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**ORIGINAL ARTICLE****The Role of Thyroid Autotransplantation In Patients With Benign Thyroid Disorders****Adel Mahmoud attia attia<sup>[1]</sup>, Alaa Mohamed Ibrahim Khalil<sup>[2]</sup>, Salah Mansour Abdelaal<sup>[3]</sup>, Mohamed.M.Alkilany<sup>[4]</sup>, Hassan Rabieh Ashour<sup>[5]</sup>**

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**ABSTRACT**

**Background:** The heterotopic thyroid autotransplantation is to leave thyroid tissue in the body that might be able to survive, gain blood supply and become functioning to avoid or reduce the severity of post thyroidectomy hypothyroidism in noncompliant patients. In the meantime, if recurrence occurs it would not be in the neck, thus avoiding the compression of the trachea and avoid dangerous re-operation deeply in the neck.

**Methods:** From November 2017 till June 2018. Patients with benign thyroid disorders were selected for heterotopic thyroid autotransplantation followed up for 12 months by duplex US, free T3, T4, TSH and  $^{99m}\text{Tc}$  to detect survival of the graft maintaining the patient euthyroid after total thyroidectomy for benign thyroid disorders.

**Results:** Ninety percent were females and ten percent males with mean age 36.2 years. The most common presentation was compressive symptoms (51.6%). Mean operative time was 124.4 min, 71% were benign follicular lesion and 29% colloid nodular goitre, 71% without early postoperative complications. Transient hypocalcaemia reported in 29% of cases. One month postoperative duplex was positive in 93.5%. Postoperative radio-isotopic scanning was positive in 93.1% after 6 months and 96.5% after 12 months. 90% of the patient reached euthyroid state.

**Conclusions:** Autotransplantation of heterotrophic thyroid tissue following total thyroidectomy for patients with benign thyroid disorders is a safe, easy and applicable technique that provides survival and function of thyroid graft achieving a postoperative euthyroid state in majority of selected patients without the need for further replacement therapy.

**Keywords:** Benign thyroid disorders, Autotransplantation, duplex US, Free T3, T4 and TSH,  $^{99m}\text{Tc}$  scanning

**INTRODUCTION**

The principle of autotransplantation of the endocrine glands was proposed for the first time by Halsted in 1909. Although autotransplantation of the parathyroid gland has been widely accepted as a useful procedure to prevent the development of

hypoparathyroidism at total thyroidectomy for thyroid cancers, successful clinical trials of thyroid autotransplantation have rarely been reported in the literature.[1]

The purpose of heterotopic thyroid autotransplantation is to leave thyroid tissue in the body that might be able to avoid or reduce

the severity of post thyroidectomy hypothyroidism in non compliant patients. In the meantime, if recurrence occurs it would not be in the neck, thus avoiding the compression of the trachea and avoid dangerous re-operation deeply in the neck.[2]

The major challenge in this new technique is the ability of the human thyroid tissue to survive and establish normal function to reach the state of euthyroidism in the absence of their native blood supply in the muscle which can be reflected through imaging techniques and thyroid function tests.[3]

#### PATIENTS AND METHODS

This study was prospectively conducted during the period from November 2017 till June 2018. Patients with benign thyroid disorders to the outpatient clinic of Zagazig University Hospitals.

Inclusion Criteria includes patients proved to have benign thyroid disorders operable and candidate for total thyroidectomy Aged between 20-44 years who agreed and consented to do the procedure. We excluded patients with high suspicion of malignancy, unfit and refused the procedure.

All patients were subjected to history taking, general and neck, laboratory investigation and imaging of thyroid gland and FNAC of the nodule. Any patients with thyroid dysfunction had received medication before surgery till becoming euthyroid. Thyrotoxic patients had received anti thyroid drugs (Carbimazole and propranolol) while the hypothyroid one had received thyroid replacement therapy (levothyroxin).

All patients were admitted the day before operation after completion of all consultations (cardiology, internal medicine and anesthesia) and the patients were documented as fit for surgery. Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for

studies involving humans. All patients are informed to be fasting for 6-8 hours before surgery time.. all patients are given preoperative antibiotics and appropriate DVT prophylaxis.

**Operative technique:** operations were done under general anesthesia with endotracheal intubation in supine position with the neck extended by padded sandbag between scapulae and head ring. Electrosurgical unit was used (electrocautery or bipolar diathermy). All patients underwent Total Thyroidectomy Transverse skin incision 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 lower flap till sternoclavicular joints. Vertical division of the midline raphe between the strap muscles then the muscles separated and retracted laterally to expose 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 dissected from its bed. The same steps were repeated for the other lobe.

