

A Case Series Study on Thyroid Autotransplantation

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Introduction: Total thyroidectomy is a common surgery nowadays, yet the use of long-life replacement therapy has its complications. Thyroid autotransplantation helps to reach a euthyroid state with an autoregulatory mechanism of the grafted thyroid tissue.

Aim of work: To assess the survival and function of autotransplanted thyroid tissue after total thyroidectomy in patients with multinodular goiter.

Patients and methods: This is a prospective case series study that was conducted in Ain Shams University Hospitals and Helwan University Hospitals from January 2022 to January 2024 including a minimum of one-year follow-up. The study included 76 patients with simple multinodular goitre who underwent total thyroidectomy with thyroid autotransplantation.

Results: All the patients reached a euthyroid state at 12 months follow up. Sixty-one patients didn't receive any replacement therapy while 15 patients (20%) received low dose (50microgram) of levothyroxine to reach the euthyroid state.

Conclusion: Thyroid tissue autotransplantation is a safe and easy procedure that can help to omit or lower the dose of replacement therapy post thyroidectomy.

Key words: Thyroid autotransplantation, thyroid function tests, thyroid scan.

Introduction

Multinodular goiter is the most common endocrine disease requiring surgical intervention. Guidelines recommend total thyroidectomy as a reliable approach in preventing recurrence.¹

Hypothyroidism is inevitable after total thyroidectomy (TT). Life-long L-T4 replacement therapy is not without complications.²⁻⁵ Poor patient compliance due to daily dependence and regular follow-up visits to reach the expected post-operative euthyroid status,⁴ unavailability of different forms, drug failure, malabsorption of L-T4 due to different reasons,⁶⁻¹⁰ long-term effect of L-T4 on bone resorption, cardiovascular system, its relation to lung cancer, and frequent dose adjustment during pregnancy,¹¹⁻¹⁴ lead to poor thyroid control and increased risk of complications and mortality.¹⁵

Autotransplantation of thyroid tissue following total thyroidectomy is an alternative to lifetime thyroid hormone replacement therapy as well as it maintains the autoregulatory mechanism of thyroxin production,^{16,17} and it does not carry the risk of neck re-exploration in case of recurrence.¹⁸

The primary aim of this study was to assess the survival and function of autotransplanted thyroid tissue after total thyroidectomy in patients with multinodular goiter.

Patients and methods

This is a prospective case series study that was conducted in Ain Shams University hospitals and Helwan University hospitals from January 2022 to January 2024 including a minimum of one-year follow-up. The study as shown in **(Fig. 1)** included 76 patients with simple multinodular goitre who underwent total thyroidectomy with thyroid tissue autotransplantation at the same setting.

Ethical considerations

This study received ethical approval from the ethical committee of the general surgery department at Ain Shams University before conducting the study. All patients signed a written informed consent.

Inclusion criteria

- Patients proved to have benign simple multinodular goitre (SMNG).
- Patients with ASA scores of 1 and 2.

Exclusion criteria

- Patients with suspicion of malignancy either clinical, or by ultrasound (TIRAD 4 or more), or pathological suspicion (Bethesda 4 or more)
- A family history of thyroid cancer
- Patients with history of previous thyroiditis, history of neck irradiation and recurrent goiter.
- Patients who refused to participate in the study.

