Implantation of thyroid tissue after total thyroidectomy in quadriceps femoris muscle

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Received: 24 September 2023
Revised: 11 October 2023
Accepted: 23 October 2023
Published: 31 January 2024

The Egyptian Journal of Surgery 2024, 43:1–8

Background

It appears to be relatively simple to control postoperative hypothyroidism after total thyroidectomy (TT) with L-T4 replacement therapy, but from the patient's perspective, a daily reliance on L-T4 administration and regular follow-up visits to the hospital may become somewhat of a burden and may interfere with reaching euthyroid status utilizing replacement therapy because of patient noncompliance.

Aim and objectives

To evaluate implantation of thyroid tissue in the thigh muscle after TT for benign simple nodular goiter to avoid lifelong use of thyroid hormones as replacement therapy and preservation of autoregulatory mechanism of thyroid hormone production.

Patients and methods

From April 2021 to September 2022, with approval from the Ethics Committee of the Faculty of Medicine at Assiut University, Assiut, Egypt, 40 individuals with simple nodular goiter who required TT participated in a prospective case series study.

Results

There was significant relation between 12 months follow up thyroid-stimulating hormone (TSH) levels and preoperative TSH levels. There was significant relation between 12 months follow up free T4 levels and preoperative TSH levels.

Conclusion

When performed on individuals who have benign thyroid disorders, TT is followed by autotransplantation of the patient's own thyroid tissue. This technique is safe, straightforward, and applicable, and it results in a postoperative euthyroid state in the vast majority of carefully selected individuals without the need for additional replacement therapy.

Keywords:
euthyroid, implantation of thyroid, in quadriceps femoris muscle, novel technique, total thyroidectomy

Egyptian J Surgery 43:1–8

1110-1121

Introduction

Total thyroidectomy (TT) is currently the standard treatment for people who have simple nodular goiter. With a thorough surgical approach and expert hands, TT can now be performed safely and with minimal complication rates [1].

Patients need to take levothyroxine (L-T4) for the rest of their lives. Although L-T4 replacement therapy seems like a simple solution for postoperative control of hypothyroidism after TT, patients may find that taking the medication every day and returning to the hospital for checkups becomes a burden. This can prevent them from achieving euthyroid status and increase the risk of complications [2]. Furthermore, exogenous L-T4 replacement medication has been connected to bone loss in premenopausal women if not closely monitored, and subclinical hypothyroidism and hyperthyroidism have been related to cardiovascular problems [3].

When benign thyroid tissue is implanted following TT, the body's own mechanisms for regulating thyroxin production are preserved, allowing patients to avoid lifetime hormone replacement treatment. Thyroid autotransplantation in the neck was done by implanting thyroid tissues at sternomastoid muscle from the same surgical approach [4], but it is still adjacent to critical structures and tight working spaces in the neck make re-exploration of the neck more difficult and liability of injury to delicate structures increases.

Thyroid autotransplantation in the thigh has been recommended to avoid reoperation at the site of earlier neck surgery in cases of recurrent goiters or hyperthyroidism, and it allows for a greater quantity of thyroid tissues to be implanted [5].

The goal of the research was to assess the implantation of thyroid tissue in the thigh muscle following TT for benign simple nodular goiter to avoid lifelong replacement therapy with thyroid hormones and to preserve the autoregulating mechanism of thyroid hormone production.

The need of long-term follow up to provide more time for the implant to gain its vascularity and function.

If recurrence or malignant transformation occurs, thyroid scan could be done to provide adequate information about site, size malignancy potential, that is cold nodule versus recurrence (warm nodule) and so we can do exploration of thigh region and this will be easier than re-exploration of the neck.

Thyroid autotransplantation can hypothetically enable the preservation of native thyroid function in an accessible site, for example in the thigh (thus, avoids the risk of regrowth in the neck region), and provides a larger amount of thyroid tissue to be implanted. If recurrence occurs it would not be in the neck, thus avoiding compression on the trachea and avoiding dangerous reoperation in the neck.

Patient safety in case of recurrence or malignancy potential

Precautions that have been taken included preoperative and operative measures. Before surgery those with a family history of thyroid cancer or neck irradiation were excluded. Thorough clinical assessment, neck ultrasound, and fine-needle aspiration cytology for any suspicious nodule were done. The slightest suspicion of malignancy disqualified the patient for autotransplantation. At operation the healthiest-looking internodular part of excised goiter was chosen for implantation. Cutting of the chosen tissue into homogeneous emulsion was too fine to allow for missing any gross change in appearance or texture.

