IJMA

International Journal of Medical Arts

Volume 6, Issue 1, January 2024

P- ISSN: 2636-4174
E- ISSN: 2682-3780

Available online at Journal Website
https://ijma.journals.ekb.eg/
Main Subject [Surgery]

Original Article

Feasibility and Safety of Thyroid Tissue Auto-transplantation after Total Thyroidectomy for Simple Multinodular Goiter

Mohamed G. El Madawy [1*], Islam Elzahaby [2], Ayman Mahmoud Elwan [1]; Nagah Atwa Salem [1]

[1] Department of General Surgery, Damietta Faculty of Medicine, Al-Azhar University, Damietta, Egypt.
[2] Department of Surgical Oncology, Mansoura Faculty of Medicine, Mansoura University, Mansoura, Egypt.

Article information

Received: 10-12-2022

Accepted: 01-10-2023

DOI: 10.21608/ijma.2024.179887.1569.

***Corresponding author**
Email: m3dawy42@yahoo.com

Citation: El.Madawy MG, Elzahaby I, Elwan AM, Salem NA. Feasibility and Safety of Thyroid Tissue Auto-transplantation after Total Thyroidectomy for Simple Multinodular Goiter. IJMA 2024 January; 6 [1]: 4082-4090. doi: 10.21608/ijma.2024.179887.1569.

ABSTRACT

Background: Total thyroidectomy is currently considered the modality of choice for treatment of benign thyroid disorders. After surgery the patient becomes dependent on replacement therapy for life, thyroid tissue auto-transplantation provides the chance to avoid the need for life-long replacement therapy and to avoid post-thyroidectomy hypothyroidism in non-compliant patients.

The Aim of the work: This work aimed to investigate the feasibility and safety of thyroid tissue auto-transplantation after total thyroidectomy for simple multinodular goiter.

Patients and Methods: This study was designed to be an observational prospective study, conducted on 30 patients who were diagnosed with simple multinodular goiter and were submitted for total thyroidectomy followed by thyroid tissue auto- transplantation.

Results: Postoperative hypocalcemia with range of serum calcium level from 7.6 to 8 mg/dl [normal value: 8.5 to 10.2 mg/dl] was found in six patients [20%], the final outcome one year after surgery showed that all the cases had a functioning viable transplanted thyroid tissue, but with different degrees of function, six cases [20%] had fully functioning implants [T3, T4, and TSH were normal during the hormonal analysis], 21 cases [70%] had minimally insufficient implants which had normal levels of thyroid hormones but they had a high level of TSH although the iodine scan showed viable functioning implants, and 3 cases [10%] had insufficient implants which had low levels of thyroid hormones and high level of TSH hormone.

Conclusion: Thyroid auto-transplantation is a safe and easy procedure that provides survival and function of the thyroid implants and offers promising results in the majority of the selected patients.

Keywords: Auto-transplantation; Total Thyroidectomy; Simple Multinodular Goiter.

INTRODUCTION

Multinodular goiter is a prevalent endocrine illness that primarily affects women in their forties and fifties. A variety of causes can contribute to the development of multinodular goiter, the most common of which is iodine deficiency [1].

Nodular goiter is typically characterized by a lump in the neck, although an expanding gland can cause pressure sensations, and hyper-thyroidism can develop in most cases of multinodular goiter after a few decades [2].

Most writers now recommend total thyroid-ectomy rather than partial thyroidectomy for the treatment of benign thyroid diseases that require surgical excision [3].

If the goiter recurs after a subtotal thyroid-ectomy, a variety of complications may arise. If this happens, additional surgery may be required, which will likely complicate matters further due to scar tissue that makes it challenging to identify vital tissues such as nerves. Moreover, a partial thyroidectomy might not remove an undiagnosed thyroid malignancy [4].

Following a total thyroidectomy, the patient is left dependent on replacement therapy for the rest of their lives. While levothyroxine appears to be a relatively simple way to control hypo-thyroidism, this approach is not thought to be ideal because it is limited by the patient's adherence to the treatment, the frequency of hospital visits to check hormone levels, malabsorption, and the inability to adjust for everyday physiological changes also play a role in reaching an euthyroid status using replacement therapy [5].

