



Parathyroid gland autotransplantation after total thyroidectomy in surgical management of hypopharyngeal and laryngeal carcinomas: A case series



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HIGHLIGHTS

- Persistent hypoparathyroidism is a frequent complication after total thyroidectomy.
- This study was to assess the feasibility of parathyroid gland autotransplantation after total thyroidectomy.
- Parathyroid gland autotransplantation is a simple safe technique with high success rate in preventing persistent hypoparathyroidism.

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ABSTRACT

Background and objectives: Total thyroidectomy is indicated in most cases with postcricoid carcinoma, circumferential hypopharyngeal carcinoma and in advanced laryngeal carcinoma. Persistent hypoparathyroidism is a frequent complication after total thyroidectomy which is difficult to manage unlike hypothyroidism. This study was to assess the feasibility of parathyroid gland autotransplantation after total thyroidectomy in advanced carcinomas and their effectiveness in preventing persistent hypoparathyroidism.

Methods: This study included 26 patients with hypopharyngeal and laryngeal carcinoma presented to National Cancer Institute, Cairo University. Total thyroidectomy and total parathyroid gland excision were performed as a part of adequate oncologic surgical procedure. The parathyroid glands were identified, resected and stored in iced saline. Histological confirmation was necessary before implantation into separated muscle pockets in the anterior forearm muscles. Regular samples were drawn to assess serum parathormone and calcium levels.

Results: All patients experienced hypocalcaemia within 1–5 days after operation. Only one patient experienced parathyroid graft failure while the remaining patients were normocalcemic during follow up after surgery, indicating functioning parathyroid grafts.

Conclusions: Parathyroid gland autotransplantation is a simple safe technique with high success rate in preventing persistent hypoparathyroidism after total thyroidectomy in surgical management of advanced hypopharyngeal and laryngeal carcinomas.

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1. Introduction

There is still controversy about the proper management of thyroid and parathyroid glands in surgical management of

hypopharyngeal and laryngeal carcinomas. Most surgeons agree that at least one thyroid lobe with its related parathyroid glands could be preserved in most cases with pyriform carcinoma and unilateral laryngeal carcinoma. Only the ipsilateral thyroid lobe is resected en block with the surgical specimen preserving the contralateral thyroid lobe in these cases [1].

There is high incidence of thyroid gland invasion in postcricoid carcinoma thus total thyroidectomy is indicated in most cases with postcricoid carcinoma and in circumferential hypopharyngeal

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carcinoma [2]. Also total thyroidectomy is indicated in advanced laryngeal carcinoma with bilateral thyroid cartilage invasion or subglottic extension [3].

Persistent hypoparathyroidism is frequent after total thyroidectomy which is difficult to manage unlike hypothyroidism [4,5].

Many series had described parathyroid autotransplantation after total thyroidectomy in thyroid carcinoma [6–8] but few studies were reported regarding parathyroid autotransplantation after total thyroidectomy in hypopharyngeal and laryngeal carcinomas [9]. Parathyroid autotransplantation was first performed in humans by Lehey [10] in 1926. Parathyroid autotransplantation may be immediate or delayed. The intraoperative autotransplantation is in another location rather than the delayed cryopreserved gland is in the subject of this manuscript. The routine parathyroid autotransplantation decrease the incidence of permanent hypoparathyroidism to less than 1% [11] In this study we tried to assess the feasibility of parathyroid gland extraction and immediate autotransplantation in the forearm after total thyroidectomy in advanced hypopharyngeal and laryngeal carcinomas and the effectiveness of this technique to prevent the occurrence of persistent hypoparathyroidism.

2. Patients and methods

This study included 26 patients with hypopharyngeal and laryngeal carcinoma presented to our unit at National Cancer Institute (Cairo University) in the period from March 2011 to June 2013. This study was approved by the ethical committee review board of National Cancer Institute, Cairo University in accordance with the Helsinki guidelines for the protection of human subjects. Written informed consent was obtained from all participants. These patients were diagnosed either outside or at our institute by direct laryngoscopy or hypopharyngoscopy and adequate biopsy from the tumor. Preoperative medical assessment included routine complete blood picture, liver and kidney functions, fasting blood sugar, bleeding and coagulation profile and cardiological assessment. The stage of the disease was evaluated by clinical assessment, fiberoptic laryngoscopy, locoregional (CT or MRI), routine CXR and other metastatic workup as indicated.