Theoretically a goiter in the thigh is less likely to be visible or to compress important structures. Surgery for such a swelling would certainly be less serious than reoperation in the neck [6].

Patients and methods

From April 2021 to September 2022, 40 patients with simple nodular goiter who required complete thyroidectomy were enrolled in a case series prospective research conducted in the General Surgery Department at Assiut University Hospital. Approval by the Assiut University Medical School's Ethics Committee. Every individual provided their informed written permission that involved a statement recognizing the value of consistent follow-up.

Inclusion criteria: patients ages 18 and up having a preoperative diagnosis of simple nodular goiter, patients deemed anesthetic-safe (ASA scores of 1 and 2), and patients willing to provide their contact information and short-term outcomes.

Exclusion criteria: individuals with a high ASA score, people with a malignant or recurrent goiter, participants who were unwilling to undergo surgery, patients with any clinical or ultrasound suspicion of malignancy, and those with a family history of thyroid cancer and a history of neck irradiation due to a high risk of developing thyroid cancer were all excluded.

Methods

Every individual underwent a comprehensive clinical evaluation consisting of a thorough history and physical examination in addition to the standard preoperative laboratory investigations such as complete blood count, liver function tests, kidney function tests, thyroid function tests [free T3 (FT3), free T4 (FT4), and thyroid-stimulating hormone (TSH)], serum calcium, ECG, and chest radiograph.

Every individual had both fine-needle aspiration cytology and neck ultrasound. Prior to surgery, laryngoscopy was performed on all patients to assess the range of motion of the vocal cords.

All patients were admitted to the hospital the day before their surgeries and required to fast for 8 h before the procedures.

Antibiotic prophylaxis in the form of sulbactam/ampicillin 1500 mg was administered intravenously at the time of anesthetic induction and then again 12 h later.

Every single individual had total thyroid removals while under general anesthesia. One of the surgeons prepared the patient for autotransplantation while the others attended to postexcision hemostasis and closure. During the procedure, the section of the thyroid that looked the healthiest was selected.

Implants weighing 10 g were used for each individual.

Transplanted tissues were very finely split with scissors and then mixed with normal saline (0.9%) in a 20 ml syringe to create an emulsion (Fig. 1).

Tissue homogenization was achieved by transferring the emulsion among two 20 ml syringes linked by tubing and a three-way stopcock (Fig. 2).

Then the homogenized emulsion attached to a fat transfer needle (2.4-mm-caliber needle).

An anterolateral snip was made along the middle third of the thigh that is closest to the front of the body. Thyroid tissue emulsion was injected into the thigh muscles at eight to ten different places through this incision by varying the needle's insertion direction and depth (Fig. 3).

Postoperative follow up

Thyroid function tests FT3, FT4, TSH, and Tc m99 scan were done at 2, 6, and 12 months (when possible) after the operation.

To avoid the development of hypothyroidism, till the take of the graft, all patients were given a relatively low replacement dose (50 μg levothyroxine daily) was chosen to maintain a high TSH would enhance implant survival and function. Replacement therapy was discontinued 2 weeks before assessment of its function. This provide enough time for the replacement therapy to disappear from the circulation (the half-life of T4 being 1 week and that of T3 1 day).

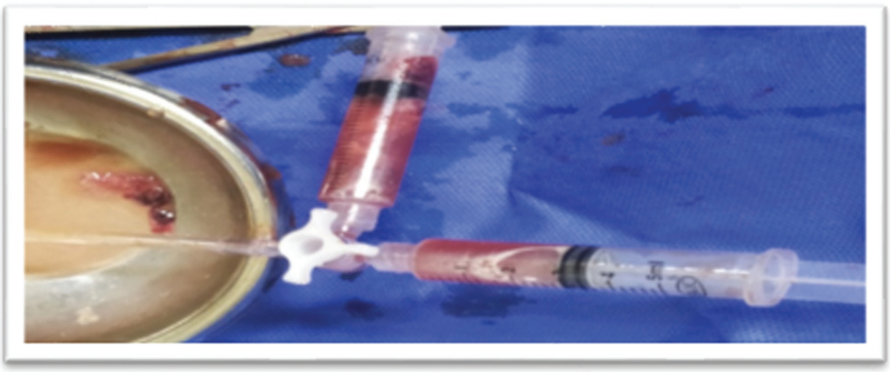
Statistical analysis

SPSS 26.0 for Windows (SPSS Inc., Chicago, Illinois, USA) was utilized for data collection, tabulation, and

Figure 1

Thyroid emulsion into 20 ml syringe.

Figure 2



Emulsification of thyroid tissue through three-way cannula.