In the field of parathyroid surgery, the clinical use of transplantation in the endocrine field by auto-transplantation of endocrine organs for hormone replacement has already been established. Prior to applying the same ideas to the human thyroid gland, research on animals has been conducted. Remarkably few human studies have addressed this issue; autologous transplantations were shown to be successful in 70% of instances, and histological exams revealed normal thyroid architecture [6].

Thyroid tissue auto-transplantation aims to preserve thyroid tissue in noncompliant patients that may be able to prevent or lessen the degree of hypothyroidism following thyroidectomy while also evaluating the procedure's safety and effectiveness. Meanwhile, should a recurrence happen If a recurrence happens in the interim, it won't be in the neck, preventing pressure on the trachea and the potentially harmful consequences of doing another neck operation [7].

The aim of this study is to investigate the feasibility and safety of thyroid tissue auto-transplantation after total thyroidectomy for simple multinodular goiter.

PATIENTS AND METHODS

This study was designed to be an observational prospective study, conducted on 30 patients who were diagnosed with simple multinodular goiter and were candidates for total thyroidectomy followed by thyroid tissue auto-transplantation. This study was approved from the Ethical committee of Al-Azhar university, and was conducted at Al Al-Azhar university hospital [New Damietta] and at Oncology Center – Mansoura University in the period from July 2020 till July 2022. Informed written consent was obtained from every patient at the time of recruitment.

The Inclusion criteria were

1) Patients with simple multinodular goiter – proved by clinical examination, fine needle aspiration and neck ultrasonography – who were indicated for total thyroidectomy; 2) age: 25 – 60 years; 3) Fit for general anesthesia [ASA I & II]; and 4) both genders were included.

The Exclusion criteria were

1) Not fit for general anesthesia [ASA III or more]; 2) Refusal to undergo thyroid tissue auto-transplantation; 3) Clinically or radiologically suspicious criteria of the thyroid gland or pathologically proved thyroid cancer [Bethesda IV or more]; 4) Toxic goiter; 5) History of neck irradiation; 6) Family history of thyroid cancer; and 7) Recurrent cases of multi-nodular goiter.

Data collection

All patients were subjected to detailed medical history taking and clinical examination, routine laboratory investigations including complete blood picture, kidney function tests, liver function tests, coagulation profile, blood glucose level, and thyroid profile.

The following investigations were done for every patient; neck ultrasonography, fine needle aspiration cytology to exclude presence of malignancy, and indirect laryngoscopy to assess vocal cords. Thyroid autoantibodies were measured when autoimmune thyroiditis was suspected based on clinical, sonographic, and pathological findings. All patients were admitted to the hospital the day before surgery after completion of all consultations [cardiology, internal medicine and anesthesia] and the patients were documented as fit for surgery and a written informed consent was obtained from all participants.

Surgical technique

Surgical procedures were performed under general anesthesia with endotracheal intubation in supine position with the neck extended by padded sandbag between the scapulae and a head ring, electrosurgical unit was used [electrocautery or bipolar diathermy].

All patients underwent total thyroidectomy starting by a transverse skin incision which was made about 2 fingers breadth above the sternal notch along Langer lines then division of platysma and formation of the upper flap till thyroid notch and the lower flap till sternoclavicular joints, vertical division of the midline raphe between the strap muscles then the muscles separated and retracted laterally to expose the thyroid lobes.

Retraction of the strap muscles to one side and the middle thyroid vein identified, clamped, divided then tied with vicryl 3/0, exposure of the upper pole of the thyroid and the superior thyroid vessels are identified, clamped, divided, and doubly tied near the upper pole with preservation of external branch superior laryngeal nerve, ligation and division of branches of the inferior thyroid vessels to avoid injury of recurrent laryngeal nerve by division of them at the capsule with preservation of the blood supply of parathyroid glands, the lobe was then dissected from its bed, the same steps were repeated for the other lobe.

The gland was then dissected from the trachea and removed after its gross exam to ensure preservation of parathyroid glands. After ensuring absolute hemostasis of the field a suction drain was inserted in the thyroid bed, closure of fascia of the strap muscles by interrupted sutures then approximation of platysma and finally subcuticular sutures by proline 3/0 or absorbable vicryl sutures.

