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Research Article

Malignancy of Thyroid: The 8 Years Institutional Experience

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Abstract: The aim was to study the epidemiological, pathological parameters and survival of patients with thyroid malignancy. It is a retrospective review of all patients of thyroid malignancy who were managed at our institution. Chi-square test was used for statistical analysis & Kaplan – Meier method was used for calculating survival. A total of 182 patients were included in the study. Parameters evaluated included age, sex, predisposing factors if any, fine needle aspiration cytology diagnosis, nodal status at presentation, intraoperative findings, final histopathological diagnosis, perioperative complications, follow up and survival. Papillary carcinoma was the commonest malignant lesion with a frequency of 87.91% followed by 7.91% for follicular carcinoma, 3.29% medullary carcinoma, 0.89% anaplastic carcinoma. Female predominance was seen (M: F - 5.06:1). The 5 year & 6 year survival rates were 89% and 73 % respectively. The most common postoperative squeal observed was temporary hypocalcaemia seen in 15% patients, followed by permanent hypocalcaemia seen in 8.79%. Temporary recurrent laryngeal nerve palsy was seen in 6.59% patients while permanent recurrent laryngeal nerve paralysis was seen in 4.39% patients. Thyroid malignancies affect all age groups. There was decreased morbidity after lobar or subtotal thyroidectomy as compared to total thyroidectomy.
Keywords: Papillary carcinoma, Morbidity, Female predominance, Nodule size, Tumor recurrence, Thyroidectomy.

INTRODUCTION

Malignancies of thyroid gland are the most common malignancies of the endocrine system [1]. These can be follicular, papillary, medullary, anaplastic and other rare varieties like mucinous, squamous cell, and mucoepidermoid carcinomas [2, 3]. Thyroid nodules are approximately more common in women than in men [4]. The median age at diagnosis is 47 years, with a peak in women at 45 to 49 years and in men at 65 to 69 years [5]. Papillary carcinoma is the most common type of thyroid malignancy, accounting for 65–80% of all thyroid cancers [6, 7]. New nodules develop at a rate of approximately 0.1% per year beginning in early life, but at a much higher rate (~2% per year) after exposure to head and neck irradiation [7, 8]. Follicular and anaplastic thyroid carcinomas occur more commonly in areas of endemic goiter [9, 10]. Additionally, two particularly important risk factors, exposure to radiation and a family history of thyroid cancer, have been studied extensively in world literature [12, 13].

Prolonged survival, even with recurrent disease, has led to controversy regarding the extent of thyroidectomy for patients with well-differentiated thyroid carcinomas [14]. Total thyroidectomy is considered as the surgical option for papillary and medullary carcinomas [15, 16] and hemi thyroidectomy is considered as the surgical option for follicular and hurthle cell neoplasms [17, 18]. A study reported that 10-year relative survival rates for patients with papillary, follicular, and Hürthle cell carcinomas were 93%, 85%, and 76% respectively [1]. This study aimed to retrospectively review the cases of thyroid malignancies operated in a tertiary care Centre with 6 yrs. of follow up to study the epidemiological, pathological and survival rates in various thyroid malignancies.

MATERIALS AND METHODS

Total 182 patients were included in this study. Parameters evaluated included age, sex, predisposing factors like family history of thyroid cancer, associated with other carcinoma. Diagnosis was made with nodal

status at presentation, Fine needle aspiration cytology used for making diagnosis, intraoperative findings, and final histopathology. Cases of thyroid malignancies previously operated in our institute in last 8yrs and on regular post-operative follow up were included in the study by studying the hospital records retrospectively. Patients with age ranging from 28 to 75 were taken and have been managed as per institutional protocol. All the patients were evaluated with a detailed history and clinical examination at the time of presentation and then investigated with the routine hemogram, serum electrolytes, liver and renal function tests along with thyroid function tests, radiological evaluation with ultrasonography of neck and computerized tomography of neck, fine needle aspiration cytological examinations and radioiodine scans preoperatively.

The work up also included routine work up for general anesthesia and detailed metastatic work up pre-operatively. Neck dissections were done along with the primary surgery in all those patients with clinically palpable FNAC proven cervical lymphadenopathy and in patients with clinically suspicious involved lymph nodes intraoperative. Surgical specimens were investigated with histopathological examination. Post operatively patients were kept on follow up and were routinely investigated with serial ultrasonography, thyroglobulin levels and radioiodine scans. Majority of the surviving patients are still under institutional follow up.