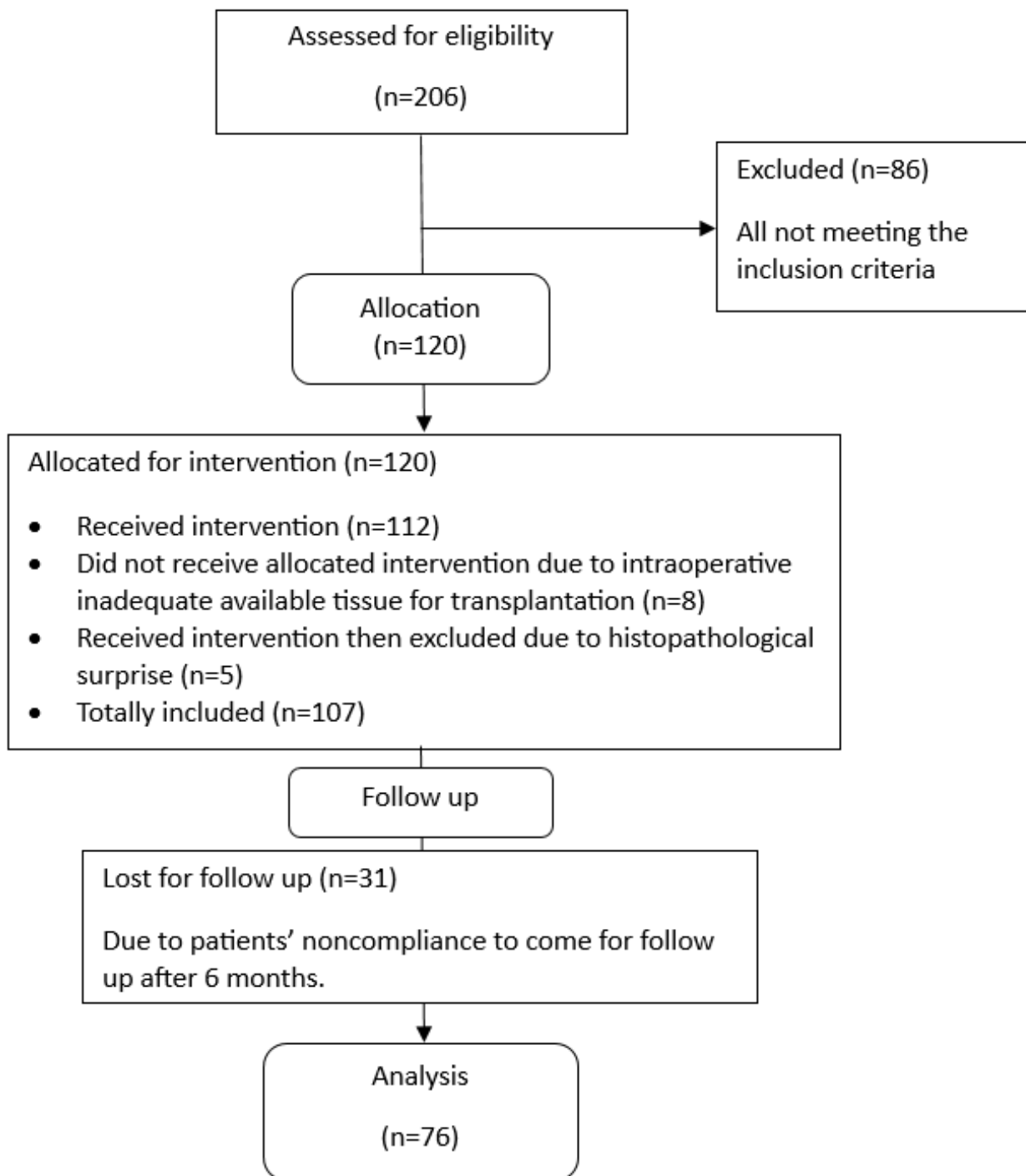


Figure 1: The Consort Flowchart of the Study.

Study tools:

All patients were candidates for:

Clinical assessment:

- Detailed medical, surgical and family history regarding thyroid cancer in any of the relatives.
- Full general examination.
- Full local neck examination for the thyroid mass and any cervical lymph nodes.

Investigations:

- Thyroid function tests FT3 FT4 TSH,
- Anti-thyroid peroxidase Abs, anti-thyroglobulin Abs
- Neck US and US-guided FNAC from all patients.
- Indirect laryngoscopy for vocal cord assessment.
- Routine preoperative laboratory investigations,

Surgical technique:

Under general anesthesia, standard total thyroidectomy was done with preservation of the parathyroid glands.

Thyroid tissue grafting

- a. Preparation of the specimen by
 - ▶ Selection of 15gm of the healthiest-looking part of the excised gland
 - ▶ stripping of the fibrous Capsule
 - ▶ Mincing into 1-2 grams using intraoperative fine digital scale under complete aseptic condition. **(Fig. 2a)**
 - ▶ Placement in warm saline
- b. Sterilization and preparation of the surgical field of the recipient site (Rt thigh)
- c. Creation of a 3-4 cm incision in the anterolateral aspect of mid-thigh opposite to iliotibial tract and vastus lateralis muscle. **(Fig. 2b)**
- d. Opening of the iliotibial tract and blunt creation of small pockets in vastus lateralis muscle
- e. Transplanting the thyroid slices into the pockets created in the vastus lateralis muscle. **(Fig. 2c)**
- f. Marking the implantation site with a prolene suture through the muscle sheath was done.
- g. Closure of the wound.