After completion of the total thyroidectomy procedure, a member of the operating team performed the auto-transplantation procedure, the healthiest thyroid tissue was grossly chosen and the slightest gross malignancy suspicion led to termination of the procedure which was not encountered during any of our procedures.

We measured 10-15 gm of grossly non-nodular healthy thyroid tissue of the excised gland which was immediately immersed in lactated Ringer's solution.

The fibrous capsule was removed and the tissue was finely minced into 1-mm to 2-mm pieces using scalpel. The tissue was then made into emulsion together with the previously added lactated Ringer's solution in a 20-mL syringe, and was further homogenized by passing the emulsion between two 20-mL syringes connected by a rubber tube, so the emulsion can be easily injected into the thigh muscle. A specially designed 2.4-mm caliber metallic needle was attached to the syringe.

A 3-mm incision was made in the anterolateral aspect of the middle third of the thigh, through this incision the thyroid tissue emulsion was injected in 8-10 sites in the vastus lateralis muscle of the thigh by changing the direction and depth of the needle introduction.

Light dressing of the incision site, the drain, and the transplantation site. During removal of the endotracheal tube, the anesthesiologist was asked to check the mobility of the vocal cords and both vocal cords were mobile in all of our patients, the operative time was documented. and the excised thyroid gland specimen was sent for histo-pathological examination.

All cases were admitted to the inpatient department with a source of oxygen beside their beds. Regular check of the vital signs every 2 hours and observation of the dressing and the drains regarding the amount and nature of the discharge. Oral fluids were allowed 2 hours after recovery and soft diet allowed at the evening if the patient tolerates the oral fluids. In the next day, serum calcium is estimated and prophylactic calcium supplementation is started for a month.

Postoperative complications, including recurrent laryngeal nerve injury, hypocalcemia, hemorrhage, neck wound infection, neck seroma/ hematoma formation, implantation site infection, or implantation site numbness, if any, were all recorded. Most patients were discharged in one to

three days after operation and received a follow up card, the patients were instructed to follow up at the outpatient clinic 1 week later, then after 2 weeks and monthly.

Histopathological examination of the total thyroidectomy specimen was performed to confirm its benign nature and exclude any malignancy. A dose of 50 micrograms/day of L-thyroxin drug was started after the final benign pathology of the excised gland was confirmed, and none of our patients had a malignant final pathology.

At 3-, 6- and 12-months' intervals after surgery, assessment of the auto-transplanted thyroid tissue function was performed by measuring the thyroid hormones levels [FT3, FT4 and TSH], exogenous hormone replacement was stopped 3 weeks before each assessment to measure the function of the auto-transplanted thyroid tissue.

A whole-body isotope scans were performed at 3 and 6 months after surgery to assess the viability of the transplant and its proper engraftment and function by injection of 5-10 mCi of 99mTc pertechnetate and imaging after 20 minutes [whole body scan, followed by calculating the uptake ratio in the thigh region].

The final results were confirmed at one year after the surgery and we classified the results into:

1) Fully functioning graft with normal levels of FT3, FT4, and TSH.
2) Minimally insufficient graft with normal levels of FT3, FT4, but a higher-than-normal TSH level.
3) Insufficient graft with positive uptake at the thigh region on 99mTc scan, but below-normal levels of FT3 and/or FT4.
4) Non-functioning graft with absent uptake in the thigh region on 99mTc scan and below normal levels of FT3 and FT4.

Statistical analysis

Data analysis was done using Microsoft Excel Software. The quantitative values were presented as mean and standard deviation. The qualitative values were presented as numbers and percentages.

RESULTS

Fulfilling our inclusion and exclusion criteria, our study included a total number of 30 patients. Age of the Patients in our study ranged between 25 - 57 years and had a mean age of 38.7 ± 9.537 years. There were 24 female patients [80%] and 6 male patients [20%].

All the cases [100%] in our study were diagnosed as benign multinodular goiter and all patients scored Bethesda II by fine needle aspiration cytology that was done before the surgery. The weight of the auto-transplanted thyroid tissue in all of our patients was about 10 - 15 grams. The operative time ranged between 90 - 150 minutes, and the mean operative time was 114 ± 21.066 minutes.