RESULTS

Papillary carcinoma was the commonest malignant lesion with a frequency of 87.91% followed by 7.91% for follicular carcinoma, 3.29% medullary carcinoma, 0.89% anaplastic carcinoma.

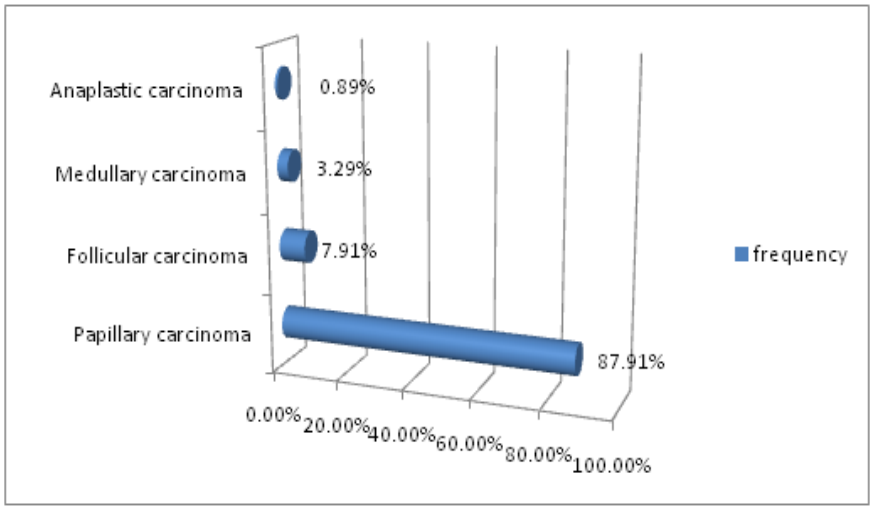

Fig. 1: Frequency of different thyroid carcinomas

Female predominance was seen (M: F - 5.06:1).

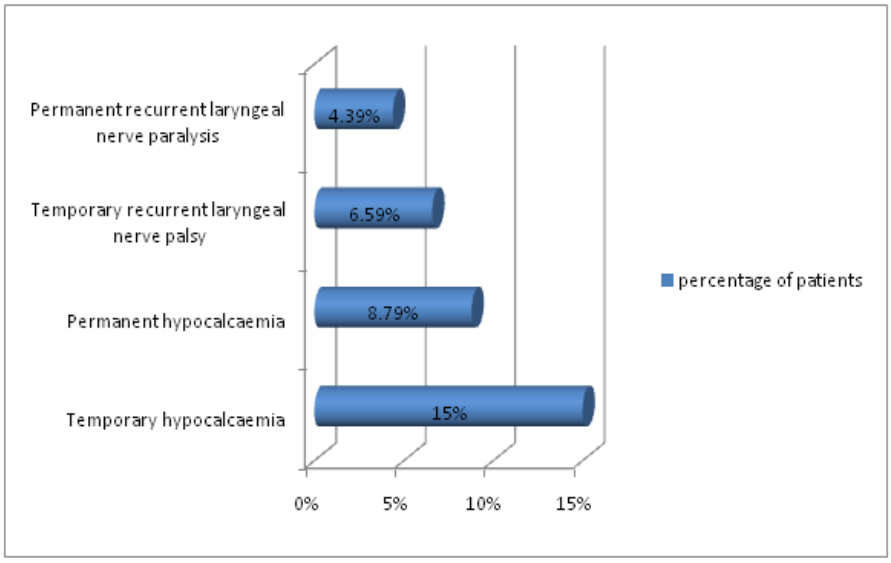

Fig. 2: Complications of thyroidectomy

The most common postoperative squeal observed was temporary hypocalcaemia seen in 15% patients, followed by permanent hypocalcaemia seen in 8.79% .Temporary recurrent laryngeal nerve palsy was seen in 6.59% patients while permanent recurrent laryngeal nerve paralysis was seen in 4.39% patients. Papillary thyroid carcinoma is the most common malignant thyroid neoplasm in countries with sufficient iodine diets and comprises up to 80% of all thyroid malignancies. It occurs in all age groups but is most common in the 3rd to 5th decades.