Fig 2a: Sliced healthy thyroid tissue ready for transplantation.



Fig 2b: Incision in the lateral aspect of the mid thigh.



Fig 2c: The opened artery forceps exposes the thyroid slice inside one of the thigh pockets.

Discharge instructions

Every other day dressing for both wounds, prophylactic low dose of calcium and vit D for the first month postoperative.

To prevent the onset of hypothyroidism until the graft uptake, all patients received a relatively low substitution dose (50 µg of levothyroxine daily) for 1 month to maintain a high serum TSH level, which would facilitate graft survival and function.

Postoperative follow up

The patient was advised to come to the outpatient clinic for follow up for stitches removal and clinical assessment of both neck and thigh wounds to ensure absence of any wound complications like hematoma or wound infection.

Routine postoperative histopathological examination of the specimen was done.

At 2 months the patient was ordered a thigh ultrasound to ensure adequate uptake and viability of the transplanted tissue

Then the patient would come at 2, 4, 6, and 12 months for follow up of pulse and thyroid function tests.

Thyroid scan was ordered at 12 months follow up.

Results

Demographic data:

This study included 76 patients with benign simple multinodular goitre. Fifty-nine (77.6%) of which were females while 17 (22.4%) were males. The mean age was 34.91±6.71 years.

Operative data

The mean time of thyroid tissue transplantation was 19.94±1.99 minutes.

No intraoperative complications were encountered, neither in the neck nor the graft site.

Postoperative data

All patients were discharged 24 hours postoperative. No significant postoperative complications were encountered, neither related to thyroidectomy nor the transplantation site.

Five of our patients showed a histopathological surprise in the form of papillary carcinoma that

was missed preoperatively. Those patients were excluded from the study.

The pulse rate showed relative bradycardia compared to the patient's preoperative pulse. Yet the pulse rate showed gradual return to the normal preoperative level within 6 months postoperative (**Fig. 3**).

Thigh ultrasound was done on the second months postoperative and showed viable thyroid graft in 75 (98.68%) of patients. Most probably, the graft was obscured by persistent edema at the site of operation and this patient didn't regain the whole function of the gland. Yet she is euthyroid on only 100 µg of thyroid replacement therapy.

Postoperative thyroid function tests (Free T3, free T4 and TSH) were assessed at 2, 4, 6, and 12 months after total thyroidectomy without hormone replacement therapy. They showed an early hypothyroid state in the form of decreased serum fT3 and fT4 levels, which started to elevate to a nearly euthyroid level with the level of TSH still high in 60% of patients. Serum TSH levels were high at 2 months postoperative and decreased gradually to return to normal level after twelve months follow up (**Fig. 4**).

Normal references of TFTs in the lab were:

- ▶ Free T3: 1.7-4.2 picograms per milliliter of blood (pg/ml)
- ▶ T4: 0.89 – 1.76 nanograms per deciliter of blood (ng/dl)
- ▶ TSH: 0.55 – 4.78 micro-international units per milliliter (uIU/ml)

At 12 months follow up, all patients showed normal levels of FT3, FT4, TSH, yet 15 patients (20%) showed euthyroid state with adding 50 µg/day of levothyroxine replacement therapy.

Thyroid scan was done at 12 months postoperative using radioactive iodine. Spot view on lower limbs showing uptake by the implant was accepted positive result. Only 30 patients agreed to do the scan, yet all of them showed positive results at the site of implantation (**Fig. 5**) denoting survival of implanted thyroid tissue with no uptake at the neck indicating neck free from any residual thyroid remnant which confirms that the thyroid hormone was released from implant only and not from any thyroid remnant in the neck.