The final pathological examination of the excised thyroid gland confirmed that 27 patients [90%] had benign multinodular goiter and only 3 of them [10%] had multinodular goiter with lymphocytic thyroiditis.

Hypocalcemia was encountered after the surgery, it appeared as slight numbness and tingling around the mouth and sometimes in the fingers, Postoperative hypocalcemia with range of serum calcium level from 7.6 to 8 mg/dl [normal value: 8.5 to 10.2 mg/dl] was found in 6 of patients [20%], and it was treated by intravenous calcium gluconate infusion until disappearance of the symptoms followed by oral calcium and vitamin D supplementations for one month.

Seroma in the neck wound was encountered in 2 patients [6.6%], in both patients it resolved spontaneously after few days, neck wound hematoma and wound infection were not encountered in any patient [0%], and temporary hoarseness of voice due to vocal cord edema was encountered in 3 patients [10%] and the vocal cords regained their function within the first week after surgery, stridor was not encountered in any patient [0%]. Numbness at the injection site in the thigh was not found in any patient [0%], there were no injection site hematoma, seroma, or abscess formation detected in any patient [0%] [Table 1].

Uptake of radioactive I ^{131} after 3-6 months of transplantation showed functioning viable thyroid tissue in the thigh in all of the patients [100%]. Thyroid tissue residues were found in the neck during the radioactive iodine scan in all

patients, though neck us detected no residue in the operative bed.

All patients started with the lowest possible dose of the post-operative hormone replacement drug [50 micrograms/day] which was not given 3 weeks before every hormonal assessment.

The mean value of T3 and T4 were within normal range at 3 months after transplantation in all the patients. Twenty-seven patients [90%] had normal levels of T3 and T4 at one year after the surgery and three patients had low levels of serum T3 and T4.

The mean serum T3 one year after surgery was 1.0397 ± 0.2502 nmol/L and the mean serum T4 one year after surgery was 6.7966 ± 1.641 ug/dL.

The mean value of TSH gradually increased until 6 months after the surgery, then a gradual decrease until one year after the surgery. The mean value of TSH at 3 months was 40.37 ± 34.86 mIU/mL, then showed a gradual rise at 6 months which was 46.682±29.142 mIU/mL, and at 12 months it showed a gradual decline to 33.637 ± 28.647 mIU/mL. The final outcome one year after surgery showed that all the cases had a functioning viable transplanted thyroid tissue, but with different degrees of function. Six cases [20%] had fully functioning implants [T3, T4, and TSH were normal during the hormonal analysis], these cases took a replacement therapy dose of 50 micrograms/day that was stopped 3 weeks before the hormonal assay.

The other 24 cases had partially functioning implants. These cases were classified into two categories; The first category included 21 cases [70%] who had minimally insufficient implants which had normal levels of thyroid hormones but they had a high level of TSH although the iodine scan showed viable functioning implants, those patients were prescribed 100 micrograms/day of the hormone replacement therapy.

The second category included 3 cases [10%] who had insufficient implants which had low levels of thyroid hormones and high level of TSH hormone although the iodine scan showing a viable functioning implant. Three months after transplantation, those patients had hypothyroid symptoms while the remaining cases were asymptomatic.

Symptoms included regular daily work intolerance, sleepiness, and increasing body weight, these symptomatic patients required a higher dose of replacement therapy to eliminate the symptoms which was 150 micrograms/day of the hormone replacement therapy [Table 2].

At the end of the duration of our study, all of the implants were viable and functioning as proved by the iodine scan. However, all of the cases still take exogenous hormone replacement drug [L-thyroxin] but with different doses. Six cases [20%] take 50 micrograms/day, twenty-one cases [70%] take 100 micrograms/day and three cases [10%] take 150 micrograms/day.