A total of 182 patients were included in the study by retrospective hospital record review.

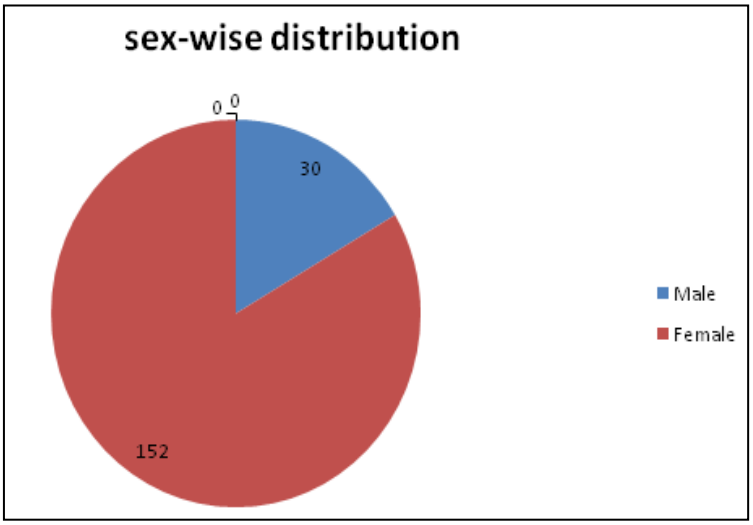

Fig. 3: Number of patients according to sex

The age of the patients ranged from 18 to 75 years with 30 males (16%) and 152(84%) females.

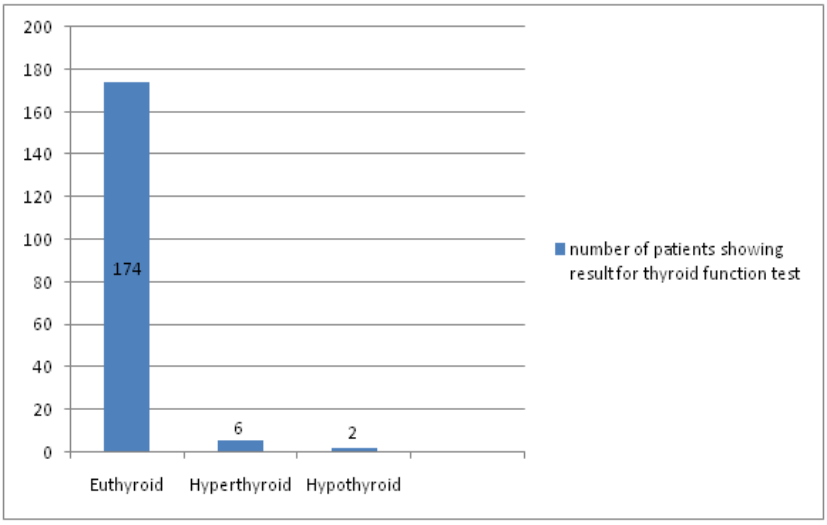

Fig. 4: Thyroid function test

Thyroid function tests were done on all those patients at presentation who showed euthyroid state in 174 patients. The 6 patients were found to be hyperthyroid and 2 patients to be hypothyroid. Total thyroidectomy was done in 180 patients. Rest 2 patients of anaplastic carcinoma were treated with palliative treatment. Post-operative histopathology showed papillary carcinoma to be the most common malignant lesion with a frequency of 87.91% followed by follicular carcinoma in 7.91% of patients, medullary carcinoma 3.29% of patients and anaplastic carcinoma in 0.89% of patients.

Table-1: Distant metastasis

Metastasis	Number of patients
Laryngotracheal invasion	33
Lymph node metastases	56
Bilateral lymph node metastases	23 among lymph node metastasis patients

Laryngotracheal framework invasion was found in 33 patients. Lymph node metastases were found in 56 patients and among them 23 patients had bilateral lymph node metastases. Lymph node metastasis without obvious thyromegaly was found in 16 patients and systemic metastasis .as found in 23 patients.

Discrepancy between pre-operative FNAC and postoperative histopathology was found in 21 patients.

