatively ($P<0.001$). According to recent research conducted by Mohsen et al.[12], there was a statistically significant difference between the 10 and 5 g implants after 12 months ($P=0.04$). Additionally, generally, the 10 g implants resulted in higher FT3 levels. Both the 5 g implants' and the 10 g implants' FT3 levels increased significantly over time ($P=0.02$), although the difference was less for the 5 g implants.

Our findings confirm that there was a correlation between the passage of time and longer follow-up with a higher uptake of 99mTc dosage.We carefully analyze several parameters in order to achieve a specific end, specifically the functional outcome of thyroid implantation in patients with preoperative euthyroid status and simple nodular goiter. There was a significant association between 99mTc uptake and preoperative serum FT3 and FT4 levels at 12 months post-transplantation. Additionally, there was a negative correlation between 99mTc uptake and preoperative TSH level.

After a period of 2 and 12 months, a 99mTc scan was performed on Saleh [13]. The utilization of duplex ultrasonography and monitoring thyroid function with FT3, FT4, and TSH resulted in a 50% reduction in the frequency of 99mTc scans one month following surgery.

Implications for Clinical Practice

The results of this study suggest that preoperative thyroid function, particularly TSH and FT3 levels, are critical factors in predicting the success of thyroid tissue autotransplantation. Patients with better thyroid function preoperatively are likely to experience more favorable postoperative outcomes. The progressive increase in 99mTc uptake and improvement in thyroid function markers over 12 months indicate the potential for thyroid tissue autotransplantation to restore thyroid function effectively.

Conclusion:

In summary, this study demonstrates that thyroid tissue autotransplantation can lead to significant improvements in thyroid function over a 12-month period. Preoperative TSH and FT3 levels are important predictors of postoperative success, highlighting the need for careful patient selection and preoperative assessment in clinical practice. Further research with larger sample sizes is needed to confirm these findings and optimize the approach to thyroid tissue autotransplantation.

Limitations:

The study's limitations include its small sample size and the gender imbalance, which may affect the generalizability of the findings. Future studies should aim to include a larger and more diverse cohort to validate these findings and explore the influence of other potential variables on postoperative outcomes.

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Ethical statement:

Institutional ethical committee accepted this study. The study was approved by the institutional human ethics committee, Annapoorana Medical College & Hospitals in Salem, Tamil Nadu. Informed written consent was obtained from all the study participants and only those participants willing to sign the informed consent were included in the study. The risks and benefits involved in the study and the voluntary nature of participation were explained to the participants before obtaining consent. The confidentiality of the study participants was maintained.

Data Availability:

All datasets generated or analyzed during this study are included in the manuscript.

Informed Consent:

Written informed consent was obtained from the participants before enrolling in the study

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