Table [1]: Postoperative complications

Complication	Number of patients	Percentage
Hypocalcemia	6	20%
Neck wound seroma	2	6.6%
Neck wound hematoma	0	0%
Neck wound infection	0	0%
Vocal cord edema	3	10%
Stridor	0	0%

Table (2) showing the percentage of sufficiency of each implant

category	cases	percentage	Dose of replacement therapy
Fully functioning implants	6	20%	50 micrograms/day
Minimally insufficient implants	21	70%	100 micrograms/day
Insufficient implants	3	10%	150 micrograms/day

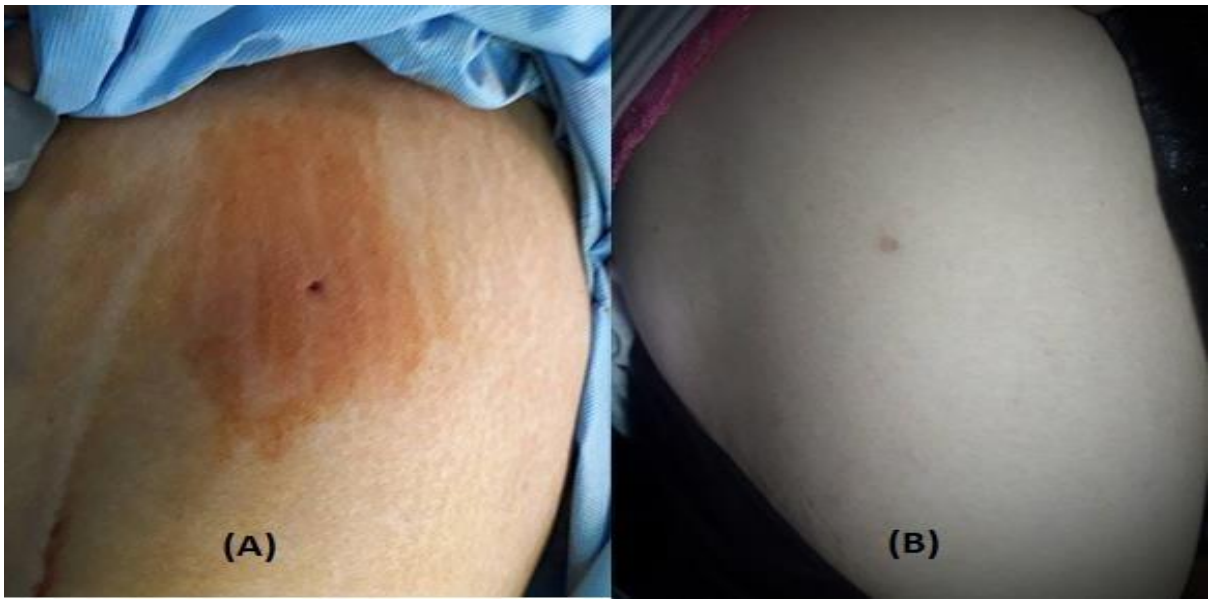

Figure [1]: [A] Injection site intraoperatively, [B] 3 months after surgery

Figure [2]: [A] Total thyroidectomy specimen, [B] Thyroid tissue emulsion ready for injection