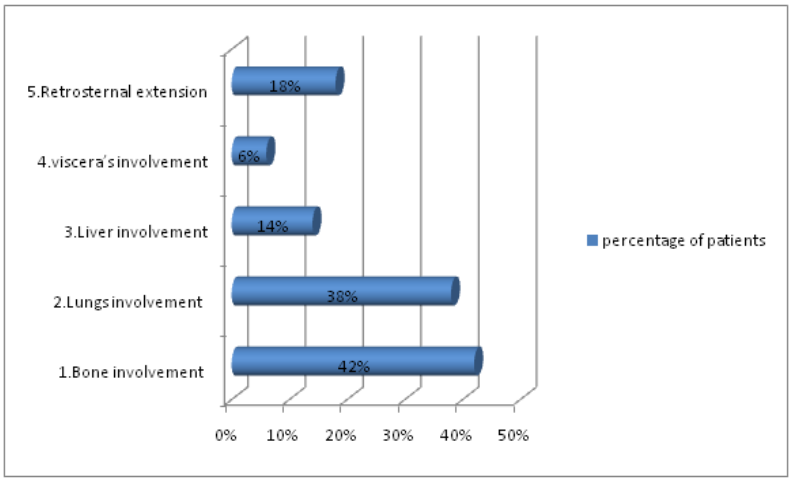

Fig. 5: Organs involved

Table-2: Parathyroid co-surgery

Parathyroid gland co-surgery	Number of patients
One parathyroid was preserved	52
Parathyroid reimplantation	15

Coexistent Lymphocytic thyroiditis was seen on histopathological examination in 38 patients. Clinical evaluation, thyroglobulin monitoring, serial USG & radioiodine scanning were done for postoperative monitoring.

Post-operative hematoma was observed in 4 patients. Average 5 years survival rates observed in differentiated thyroid carcinomas was 89%.

Table-3: Radiotherapy treatment

Radiotherapy	Number of patients
Radioiodine ablation	92
Underwent radioiodine ablation for the second time	26

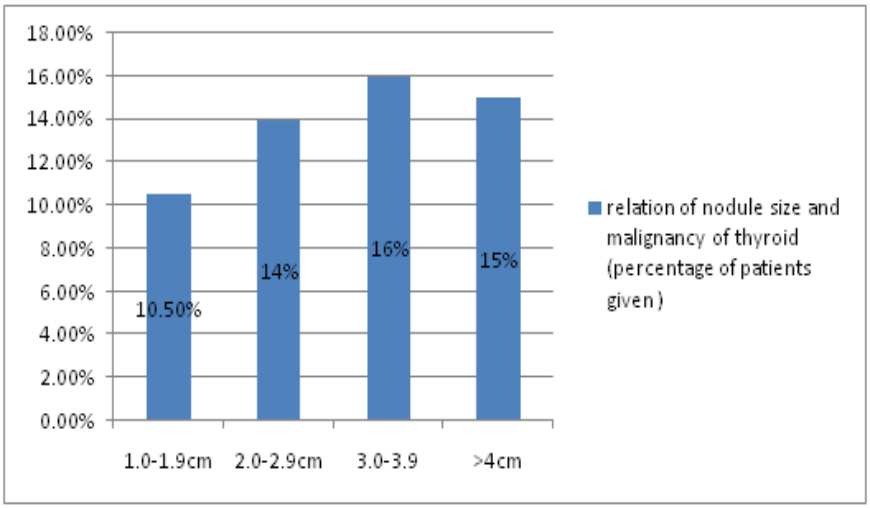

Fig. 6: Malignant Thyroid carcinomas and nodule size

Of that 1.0 to 1.9 cm in diameter, 10.5% were cancerous. In contrast, of those >2.0 cm, 15% were cancerous (p< .01). However, nodules 2.0 to 2.9, 3.0 to 3.9, and >4 cm were cancerous in 14%, 16%, and 15% of cases, respectively, demonstrating no graded increase in risk beyond the 2-cm threshold.