Figure 3

Injection of emulsified thyroid tissue into quadriceps femoris muscle.

statistical analysis. Quantitative and percentage descriptions were used for qualitative information. Minimum and maximum values, as well as the mean, median, and SD, were utilized to characterize the quantitative data. Two-tailed significance testing was performed on all data. *P* value less than or equal to 0.05 is significant, *P* value less than 0.001 is extremely significant, and *P* value more than 0.05 is not significant.

The used tests were χ^2 test of significance: was used to compare proportions among qualitative parameters and independent *t* test: was utilized to compare among two independent groups with parametric quantitative data.

Results

The study included 40 patients, 37 (93%) females and three (7%) males. The age extended from 31 to 50 years with mean±SD=40.5±5.2 (Table 1).

Two-month follow up 99mTc uptake by the implant among the study population: varied from 0.2 to 0.8 with mean±SD=0.45±0.14 (Fig. 4).

Table 1 Demographic characteristics among the study population

	N=40) [*n* (%)]
Sex	
Male	3 (7)
Female	37 (93)
Age (years)	
Mean±SD	40.5±5.2
Median (IQR)	40.5 (38–45.25)
Range (minimum–maximum) (years)	31–50

IQR, interquartile range.

Six-month follow up 99mTc uptake by the implant among the study population: varied from 0.2 to 1 with mean±SD=0.61±0.17 (Fig. 5).

Six-month follow up of 99mTc uptake by the implant (two white arrows) with spot view on lower limbs. Black arrow showing urinary bladder.

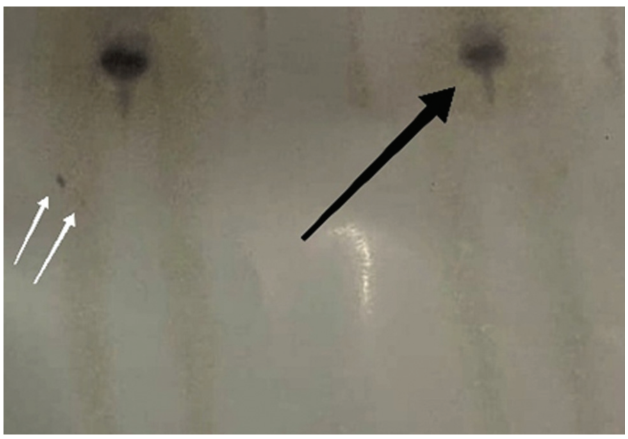
Twelve-month follow up 99mTc uptake by the implant among the study population: varied from 0.4 to 1 with mean±SD=0.73±0.17 (Table 2).

Two-month follow up TSH levels among the study population varied from 10.2 to 75.1 (mean±SD=46.2 ±16.7). Six-month follow up TSH levels among the study population extended from 4.7 to 68 (mean ±SD=37.2±14.7). Twelve-month follow up TSH levels among the study population extended from 5.3 to 41.6 (mean±SD=22.9±9.92).

Figure 4

Thyroid scan m99Tc with spot view on lower limbs showing m99Tc uptake by the implant (arrow).

Figure 5



Six-month follow up whole body thyroid scan showing functioning thyroid implant (2 arrows) in th thigh.

Table 2 Postoperative thyroid scan (^{99m} tc) uptake by implant among the study population follow-up

	2 months	6 months	12 months
99 m Tc			
Mean±SD	0.45±0.14	0.61±0.17	0.73±0.17
Median (IQR)	0.4 (0.3–0.52)	0.6 (0.5–0.7)	0.7 (0.6–0.8)
Range (minimum–maximum)	0.6 (0.2–0.8)	0.8 (0.2–1)	(0.4–1)

Two-month follow up FT3 levels among the study population ranged from 1 to 3.3 (mean±SD=2.2 ±0.62). Six-month follow up FT3 levels among the study population extended from 2 to 3.8 (mean ±SD=2.63±0.42). Twelve-month follow up FT3 levels among the study population ranged from 2.1 to 5.7 (mean±SD=3.96±1.1).

Two-month follow up free T4 levels among the study population ranged from 0.4 to 0.8 (mean ±SD=0.67±0.13). Six-month follow up free T4 levels extended from 0.6 to 1.4 (mean±SD=1.05 ±0.21). Twelve-month follow up of FT4 levels ranged from 0.6 to 1.4 (mean±SD=1.05±0.21) (Table 3).