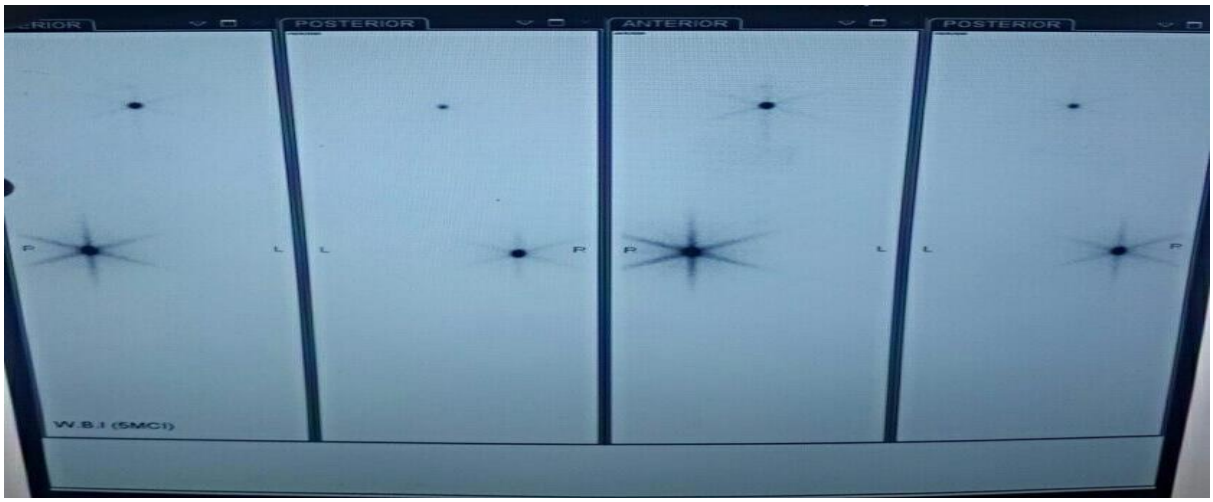

Figure [3]: Thyroid scan 6 months after surgery

DISCUSSION

According to several publications, the gold standard for treating benign thyroid diseases that necessitate surgical excision is a whole thyroidectomy rather than a partial thyroidectomy. Regretfully, after a total thyroidectomy, hypothyroidism is unavoidable, hence hormone replacement treatment is always recommended to keep thyroxin levels stable. However, levothyroxine dosage needs to be closely supervised [8]. With thyroid tissue auto-transplantation, it is possible to preserve a healthy portion of the removed thyroid gland in a location that is easily accessible and away from the neck. This reduces the risk of a localized recurrence in the neck with its many dangerous complications, eliminates the need for lifelong thyroid hormone replacement therapy, and keeps the body's natural ability to produce thyroxin in response to its own needs [9].

Thirty patients underwent total thyroidectomy for simple multinodular goiter and thyroid tissue auto-transplantation in the thigh away from the primary site of surgery in the neck in our current study to see if the implanted thyroid tissue could restore euthyroid status without the use of exogenous replacement therapy.

Because hypothyroidism is one of the possible complications of thyroid tissue auto-transplantation, patients with cardiovascular diseases were excluded, and the least amount of exogenous hormone replacement drug was given to avoid hypothyroidism symptoms until the implant was fully functional. Children and pregnant women were also excluded to avoid the procedure's associated side effects of transient hypothyroidism.

The majority of human studies documented the survival and function of thyroid tissue implanted in muscles using various methods of implant preparation. Some used frozen implants, while others used fresh implants with variable implants weight. **Shimizu *et al.*** [10] implanted 2.5 - 3.5 gm per Graves' disease patient, a portion of the excised thyroid was stored frozen at -196oC then transplanted in the forearm muscles. **Sankar *et al.*** [11] implanted 3 to 5 gm of thyroid tissue in the sternocleidomastoid muscle. **Mohsen *et al.*** [12] used fresh thyroid auto-transplantation on 40 patients in Egypt, five gm of the patients' own thyroid tissue was implanted in the thigh muscles, while 10 gm was injected for the other 28 patients. They came to the conclusion that 10 gm implants had higher isotope uptake than 5 gm implants. This difference, however, was not reflected in the thyroid hormone profile. Because the volume of a healthy thyroid gland ranges from 15 to 25 gm, it is prudent not to auto-transplant less than 10 gm. Therefore, in our study, we decided to emulsify and implant 10 gm of thyroid tissue for all of our patients in order to gain more benefit and reduce the failure rate.

Regular laboratory investigations were used in our study to determine whether our patients had reached the euthyroid state, had not reached it, or simply needed to continue the primary dose of the supporting replacement therapy. **Shimizu *et al.*** [10] studied four patients, one of whom developed hypothyroidism and required replacement therapy six months after auto-transplantation.

Sankar *et al.* [11] included 15 patients in their study. Seven had Graves' disease, six had simple multinodular goiter [MNG], and two had nodular toxic goiter. Six patients with MNG and four patients with Graves' disease received functional implants; all patients with MNG who received functional implants became euthyroid six months after surgery. Only one of the four patients with Graves' disease who received functional transplanted tissue became euthyroid, while the other three required postoperative hypothyroidism treatment. **Mohsen *et al.*** [12] used 5 gm and 10 gm emulsified injections of their own thyroid tissue in the thigh muscles on 40 patients with simple MNG. After 2, 6, and 10 months, 99mTc, Free T3, Free T4, and TSH levels were measured They reported that all transplants survived with varying degrees of function and that all improved with time.