The extent of surgical resection and the technique of reconstruction with its potential complications and parathyroid autotransplantation were discussed preoperatively with the patient with combined signed consent by the patient and the surgeon performing the operation. Total thyroidectomy and total parathyroid gland excision were performed in those 26 patients as a part of adequate oncologic surgical procedure.

Total laryngo-pharyngo-esophagectomy and total thyroidectomy was done in 19 cases with hypopharyngeal carcinoma. Eleven cases had advanced post-cricoid carcinoma and eight cases had circumferential lesions. Reconstruction was done by gastric transposition in all of the cases. This technique is the most commonly used after pharyngolaryngo-oesophagectomy in patients with hypopharyngeal carcinoma in our institute, owing to increased multidisciplinary experience in this form of surgery and in relation to the advanced pathological stage of hypopharyngeal carcinoma at presentation in which total oesophagectomy is needed to obtain proper lower safety margin [12,13].

Total laryngectomy and total thyroidectomy was performed in 7 patients with laryngeal carcinoma as all patients had advanced disease. In five cases the tumor had invaded the thyroid cartilage bilaterally and in 2 cases there were subglottic extension. Five cases were treated primarily by surgery and in 2 cases salvage surgery was done after failure of previous radiotherapy.

2.1. Technique of parathyroid autotransplantation

The search of parathyroid glands was begun at the point where the recurrent laryngeal nerve crosses behind the inferior thyroid artery. The inferior parathyroid glands were usually found below this point. The superior glands were often found within 1–2 cm above this point. This technique was described in detail by Kaplan in 1984. The parathyroid glands were identified, resected and stored in iced saline until completion of the operation. Part of the extracted supposed parathyroid glands and the surrounding fat tissue was sent for frozen section examination to confirm being parathyroid glands and to exclude malignant invasion. Each parathyroid gland was sliced into 1–3 mm slices and three or four grafts were implanted into separated muscle pockets in the anterior forearm muscles (in brachioradialis muscle), then the muscle is closed with non absorbable sutures [14,15].

2.2. Follow up and assessment of function of grafted parathyroid glands

Blood samples were drawn from both forearms 24 h, 3 days, 2 weeks and one month after surgery to assess parathormone level. Prolonged use of tourniquet was avoided before blood sampling. Serum calcium was also measured every 12 or 24 h postoperatively, 2 weeks, 2 months, 4 months and 6 months postoperatively. Vitamin D (calcitriol, 25–50 ug), calcium (ca carbonate 2–3 g) and thyroxine (200 ug) supplementation started on first post-operative day via the feeding tube. Patients who experienced symptoms or signs of hypocalcemia or a fall in serum calcium below 8 mg/dL were given oral 1,25-Dihydroxycholecalciferol 0.5–1.0 ug/day and oral calcium carbonate 1 g/day. Patients with severe symptoms of hypocalcemia or a [Ca+2] level less than 7 mg/dL were given intravenous calcium gluconate. Patients were deemed ready for hospital discharge as soon as the serum calcium reached 8.0 mg/dL. All patients with a [Ca+2] level less than 8.0 mg/dL were maintained on supplemental calcium carbonate and vitamin D after hospital discharge.

Data of all patients were collected and analyzed including primary sites of malignancy, Perioperative complications, number of autotransplanted parathyroid glands, and postoperative serum levels of parathormone and calcium.

3. Results

The mean age of our patients was 52.3 years (range 34–65 years). The primary sites of malignancy are presented in Table 1. Primary site of tumor was the hypopharynx in 19 cases and the larynx in 7 cases. Total thyroidectomy and parathyroid excision were done in all cases as a part of adequate oncologic procedure. Two cases were found to have malignant infiltration of the extracted parathyroid specimens by frozen section and were excluded from our study.

The number of glands used for transplantation ranged from 1 to 5 glands Table 2. The right and left forearms were used for

Table 1
Primary sites of malignancy.

Primary site of tumor	No. of cases
Hypopharyngeal carcinoma	19
Postcricoid ca	11
Circumferential carcinoma	8
Laryngeal carcinoma	7
Advanced with bilateral thyroid cartilage invasion	5
Advanced with subglottic extension	2

parathyroid autotransplantation in 2 and 22 cases respectively as our rationale was to use the non dominant forearm.