Table 3 Postoperative thyroid function follow up (free T3–free T4–thyroid-stimulating hormone)

	2 months follow up	6 months follow up	12 months follow up
Free T3			
Mean±SD	2.2±0.62	2.63±0.42	3.96±1.1
Median (IQR)	2.05 (1.58–2.6)	2.55 (2.3–2.72)	3.95 (2.98–4.8)
Range (minimum–maximum)	2.3 (1–3.3)	1.8 (2–3.8)	(2.1–5.7)
Free T4			
Mean±SD	0.67±0.13	0.8±0.18	1.05±0.21
Median (IQR)	0.7 (0.6–0.8)	0.8 (0.7–0.9)	1.1 (0.9–1.2)
Range (minimum–maximum)	0.4 (0.4–0.8)	0.6 (0.5–1.1)	(0.6–1.4)
TSH			
Mean±SD	46.2±16.7	37.2±14.7	22.9±9.92
Median (IQR)	47.65 (38–55)	37.85 (25.12–47.12)	21.8 (15.85–30.52)
Range (minimum–maximum)	64.9 (10.2–75.1)	63.3 (4.7–68)	(5.3–41.6)

TSH, thyroid-stimulating hormone.

Table 4 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	−0.020	0.011	−0.017	0.022
P value	0.196	0.505	0.276	0.172
Preoperative TSH levels				
r	−0.27*	0.21*	0.4*	0.18*
P value	0.0092	0.018	0.007	0.025
Preoperative FT3 levels				
r	0.4*	−0.011	−0.007	0.009
P value	0.00813	0.490	0.648	0.580
Preoperative FT4 levels				
r	0.016	0.012	0.023	0.009
P value	0.304	0.439	0.151	0.573

FT3, free T3; FT4, free T4; TSH, thyroid-stimulating hormone.

Table 4 shows that there was significant relation between 12 months follow up 99mTc uptake by the implant and preoperative TSH levels and preoperative FT3 levels.

There was significant relation between 12 months follow up TSH levels and preoperative TSH levels. There was significant relation between 12 months follow up free T4 levels and preoperative TSH levels.

Discussion

Our study show that the age of our participants varied from 31 to 50 years (mean±SD=40.5±5.2) and 37 (93%) of cases were female.

Our findings were matched with Sakr *et al.* [7] who found that the mean age of individuals with benign thyroid disorders was 36.65±12.19 years and the majority of cases were women (75%). Similarly, Alawady *et al.* [8] revealed that the mean age of individuals with benign thyroid disorders was 36.2 years and the majority of cases were women (90%).

At our study, all patients underwent routine neck ultrasound with fine-needle aspiration cytology and thyroid function test.

As regard neck ultrasound, all patients show multinodular goiter with benign featuring thyroid nodules and no cervical lymphadenopathy and normal neck vessels (not compressed or infiltrated by a tumor). Fine-needle aspiration cytology: all cases were colloid goiter. Thyroid function tests (TSH, FT3, and FT4): revealed that all cases were at euthyroid state: where TSH levels ranged from 1.3 to 4.6 with mean±SD=2.9±0.91. FreeT3 was ranged from 2.4 to 4.5 with mean±SD=3.33±0.61. Free T4 levels ranged from 0.8 to 2 with mean±SD=1.08±0.25.

These results were similar to Alawady *et al.* [8] as regard neck ultrasound and laboratory investigations and histopathological examination.

At our study, all cases underwent TT with implantation of thyroid tissue at quadriceps femoris muscle at the same operation unlike who cryopreserved thyroid tissue to be autransplanted later on when patient develop hypothyroidism.

The advantage of using the thigh muscle as an autotransplantation site is being bulky and with good vascularity and so we can implant sizable weight of thyroid tissue with no fear of graft ischemia, on the other hand the thigh is accessible site helping in feasibility of removal in cases of recurrence.

Some studies, for example, Gamal *et al.* [4] implanted thyroid tissue in sternomastoid muscle at the same approach for TT with no further incision, for example in the thigh but still carrying the risk of injury of critical structures in the neck in cases of recurrence.

The weight of 10 g of thyroid tissue was chosen to be autransplanted because other studies, for example Sakr *et al.* [7] shown that less than that weight will not be functioning very well, however Mohsen *et al.* [9] show no statistical difference between 5 and 10 g implant.

Monib *et al.* [10] sliced and mixed with saline and injected in various pockets by microskin puncture with a 20-ml syringe coupled to a 1 mm blunt tip fat transfer needle into the anterolateral portion of the left thigh (nondominant thigh).

Histopathological examination: at our study, histopathological examination of the removed specimens demonstrated that 20 (50%) cases had colloid nodular goiter, 18 (45%) patients had nodular thyroid hyperplasia, one patient had primary toxic goiter (2.5%) and one patient had Hashimoto thyroiditis (2.5%).