Following our study's follow-up period, all of the implants were viable and functioning, as evidenced by an iodine scan which was done at the follow up periods at 3 and 6 months after surgery. Six out of thirty patients [20%; with normal T3, T4, and TSH, and no exogenous replacement drugs during the hormonal assessment] had fully functioning implants. This is a promising result because the implants maintained a normal TSH serum level throughout the study and after discontinuing exogenous replacement therapy for three weeks at a low dose of the drug [50 micrograms of L-T4 daily].

Twenty one of 30 patients [70%] had minimally insufficient implants with normal thyroid hormone levels but a high level of TSH. Although these implants kept thyroid hormone levels within the normal range, they did not achieve one of the study's main goals, which was to use the TSH feedback mechanism to respond to the patient's need for thyroid hormones, so those patients were given a higher dose of exogenous hormone replacement therapy [100 micrograms of L-T4 daily]. Three patients out of thirty [10%] had insufficient implants with low thyroid hormone levels and high TSH hormone levels. Due to symptomatic hypothyroidism three months after surgery, those patients were given higher doses of exogenous hormone replacement therapy [150 micrograms of L-T4 daily].

Three cases out of 30 patients [10%] had insufficient implants which had low levels of thyroid hormones and high level of TSH hormone. At 3 months after the surgery due to symptomatic hypothyroidism those patients were given higher doses of the exogenous hormone replacement therapy [150 micrograms of L-T4\day].

Because the implants required more time to fully function, the duration of our study was insufficient to fully judge their full capacity. A longer study duration was required to monitor whether there was further improvement or decline in graft function. There is a major concern that a period of clinical or subclinical hypothyroidism may occur until the implant is fully functional, so patients must be given an exogenous hormone replacement drug with regular hormonal profile follow up and replacement therapy dose adjustment.

To avoid implanting cancerous tissue, we performed a full preoperative clinical, radiological, and pathological evaluation on all of our cases. As **Prades *et al*.** [13] documented that the role of frozen section in the diagnosis of a thyroid nodule has decreased with the more widespread use of FNAC, in the majority of cases, frozen section no longer represents the first-line diagnostic procedure, and should only be preserved to supplement the FNAC findings of suspicious lesions, intraoperative frozen section was not required.

The gross assessment of gland texture intraoperatively was also important in our study because we excluded any cases with grossly suspicious tissue. All patients in our study had no malignancy on final pathology.

Accurate marking of the transplantation site by a stitch over the injection site was performed to make it easier to identify the injection site for any possibility of presence of malignant tissue. In theory, the implant resembles the thyroid remnant after subtotal thyroidectomy, but in this case, the swelling will be difficult to detect because the thigh muscles are large and detecting the swelling early on is hard, so ultrasound and CT imaging could be used to detect it if needed.

Only one case of parathyroid carcinoma arising from auto-transplanted parathyroid tissue in a chronic kidney disease patient with secondary hyperparathyroidism has been reported in the literature [14].

Because thyroid auto-transplantation is a new field, the transplantation site requires close monitoring with FNAC and ultrasound imaging for fear of malignant transformation, even if the transplant was initially benign. Another issue that could arise is pain or numbness at the site of the transplantation, but none of our patients experienced this.

Regardless of the study's outcome, our study's patients were consulted to continue their hormonal profile follow-up to detect any changes and adjust the dosage, if necessary, until reaching a stationary level of TSH. The operative time and the patients' ages had no effect on the hormone profile one year after surgery.

Conclusion: Thyroid auto-transplantation is a safe and easy procedure that provides survival and function of the thyroid implants and offers promising results in the majority of the selected patients and allows them to maintain the native feedback mechanism of the thyroid hormones and reach a postoperative euthyroid state. and we recommend further studies should be done on a larger population scale and over longer duration to assure the validity of this procedure, its applicability on other benign pathologies other than multinodular goiter such as Graves' disease, and follow up of transplantation site for fear of recurrence of the original disease or malignant transformation.

Disclosure: The authors declare there was no specific funding source for the study and declare no conflicts of interest.