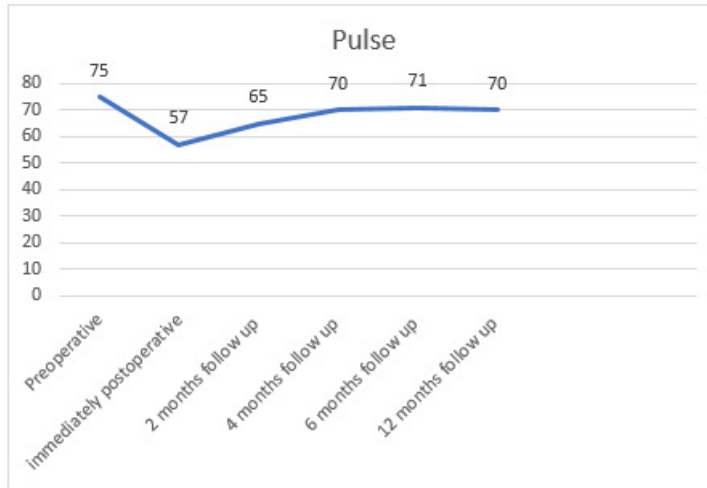


Fig 3: Pulse rate.

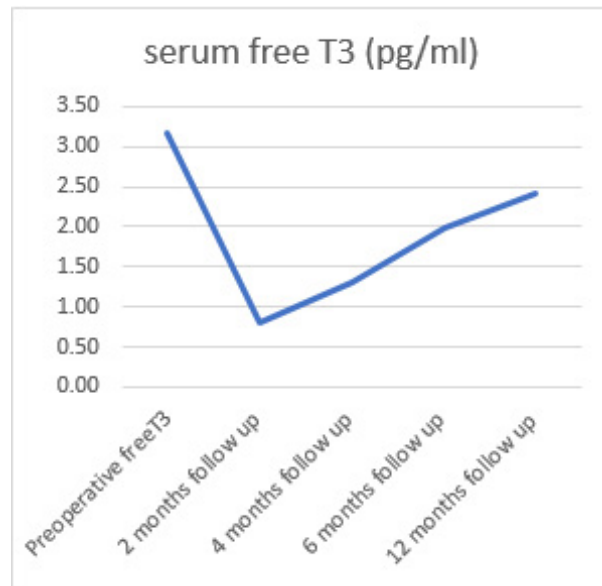


Fig 4a: Serial free T3 level.

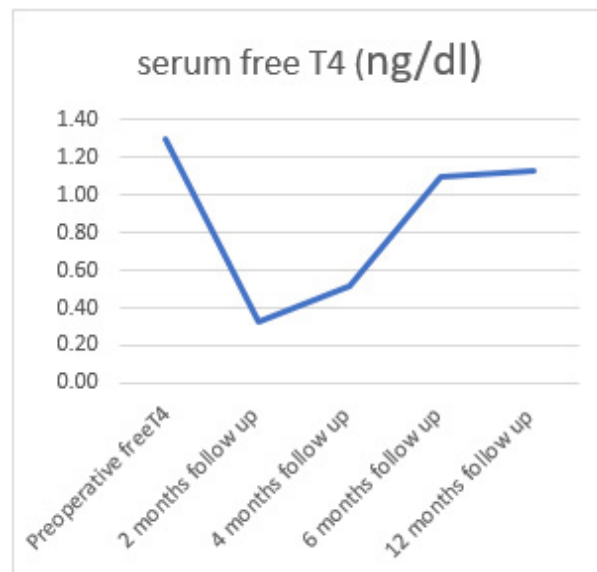


Fig 4b: Serial free T4 level.

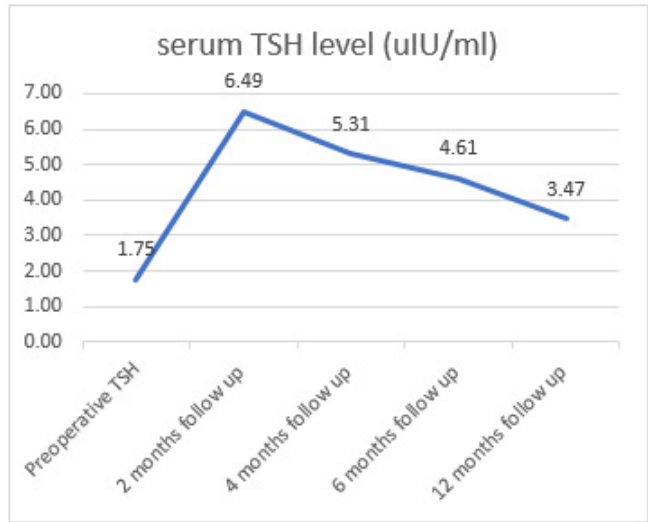


Fig 4c: Serial serum TSH level.