The gland dissected from the trachea and removed after its gross exam to ensure preservation of parathyroid glands. Ensure absolute hemostasis of the field then insertion of suction drain or rubber drain in thyroid bed. Closure of fascia of the strap muscles by interrupted sutures then approximation of platysma and finally subcuticular sutures by proline 2/0 or absorbable vicryl sutures.

Preparation of our field of transplantation subplatysmal and over the sternomastoid muscle. Exploration of our gross specimen to exclude suspicious samples with fear of malignancy like degeneration cysts and

choosing the best part suitable for transplantation .10 gm of the gland are dissected with fine pair of fine scissors and part buried into the sternomastoid gland sutured with proline 5/0 as a mark and another part was emulsified by adding to 10 cm normal saline and injected to multiple places into the sternomastoid muscle. A part from the rubber drain pass through sublatysmal space beside our transplant to outside through the angle of the wound.Light dressing of the incision site and the drain. Asking the anesthesiologist to check the mobility of the vocal cords.

Excised thyroid gland specimen was sent for histopathological examination. Postoperative follow up; all cases at the inpatient department with near source of oxygen beside the patient bed. Regular check of the vital signs every 2hours and observation of dressing and the drains regarding the amount and nature of the discharge. Oral fluids are 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 calcium supplementation is started for a month. vocal cord mobility and voice of the patients are checked.Wound , dressing and drains is closely monitored for early detection of signs of rejection and inflammation . removal of rubber drains after 48 hours after exclusion of signs of rejection.

Discharge; most patients were discharged in the 3rd after operation after estimation of serum calcium, vocal cord mobility and removal of the drain and had received a follow up card. Discharge medications include antibiotics, analgesics, thyroid replacement therapy (levothyroxin ). We start with 50 µg for three weeks as an initial dose.oral calcium supplementation in the form of (calcium and 1, 25 D3). The patient warned about the emergent signs; hematoma, respiratory distress and how to deal with them and with the drain if discharged with it. The patients are instructed for follow up at the outpatient clinic 1week later, then after 2weeks and monthly. The

histopathology report usually interpreted at the first post operative visit.

Patients diagnosed on final pathology as benign pathology , no fear of recurrence and suitable for continuing the study. At first duplex us was done after one month to make sure that all transplants has a good blood supply with no atrophy or fibrosis . Positive duplex cases start a regimen to test free t3 ,free t4 , tsh after 1 ,3 ,and six months . patients with normal values stopped eltroxin therapy while cases with hypothyroidism clinically and by laboratory investigation we increase the dose of eltroxin 50 µg till control of symptoms and improvement of laboratory finding.

Scans were done by intravenous injection of 5e10 mCi of radioactive technetium (<sup>99m</sup>Tc).Imaging was done 20 minutradionuclide was done after 6 months for all patients, repeated only for patient with still poor uptake after 12 months .

#### **Statistics:**

Mean age of the studied patients was 36.2 years old and most of them were females. Almost half (51.6%) of the studied patients had MNG compressive symptoms and 38.7% had thyroid swelling. almost half (51.6%) of the studied patients had Diffuse irregular swelling of thyroid and 29.0% had Left lobe solitary swelling. Pathological examinations showed 71.0% of the studied patients had benign follicular lesion and 29.0% had Colloid nodular goiter. 70.97% of the studied patients had no early postoperative complications and 29.03% had Transient hypocalcaemia. 93.55% of the studied patients had Positive duplex and 6.45% had Negative duplex one month postoperative table [1].

#### **RESULTS**

Our study included 31 patients , ninety percent were females and ten percent males with mean age 40 years. The most common presentation was compressive symptoms (52%), the mean time of operation was 124 min , 71% were benign follicular lesion and 29% colloid nodular goitre , one month postoperative duplex us positive was 93.5 % of the patients, table [1].

Six months postoperative radio-isotopic scanning of the studied patients 93.1 % and

after 12 months 96.5, table [2].