In other studies as Sakr *et al.* [7] eight individuals (40%) were found to have colloid nodular goiter; another five people (25%) were found to have nodular thyroid hyperplasia; four individuals (20%) were found to have Grave disease; a single person (5%) was found to have follicular adenoma in the context of colloid nodular goiter and two cases (10%) were found to have papillary thyroid carcinoma.

In our study the postoperative follows up of thyroid function tests was as follow: TSH: at 2 months follow up, TSH levels extended from 10.2 to 75.1 with mean ±SD=46.2±16.7. Six months follow up TSH levels extended from 4.7 to 68 with mean±SD=37.2±14.7. At 12 months follow up, we also found that TSH levels ranged from 5.3 to 41.6 with mean±SD=22.9±9.92. So, the current study showed that TSH levels significantly reduced with time passage for 10-g implants (P=0.018).

Our findings indicated by Alawady *et al.* [8] who revealed that TSH level significantly increased at 1 month postoperatively, then gradually decreased at 3, 6, and 12 months postoperatively ($P<0.001$).

Free T3: our results showed that there was significant increase in FT3 levels by passage of time. At 2 months follow up FT3 levels ranged from 1 to 3.3 with mean ±SD=2.2±0.62. As well, at 6 months follow up FT3 levels ranged from 2 to 3.8 with mean±SD=2.63±0.42. At 12 months follow up FT3 levels it ranged from 2.1 to 5.7 (mean±SD=3.96±1.1) (P=0.648).

Depending on the current research Mohsen *et al.* [9] showed that at 12 months, the distinction among the 10 and 5 g implants was statistically significant (P=0.04), while FT3 levels were greater with the 10 g implants overall. Both the 5 g implants' and the 10 g implants' FT3 levels rose substantially over time (P=0.02), however the difference was less for the 5 g implants.

FT4: our results showed that there was significant increase in FT4 levels by passage of time. At 2 months follow up FT4 levels varied from 0.4 to 0.8 with mean±SD=0.67±0.13. At 6 months follow up FT4 levels varied from 0.5 to 1.1 with mean±SD = 0.8 ±0.18. at 12 months follow up FT4 levels ranged from 0.6 to 1.4 with mean±SD=1.05±0.21 (P=0.57).

In other studies, as Mohsen *et al.* [9] showed that although there was a trend toward greater FT4 levels with the 10 g implants, the variation among them and the 5 g implants did not approach statistical significance until much later. However, both the 5 g implants (Z=0.02) and the 10 g implants had substantial increases in FT4 levels over time.

Our results approve that the was associated with high ^{99m}Tc dose uptake with passage of time and longer follow up.

There are many factors we put it in consideration to gain certain outcome so we can obtain thyroid implant function outcome in relation to preoperative euthyroid status of simple nodular goiter patients. The 99mTc uptake was significantly associated when considering 1% 99mTc uptake as a cutoff point, positive correlation was found between 99mTc uptake at 12 months post-transplantation and preoperative serum FT3 (r=0.4; P=0,0081), preoperative FT4 (r=0.016; P=0.304), whereas a negative correlation was found with preoperative TSH level (r=−0.27; P=0.0092).

Saleh [11] after 2 and 12 months, ^{99m}Tc was conducted. The frequency of ^{99m}Tc scans was cut in half by using duplex ultrasonography 1 month after surgery and tracking thyroid function with FT3, FT4, and TSH.

In our study five (12.5%) patients developed complications in the form of temporary hoarseness of voice in two (5%) patients, two (5%) patients developed implantation site numbness which respond very well to neurotonic tablets and one (2.5%) patient developed transient hypocalcaemia.

In other studies, as Sakr *et al.* [7] show in two patients, neither the preoperative evaluation nor the intraoperative characteristics indicated suspicion of malignancy, but the postoperative histological analysis reveals follicular form of papillary thyroid cancer. These two individuals were removed from the trial because they required readmission for surgical excision of the auto graft.

Limitations of the study

Strict follow up could not be obtained in few patients at 12 months follow up due to noncompliance patients and nonavailability of isotope scan study regularly.

Conclusion

Autotransplantation of thyroid tissue following TT is a simple, safe, simple, and applicable technique that results in survival and function of thyroid graft, achieving postoperative euthyroid state in the majority of selected individuals without the need for further replacement therapy in those with benign thyroid disorders. There was positive isotope absorption from 10 g implants. The longer the implant was in place, from 2 to 12 months, the better it appeared to work. To corroborate our results and uncover risk factors of adverse outcomes, larger-scale, longer-term follow-up investigations are required.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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