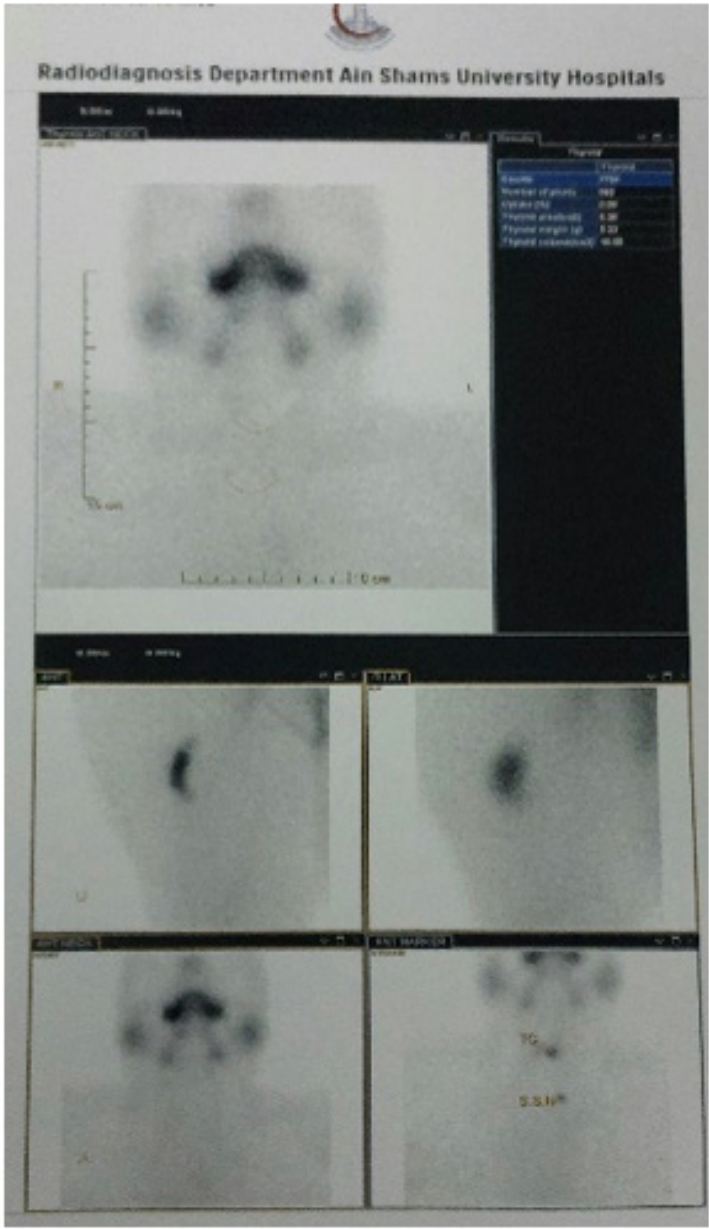


Fig 5: Postoperative whole body scan showing uptake in the thigh graft.

Discussion

Halsted introduced the idea of endocrine glands auto transplantation in 1909.¹⁹ The idea of thyroid autotransplantation followed the success and establishment of parathyroid gland autotransplantation.²⁰ One of the first trials of thyroid auto-transplantation was in 1957 in Italy, five months post-operatively, there was clinical evidence for gradual recovery of thyroid function.²¹

Although autotransplantation of the thyroid gland is controversial,^{17,22} there is reassuring evidence of its safety in providing a postoperative euthyroid state in selected patients without the need of L-T4 replacement therapy.²³

Trials of thyroid transplantation were done with total thyroidectomy,^{23,24} or with subtotal thyroidectomy.^{18,25} Also, the procedure was tried in simple goitre,^{18,23,24} and thyrotoxicosis.²³⁻²⁵

There is no single technique for thyroid transplantation. Following total thyroidectomy, grafting may be done immediately either freshly or after frozen section or the graft is frozen (Cryo-preserved thyroid tissue) till the result of histopathology of paraffin section of the specimen then the graft is applied in another session.¹⁷

The specimen may be minced, made into an emulsion, and injected into the thigh in multiple pockets through tiny skin puncture,^{18,23,26} or they may be sliced and implanted directly,¹⁷ as in our study.