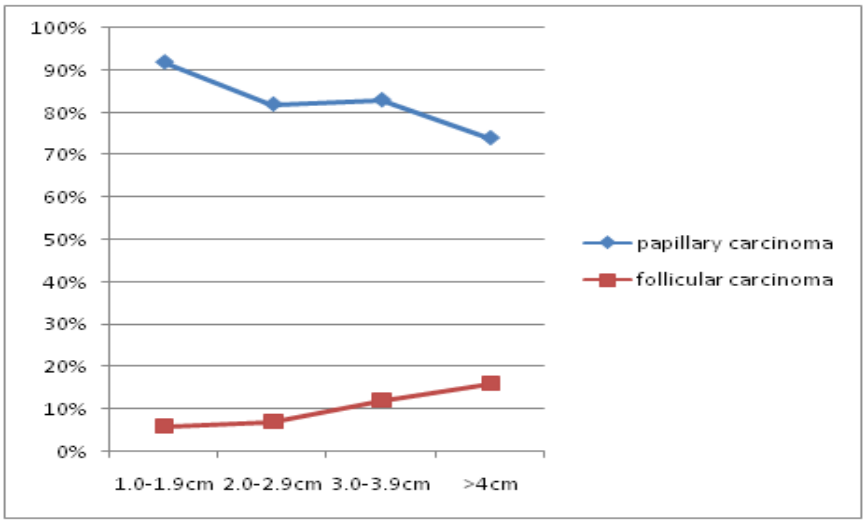

Fig. 7: Different carcinoma showing variation in nodule size with the % of malignant patients

When malignant, the proportion of papillary carcinoma decreased (nodules 1.0-1.9 cm, 92% of cases; 2.0-2.9 cm, 88%; 3.0-3.9 cm, 83%; >4 cm, 74%, while follicular carcinoma increased (1.0-1.9 cm, 6%; 2.0-2.9 cm, 7%; 3.0-3.9 cm, 12%; >4 cm, 16% (p< .01) as nodules enlarged. Nodules size did not influence cytology distribution or risk of false-negative aspirates.

DISCUSSION

Epidemiologic studies have reported the prevalence of palpable thyroid nodules to be approximately 5% in women and 1% in men living in iodine-sufficient parts of the world [19, 20]. Palpable nodules increase in frequency throughout life, reaching a prevalence of approximately 5% in the population aged 50 years and older [21, 22]. Thyroid nodules are approximately more common in women than in men [4]. Thyroid carcinoma is 6th most common malignancy in women and its incidence is getting up by 6.2 %per year [23].

Thyroid carcinoma has 3 main histologic types: differentiated (including papillary, follicular, and Hürthle cell), medullary, and anaplastic (aggressive undifferentiated tumor) [24].

Papillary and follicular cancer compromises the 90 percent of all thyroid cancers [25]. A study in America conducted for thyroid abnormality and 5 year follow up showed results for 53,856 patients who were treated for thyroid carcinoma , 80% had papillary carcinoma, 11% had follicular carcinoma, 3% had Hürthle cell carcinoma, 4% had medullary carcinoma, and 2% had anaplastic thyroid carcinoma [1]. Although thyroid carcinoma occurs more often in women, mortality rates are higher for men, because men are usally diagnosed in older ages [26, 27].

Exposure to ionizing radiation is the only known environmental cause of thyroid carcinoma, usually causing papillary carcinoma [28]. The thyroid gland is the only organ linked to risk at approximately 0.10 Gy by convincing evidence [8]. Short-lived radioiodines were potent thyroid carcinogens in children with history of ionizing radiation particularly those younger than 10 yrs [29].

Family history, long standing goiters are other studied risk factors [30, 31]. The loss of chromosomes, or aneuploidy, has been noted in 10% of all papillary carcinomas, but is present in 25% to 50% of all patients who die as a result of these lesions [32]. Similarly, the chromosome abnormality is associated with follicular adenoma is due to loss of the short arm of 11th chromosomeand transition to a follicular carcinoma seems to involve deletions of 3p, 7q, and 22q [33, 34]. There genetic changes have also been associated with certain types of thyroid carcinoma [35]. Mutations within the mitogen-activated protein kinase (MAPK) pathway play important role in papillary thyroid cancer [36]. Additionally, rearrangements or activation of RET or BRAF proto-oncogenes, which can also activate MAPK, are often found in papillary thyroid cancer [37, 38].

Differentiated (i.e., papillary, follicular, or Hürthle cell) thyroid carcinoma is commonly presents as a solitary thyroid nodule which remains asymptomatic for long periods. Approximately 50% of the malignant nodules are discovered during a routine physical examination, by serendipity on imaging studies, or during surgery for benign disease. Remaining 50% are noticed first by the patient, usually as asymptomatic nodules [21, 39].