Perioperative mortality occurred in 2 cases and they were excluded from the study. One patient died from massive myocardial infarction on third postoperative day. The 2nd patient developed sloughing of a part of the gastric tube. Reexploration and excision of the sloughed segment was done with orostome and gastrostomy, however, this patient died on 19 P.O day from severe chest infection. Perioperative complications are shown in Table 3.

Circulating levels of PTH were undetectable on the first postoperative day, however, PTH levels gradually increased, and by the third post-operative week they had reached $20 \text{ pg ml} \pm 1$. Patients were weaned of calcium and vitamin D supplements during the fourth post-operative week.

All our patients experienced a $[\text{Ca}^{+2}]$ less than or equal to 8.0 mg/dL associated with symptoms and signs of hypocalcemia within 1–5 days after operation (mean, 2.0 days).

All patients were followed for at least 6 months to assess the level of serum calcium and parathormone. Only one patient experienced parathyroid graft failure as judged by undetectable levels of circulating PTH measures by immunoassay while the remaining patients were normocalcemic at 6th months follow up after surgery, indicating the presence of functioning parathyroid grafts (see Fig. 1).

Three patients took calcium and vitamin D supplementation regularly beyond 6 months; however, only one patient required continued calcium or vitamin D replacement to maintain asymptomatic normocalcemia.

4. Discussion

The proper management of thyroid and parathyroid glands in laryngo-hypopharyngeal carcinoma is still controversial. The incidence of thyroid gland involvement in laryngo-hypopharyngeal carcinoma ranges from 0 to 23% [1–3] and this occurs mainly due to the physical proximity of the thyroid gland to the laryngopharynx. This low incidence of thyroid gland invasion explains why total thyroidectomy and parathyroid gland resection is rarely performed nowadays. However there is still subgroup of patients with advanced tumor stage who are in need for total thyroidectomy and parathyroid gland resection, and this include patients with postcricoid carcinoma, circumferential hypopharyngeal carcinoma [2] and patients with advanced laryngeal carcinoma with bilateral thyroid cartilage invasion or subglottic extension [3]. In our study, out of 56 patients with laryngo-hypopharyngeal carcinoma presenting to our center, the thyroid gland, parathyroid bodies, and regional lymph nodes was excised 'en bloc' with the primary tumor in 26 patients (46%) while in the other patients at least one thyroid lobe with its ipsilateral parathyroid glands could be preserved. This high incidence of total thyroidectomy in our patients may be explained by late presentation with advanced tumor stage at our institute.

The symptoms of hypothyroidism and chronic hypoparathyroidism occur in patients surviving after surgery and/or

Table 2
Number of autotransplanted parathyroid glands.

Number of auto-transplanted glands	Number of patients
5	1
4	2
3	4
2	10
1	7
	24 ^a

^a 2 cases were excluded due to malignant infiltration of the parathyroid glands.

Table 3
Perioperative complications.

Complications ^a	No.
Chest infection	4
Wound sepsis and fistula	6
Burst abdomen	1
Secondary hemorrhage	2
Massive myocardial infarction ^a	1
Sloughing of a part of gastric tube ^b	1

N.B. More than one complication may be present in the same patient.

^a Patient died on 3rd POD.

^b Patient died on 19 POD.

radiotherapy for squamous cell carcinoma of the larynx and hypopharynx [16,17]. However often these disorders are not noticed until symptoms are severe [18]. The diagnosis may be delayed due to lack of awareness, low index of suspicion, or both.

The reported incidence of hypoparathyroidism following thyroidectomy varies from 3% to 32% [19] but depends upon the extent of the surgery and the indications.

In a select group undergoing preoperative radiotherapy followed by surgery, 57% developed hypoparathyroidism in the month following surgery but no data was available regarding their long term parathyroid status [19]. While the management of this problem with vitamin D analogs and oral calcium may in many patients be satisfactory, hypoparathyroidism can have considerable consequences on bone metabolism, renal function, the risk of cataract formation and quality of life [20]. In patients undergoing pharyngolaryngectomy with oesophagectomy and total thyroidectomy, 50–73% were found to be hypoparathyroid in the immediate postoperative period [21,22].

Many series had described parathyroid autotransplantation after total thyroidectomy in thyroid carcinoma [6–8] but few studies were reported regarding this technique after total thyroidectomy in hypopharyngeal and laryngeal carcinomas [9].