Five of our patients showed a histopathological surprise in the form of papillary carcinoma that was missed preoperatively. Excision of the graft with safety margin of the surrounding muscle tissue was urgently performed, and histopathology of the excised graft tissue was examined and was entirely free of any malignant tissue.

Sakr and Mahmoud²³ detected the presence malignancy in thyroidectomy specimen of 2 patients out of 20, although their pre-operative fine-needle aspiration cytology was normal, and so they excised the graft of both patients. To ensure that no residual thyroid tissue remains in the neck or implantation site, and to check for metastasis elsewhere, a whole-body iodine scan is conducted following the detection of malignancy.

It is essential to remove the graft entirely in such instances due to the potential risk posed by the implanted tissue to the patient. Moreover, most of these patients are likely to require one or two post-operative doses of radioactive iodine (RAI) treatment. This treatment aims to eradicate any hidden thyroid microcarcinoma completely.¹⁷

Research has indicated that the functionality of grafts can vary due to several elements. These

include the pathology of the gland before surgery, the mass of the tissue transplanted, and the condition of the graft itself, particularly its cell density and regenerative capacity. Additionally, the success of the graft is influenced by the survival rate of the cells within the host site, the dimensions of the transplant bed, and the period over which the graft is subject to prolonged stimulation.²⁷

Revascularization of the heterotopic thyroid autograft is the main challenge for graft survival.²⁸

Efficacy of thyroid autotransplantation is still a research item. The optimal volume of thyroid graft required to maintain a euthyroid state after surgery has not yet been determined.²⁶

The weight of a healthy thyroid gland ranges from 15 to 25 g, thus it is advised to transplant not less than 10 g.^{27,29,30}

Monib et al,²⁶ observed that younger patients, as well as those who were transplanted with 15 grams of thyroid tissue, achieved an euthyroid state more promptly compared to older individuals and those who received a 10-gram graft. However, it's important to note that some patients may take an extended period to reach a euthyroid state.^{26,31}

Sakr and Mahmoud²³ noted that while the results were not statistically significant, there was a discernible enhancement in graft function as the weight of the transplanted tissue increased."

Mohsen et al,¹⁸ noted that isotope uptake with the 10-g implants was higher than that with 5 g, yet with no effect on thyroid hormone profile. They reported improvement of implant function with time.

Roy et al,³² noted an increase in the size and activity of transplanted thyroid tissue during serial 99mTc scans.

Sakr and Mahmoud,²³ observed that the sooner the graft is prepared for transplantation and the more expedited the procedure, the more favorable the outcomes. They also found a statistically significant correlation between the age of the patients and the necessity for replacement therapy, particularly when using 50 years as the threshold age.

Monib et al,²⁶ reported the survival of implanted thyroid tissue by positive isotope scan uptake from the 2nd month regardless the thyroid profile.

Sakr and Mahmoud,²³ documented that 2 months after surgery, there was an uptake of 99mTc and a steady improvement in thyroid function tests (FT3, FT4, and TSH) throughout a year-long observation period. The findings indicated that all implanted tissues were viable and functional, although to varying extents. A minority of patients, representing 27.8%, exhibited partial graft function and required additional replacement therapy in the form of 50

µg daily for three patients and 100 µg daily for two patients.

Furthermore, neither this study nor any recent literature has reported any postoperative complications stemming from the thyroidectomy or at the transplantation site, affirming the relative safety of thyroid autotransplantation.^{24,31,33}

Conclusion

Autotransplantation of heterotrophic thyroid tissue is safe, and simple. It allows an autoregulatory euthyroid for selected patients after thyroidectomy either without or with the lowest possible dose of replacement therapy.

Limitations and recommendations

The study lacks long-term follow-up of patients, which is mandatory for all patients, to monitor any fluctuations in thyroid functions and proper response to feedback mechanisms. Follow-up of the implantation site is important to detect any change in the nature of the implanted tissue.

Yearly US may detect goiter recurrence in the muscle, yet no vital structures will be compressed. Reoperation, if indicated, will be safe in comparison to reoperation in the neck.

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Nil.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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