**Table (1): One month postoperative duplex of the studied patients:**

One month postoperative duplex	Studied patients (n=31)
Positive	29 (93.55%)
Negative	2 (6.45%)

**Table (2): Postoperative radio-isotopic scanning of the studied patients:**

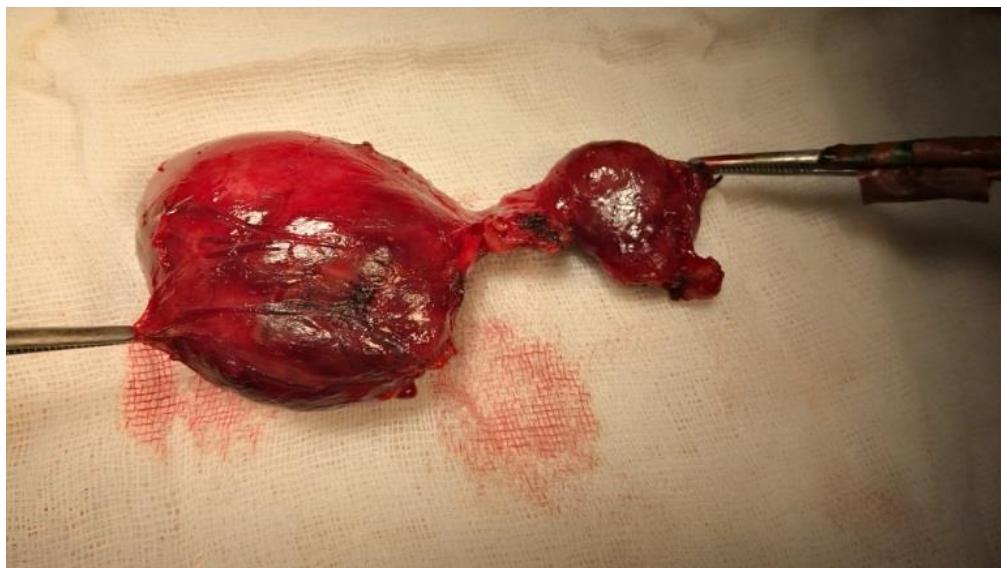
Postoperative radio-isotopic scanning	After 6 month (n=29)	After one year (n=29)
Good uptake by implanted tissue	27 (93.1%)	28 (96.55%)
Poor uptake by implanted tissue	2 (6.9%)	1 (3.45%)

**Table (3): TSH of the studied patients:**

TSH (IU/ml)	Pre-operative	After month 1	After months 3	After months 6	After months 12	F	P
Mean $\pm$ SD	1.5 $\pm$ 1.1	8.7 $\pm$ 14.6	6.7 $\pm$ 10.9	4.4 $\pm$ 6.6	3.9 $\pm$ 7.1	23.9	<0.001
Median	1.3	3.5	1.7	1.3	1.5		HS
Range	0.0 – 4.0	0.22– 52.0	1.0 – 35.0	0.9 – 20.0	0.9 – 25.0		



**Figure 1:** dissection of the upper flap through sub-platysmal plain.



**Figure 2:** exploration of the specimen to choose the best part



**Figure 3 :** 10 mg of healthy thyroid tissues fixed to the right sternomastoid muscle.

## DISCUSSION

The aim of heterotrophic thyroid autotransplantation is to leave thyroid tissue in the body enough to reach euthyroid state following total thyroidectomy and to transfer the risk of recurrence and re-operation away from deep neck structure to more superficial level with less risk of injury of deep neck structures[4]. avoid life-time thyroid hormonal replacement therapy. Another advantage of heterotopic thyroid autotransplantation is maintaining the autoregulatory mechanism of

thyroxin production inside the body according to its needs .[5]

Multiple trials before our study either included a few numbers of patients or focused only on single pathological type of benign thyroid disorders. *Okamoto et al.*,[6] carried out thyroid autotransplantation after solitary thyroid nodule for 5 patients presenting with Graves' disease. The work of *Shimizu et al.*,[7] in Japan in 2002, though involved 4 patients only, gave more insight about the technique and the results of thyroid autotransplantation . In 2003, *Roy et al.*,[8] from India gave further details about the

concept of thyroid autotransplantation. They performed modified STT and fresh tissue autotransplantation for 15 patients. These included 7 with Graves' disease, 6 with simple multinodular goiter (MNG) and 2 with nodular toxic goiter . our study included 31 patients 16 of them had multinodular goiter, 9 with left thyroid swelling ,3 with right thyroid swelling and three of them had graves disease. This gave us larger number of study and wider variety of pathological types .