Ultrasonography is considered as the standard radiological tool for evaluation of suspicious thyroid nodules [40]. Suspicious criteria that are found on using ultrasound include central hyper vascularity, micro calcifications, and irregular bordersm [28]. Fine-needle aspiration (FNA) is the preferred procedure for the evaluation of suspicious thyroid nodules [28, 41]. Limitations of FNAC examination include sometime it gives false negative results [42].

Tumor recurrences depend on initial therapy and other prognostic variables. Approximately 30% of patients with differentiated thyroid carcinoma are found to have tumor recurrences during several decades. 66% of recurrences are found to occur within the first decade after initial therapy. Recurrence rates are 2 times higher with locally invasive tumors. 33% of patients with these tumors die of cancer within a decade [43].

Enlarged cervical lymph node may be the only sign of thyroid carcinoma. In these patients, multiple nodal metastases are usually found at surgery [44]. It is approximated that 10% of patients with papillary carcinoma and 25% of those with follicular carcinoma develop distant metastases. Approximately 50% of these metastases are present at diagnosis [45].

The FNA cytologic diagnosis of follicular neoplasm is a benign follicular adenoma in 80% of cases. However, 20% of patients with follicular neoplasms are ultimately diagnosed when the final pathology is assessed. Total thyroidectomy is recommended only if invasive cancer or metastatic disease is apparent during surgery or if the patient chooses total thyroidectomy to avoid a second procedure [28]. Completion thyroidectomy is also recommended for tumors that, on final histologic sections after lobectomy plus isthmusectomy, are minimally invasive follicular carcinomas; *minimally invasive* cancer often requires examination of at least 10 histologic sections [46].

A Hürthle cell tumor or oxyphilic cell carcinoma is usually assumed to be a variant of follicular thyroid carcinoma, prognosis is worse [28, 47]. The management is similar to follicular carcinoma except that it can present with associated lymphadenopathy and need neck dissection along with primary surgery and metastatic hurthle cell lesions are less like to concentrate 131I [28]. Radioiodine therapy (100–150 mCi) should be considered after thyroidectomy for patients with stimulated Tg levels of more than 10 ng/mL who have negative scans [47].

Total thyroidectomy is the treatment of choice in patients with medullary carcinoma [48]. Patients with familial medullary carcinoma thyroid or MEN II should have the entire gland removed [49].

Anaplastic thyroid carcinomas are aggressive undifferentiated tumors, with a disease-specific mortality approaching 100% [50]. Patients with anaplastic carcinoma are older than those with differentiated carcinomas, with a mean age at diagnosis of approximately 65 years [51]. No effective therapy exists for anaplastic carcinoma [52]. Total or subtotal thyroidectomy is performed for anaplastic thyroid carcinoma [53].

CONCLUSION

Major surgeries of the thyroid is considered as difficult, and results totally depends upon the experience of surgeons and the average results is much better than the surgeons who perform the operations occasionally. Near total" and subtotal thyroidectomy are basically considered as less extensive surgery and causes less complications, but many times it is associated with higher rates of tumor recurrence and mortality.

The relation between the size of different thyroid nodules and malignancy is also shown in our patients in above mentioned graphs and increasing thyroid nodule size impacts cancer risk in a nonlinear fashion. In papillary carcinoma as the thyroid nodule size increases, malignancy risk decreases but in follicular carcinoma as the nodule size increases ,the malignancy risk also increases.

A threshold is detected at 2.0 cm, beyond which cancer risk is unchanged. However, the risk of follicular carcinomas and other rare thyroid malignancies increases as nodules enlarge [54].

The long-term complications of thyroid surgery are hypocalcaemia, a serious, difficult-to-treat condition due attendant to hypoparathyroidism; and hoarseness, due to injury to the recurrent laryngeal nerve. The complications depend upon the extent of the operation and the experience of the surgeon [55].

Papillary thyroid carcinoma is the most common malignant thyroid neoplasm in countries with sufficient iodine diets and comprises up to 80% of all thyroid malignancies, occurs in all age groups but commonly in the 3rd to 5th decades [56].

We also analyzed that there is decreased morbidity after lobar or subtotal thyroidectomy as compared to total thyroidectomy.

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