Functional assessment of parathyroid autografts has included maintenance of normocalcemia without calcium supplementation, elevated PTH concentration in blood draining from the grafted site compared with systemic blood, increase in PTH level after transplantation, and graft uptake of radioisotope [23]. In our study we assessed our graft by frequent assessment of systemic serum Ca and Parathormone level from antecubital vein of the grafted forearm. We found gradual rise of PTH level in grafted site from 12.7 ± 5.1 from day 0 postoperative to $71.7 \pm 7.1 \text{ Pg/ml}$ one month after surgery denoting a good functioning parathyroid graft. In our series All our patients experienced a $[\text{Ca}^{+2}]$ less than or equal to 8.0 mg/dL associated with symptoms and signs of hypocalcemia within 1–5

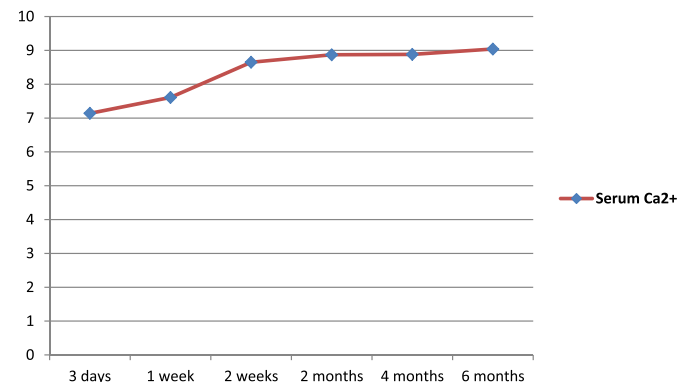


Fig. 1. Serum calcium level follow up for 6 months: shows gradual increase in serum Ca level during follow up in our patients up to 6 months.

days after operation (mean, 2.0 days). Three patients (11.5%) took calcium and vitamin D supplementation regularly beyond 6 months; however, only one patient required continued calcium or vitamin D replacement to maintain asymptomatic normocalcemia.

Only One patient experienced parathyroid graft failure as judged by undetectable levels of circulating PTH measures by immunoassay. After 6 months the remaining patients (82%) remained normocalcemic, indicating the presence of functioning parathyroid grafts and these results are comparable with other reports which showed success rates range from 55% to 100% after immediate autotransplantation of fresh parathyroid tissue [24].

Most studies on parathyroid autotransplantation in thyroid carcinomas reported autotransplantation in the neck in the same field of surgery [6–8].

However in our study we preferred transplantation of the parathyroid gland in the forearm instead of the neck as this site has many advantages. First, it is easy to assess the function of the graft by assessment of PTH level of antecubital vein of the grafted limb. Secondly, most of our patients have advanced tumor and most of them are in need for postoperative adjuvant radiotherapy or have already received preoperative radiotherapy which has an adverse effect on function and vascularity of grafted parathyroid gland. Another factor is that the sternomastoid muscle may be resected with radical neck dissection during the primary surgery or surgery for treatment of nodal recurrence. For all of these reasons, we preferred to do our transplanted parathyroid gland in the forearm instead of the neck.

5. Conclusion

Thyroid and parathyroid gland en block resection should be done in all patients with advanced laryngo-hypopharyngeal carcinoma for adequate local control. Parathyroid gland autotransplantation should be done for these patients when possible to avoid permanent hypoparathyroidism. We advice to do transplantation in the forearm as it has many advantages over the neck site.

Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this article.

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None.

Ethical approval

This study was approved by the ethical committee review board of National Cancer Institute, Cairo University in accordance with the Helsinki guidelines for the protection of human subjects. Written informed consent from all participants.

Consent

An informed consent has been obtained from all subjects after explanation of the protocol before joining the study.

The study had been conducted in compliance with the established standard methodological procedures. Participant's names will not be recorded to assure confidentiality. The confidentiality of the participants will be established by coding of the data list by a different code from their files to insure the anonymity of respondents.

All investigations will be carried out for patients free of charge.

Author contribution

Abd Elmaksoud: study design, Surgical and data analysis and writing.

Iman: data collections, data analysis and writing.

Mahmoud: data collections, data analysis and writing.

Guarantor

Dr Abd Elmaksoud.