Most human studies documented the survival and function of the thyroid tissue that was implanted in the muscle seldom achieved euthyroid status with multiple different methods of preparation of implants some used frozen other used fresh implants and variability of plants weight. **Shimizu et al.**, the workers implanted 2.5 - 3.5 g per patient with Graves' disease. **Roy et al.**, Implanted (3–5 g) was performed in the sternocleidomastoid muscle. In 2015, **Mohsen et al.**,[9] from Egypt applied the technique of fresh thyroid autotransplantation on 40 patients with simple MNG who underwent TT. For 12 patients, 5 g of their own thyroid tissue were, while 10 g were injected for the other 28 patients. In our study we decided to implant 10 g of thyroid tissue for all of patient to gain more benefit and decrease the failure rate.

The site of transplantation of heterotrophic thyroid tissue was different in each study. **Shimizu et al.**, in Japan in 2002, involved 4 patients of Graves' diseases .a part of the excised thyroid was stored frozen at -196°C. then transplanted in the muscles of the forearm after slicing them into minute pieces marked with monofilament nylon sutures. In 2003, **Roy et al.**, fresh tissue autotransplantation of thyroid tissue (3–5 g) performed in the sternocleidomastoid muscle. In 2015, **Mohsen et al.**, emulsified heterotrophic thyroid tissue were implanted in the thigh muscles using the injection technique. In our study we preferred to transplant the thyroid tissue in the sternocleidomastoid muscle in the subplatysmal plane as more superficial more accessible in

examination with easily detection of early rejection through the subcutaneous rubber drain. This helped in decreasing the time of surgery to reach the time of the ordinary total thyroidectomy and this helped in maintaining the graft viable and fresh, and if recurrence occurred it would be more easily to deal with more superficial and more accessible lesion.

A new step that has never performed before in the previous studies is the early one month duplex ultrasound of the neck for detection of uptake and vascularization of the graft or fibrosis. this gave us the chance for selection of patient who needed full replacement therapy and others who were suitable for continuation of the study.

Following up the laboratory investigation in a regular pattern was an important step as a guide that our patients have reached the euthyroid state or with complete failure or just need continuation of the primary dose of the supporting replacement therapy . **Shimizu et al.**, involved 4 patients with Graves' diseases Only 1 patient developed recurrence of hypothyroidism and had to resume replacement therapy 6 months after autotransplantation. **Roy et al.**, involved 15 patients. These included 7 with Graves' disease, 6 with simple multinodular goiter (MNG) and 2 with nodular toxic goiter. All patients with MNG who had a functional transplant became euthyroid 6 months postoperatively. Only 1 patient with Graves' disease from the four who had functional transplanted tissue became euthyroid, while the other 3 required postoperative supplemental therapy for hypothyroidism.

**Mohsen et al.**, involved 40 patients with simple MNG Follow-up was done after 2, 6, and 10 months postoperatively using <sup>99m</sup>Tc, FT3, FT4, and TSH. The authors reported survival of all transplants with different degree of function. In 2016, **Saleh et al.**,[10] performed heterotopic autotransplantation of fresh thyroid tissue for 20 patients (13 with simple MNG, 4 with Graves' disease and 3 with toxic nodular goiter). Results confirmed

that all implants survived and showed variable degree of function. In our study we involved 31 patients 16 patients with MNG , 12 patients with solitary thyroid nodules and 3 patients with thyrotoxicosis .following up the thyroid function 1 month , 3 months, 6months and 12 months after surgery showed hypothyroidism in two of the patients which had not improved on following up , only after full dose of replacement therapy while the other patients showed increasing the degree of function through out the course of follow up until reaching euthyroid state .

**Mohsen et al.**, Follow-up was done after 2, 6, and 10 months postoperatively using  $^{99m}\text{Tc}$ , while, **Saleh et al.**, performed  $^{99m}\text{Tc}$  at 2-month and at 12-month postoperatively. Using duplex ultrasound one month after surgery together with monitoring the thyroid function using free t3 . free t4 and TSH decreased the need for repeated  $^{99m}\text{Tc}$  . we performed  $^{99m}\text{Tc}$  only after 6 months for all patients and after 12 months only for patients with poor uptake at the 6 month while their thyroid function where normal .this helped in decreasing the cost and minimizing the risk for radiation exposure with good results.

So we concluded that we can use autotransplantation of heterotrophic thyroid tissue following total thyroidectomy for patients with benign thyroid disorders as a safe , easy and applicable technique that provides survival and function of thyroid graft achieving a postoperative euthyroid state in majority of selected patients without the need for further replacement therapy.

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## How to Cite

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