REFERENCES

1. Can AS, Rehman A. Goiter. 2023 Aug 14. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 32965832.

2. Saran S. Multinodular Goiter. In: Goiter - Causes and Treatment. Edited by N.K. Agrawal. Intech Open; 2020. doi: 10.5772/intechopen. 90325

3. Mooij CF, Cheetham TD, Verburg FA, Eckstein A, Pearce SH, Léger J, van Trotsenburg ASP. 2022 European Thyroid Association Guideline for the management of pediatric Graves' disease. Eur Thyroid J. 2022 Jan 1;11 (1): e210073. doi: 10.1530/ETJ-21-0073.

4. Cirocchi R, Trastulli S, Randolph J, Guarino S, Di Rocco G, Arezzo A, D'Andrea V, Santoro A, Barczyñski M, Avenia N. Total or near-total thyroidectomy versus subtotal thyroidectomy for multinodular non-toxic goitre in adults. Cochrane Database Syst Rev. 2015;2015(8): CD010370. doi: 10.1002/14651858.CD010370.pub2.

5. Hegedüs L, Bonnema SJ, Bennedbaek FN. Management of simple nodular goiter: current status and future perspectives. Endocr Rev. 2003 Feb;24(1):102-32. doi: 10.1210/er.2002-0016.

6. Jonklaas J. Optimal Thyroid Hormone Replacement. Endocr Rev. 2022 Mar 9;43(2):366-404. doi: 10.1210/endrev/bnab031.

7. Miccoli P, Materazzi G, Rossi L. Levothyroxine Therapy in Thyrodectomized Patients. Front Endocrinol (Lausanne). 2021 Jan 29; 11:626268. doi: 10.3389/fendo.2020.626268.

8. Jonklaas J, Bianco AC, Bauer AJ, Burman KD, Cappola AR, Celi FS, *et al.* Guidelines for the Treatment of Hypothyroidism: Prepared by the American Thyroid Association Task Force on Thyroid Hormone Replacement. Thyroid. 2014; 24 [12]:1670–751. doi: 10.1089/thy.2014.0028.

9. Alawady A, Khalil A, Abdelaal S, Alkilany M, Ashour H. The role Of thyroid autotransplantation in patients with benign thyroid disorders. Zagazig Univ Med J. 2019 Sep 30;0–0. doi: 10. 21608/zumj.2019.16849.1513

10. Shimizu J, Yamazaki S, Takahashi T, Ishida Y, Sakaguchi S. Stimulation of CD25+CD4+ regulatory T cells through GITR breaks immunological self-tolerance. Nat Immunol. 2002 Feb 22;3 [2]:135–42. doi: 10.1038/ni759

11. Sankar R, Roy PG, Saund MS, Thusoo TK, Roy D. Fate of Human Thyroid Tissue Auto-transplants. Surg Today. 2003 Jul 1;33 [8]:571–6. doi: 10.1007/s00595-003-2557-8.

12. Mohsen AA, Nada AA, Ibrahim MY, Ghaleb AH, Abou-Gabal MA, Mohsen AA, *et al.* Technique and outcome of autotransplanting thyroid tissue after total thyroidectomy for simple multinodular goiters. Asian J Surg. 2017 Jan;40[1]:17–22. doi: 10.1016/j.asjsur.2015.05.007.

13. Prades JM, Querat C, Dumollard JM, Richard C, Gavid M, Timoshenko AA, *et al.* Thyroid nodule surgery: Predictive diagnostic value of fine-needle aspiration cytology and frozen section. Eur Ann Otorhinolaryngol Head Neck Dis. 2013; 130[4]:195–9. doi: 10.1016/j.anorl.2012.12.005.

14. Won H-R, Kang JY, Lee IH, Kim J-M, Chang JW, Koo BS. Parathyroid carcinoma arising from auto-transplanted parathyroid tissue after Total Parathyroidectomy in chronic kidney disease patient: a case report. BMC Nephrol. 2019 Dec 15; 20 [1]:414. doi: 10.1186/s12882-019-1606-5.

IJMA

International Journal of Medical Arts

Volume 6, Issue 1, January 2024

P- ISSN: 2636-4174
E- ISSN: 2682-3780