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References

- [1] Sparano A, Chernock R, Laccourreye O, Weinstein G, Feldman M. Predictors of thyroid gland invasion in glottic squamous cell carcinoma. *Laryngoscope* 2005;115:1247–50.
- [2] Collin CF, Spiro RH. Carcinoma of the cervical esophagus changing therapeutic trends. *Am J Surg* 1984;148:460–6.
- [3] Brennan MA, Meyers AD, Jafek BW. The intraoperative management of the thyroid gland during laryngectomy. *Laryngoscope* 1991;101:929–34.
- [4] Buchanan G, West TE, Woodhead JS, Lowy C. Hypoparathyroidism following pharyngolaryngo-oesophagectomy. *Clin Oncol* 1975;1:89–96.
- [5] Mortimore S, Thorp MA, Nilssen ELK, Isaacs S. Hypoparathyroidism after the treatment of laryngopharyngeal carcinoma. *J Laryngol Otol* November 1998;112:1058–60.
- [6] Walker RP, Paloyan E, Kelley TF, Gopalsami C, Jarosz H. Parathyroid autotransplantation in patients undergoing a total thyroidectomy: a review of 261 patients. *Otolaryngol Head Neck Surg* 1994 Sep;111(3 Pt 1):258–64.
- [7] Wells SAJ, Stirman JAJ, Bolman RM. Parathyroid transplantation. *World J Surg* 1977;1:747–56.
- [8] Gamil Mohamed, Murad Magda, Abdelsalam Ibrahim. PARA thyroid autotransplantation in total thyroidectomy. *J Egypt Natl Cancer Inst* 1994;Vol. 6(3):495–503 (June).
- [9] Kourias E, Arkadopoulos N, Kostopanagiotou G, Kinoglou G, Smyrniotis V. Extended esophagolaryngeal resection with parathyroid autotransplantation diseases of the esophagus 1999;12:314–6.
- [10] Moffett JM, Suliburk J. Parathyroid autotransplantation. *Endocr Pract*. 2011;17(Suppl. 1):83–9.
- [11] Palazzo FF, Sywak MS, Sidhu SB, Barraclough BH, Delbridge LW. Parathyroid autotransplantation during total thyroidectomy-does the number of glands transplanted affect outcome? *World J Surg* 2005;29:629–31.
- [12] Abdelaziz S, Anwar H, Ramzy S, Elshafey MM, Mebed AH. Is gastric pull-up reconstruction still the versatile method in the surgical treatment for hypopharyngeal carcinoma. *Kasr El Aini J Surg* 2005;6(1):3–11.
- [13] Kaplan MM. Thyroid hormones. In: Donald RA, editor. *Endocrine disorders: a guide to diagnosis*. New York: Marcel Dekker; 1984.
- [14] Baumann DS, Wells Jr SA. Parathyroid autotransplantation. *Surgery* 1993;113:130–3.
- [15] Olson Jr JA, DeBenedetti MK, Baumann DS, Wells Jr SA. Parathyroid autotransplantation during thyroidectomy. Results of long-term follow-up. *Ann Surg* 1996;233:472–8.
- [16] Ledger GA. Hypocalcaemia and hypoparathyroidism. *Curr Ther Endocrinol Metabol* 1994;5:508–10.
- [17] Isaacson SR, Snow JB. Etiologic factors in hypo calcaemia secondary to operations for carcinoma of the pharynx and larynx. *Laryngoscope* 1998;88:1290–7.
- [18] Isaacson R. Hypocalcaemia in surgery for carcinoma of the pharynx and larynx. *Otol Clin N Am* 1980;13:181–92.
- [19] Ronga G, Fragasso G, Fiorentino A, Paserio E, Todino V, Tummarello MA. Prevalence of parathyroid insufficiency after thyroidectomy study of 1037 cases. *Ital J Surg Sci* 1988;18:151–4.
- [20] Cusano NE, Rubin MR, Sliney Jr J, et al. Mini-review: new therapeutic options in hypoparathyroidism. *Endocrine* 2012;41:410–4.
- [21] Shoback D. Clinical practice. Hypoparathyroidism. *N Engl J Med*. 2008;359:391–403.
- [22] Osborne DA, Jones WI. Parathyroid dysfunction following surgery of the pharynx and larynx. *Br J Surg* 44:166–171.
- [23] Saxe A. Parathyroid transplantation: a review. *Surgery* 1993;113:130–3.
- [24] Feldman Andrew L, Sharaf Renu N, Skarulis Monica C, et al. Results of heterotrophic parathyroid autotransplantation: a 13-year experience. *Surgery* 1999;126:1042–8.