PROSPECTIVE ANALYSIS OF 518 CASES WITH THYROIDECTOMY IN TURKEY

FERIT TANERI, OSMAN KURUKAHVECIOGLU, BAHADIR EGE, UTKU YILMAZ, ERCUMENT TEKIN, CAGATAY CIFTER, ERHAN ONUK

Gazi University Faculty of Medicine, Department of Surgery, Ankara, Turkey
E-mail: okurukahveci@yahoo.com

Objective. Thyroid malignancies can present in different manners, among them as asymptomatic solid nodule being the most puzzling. Nodules have been found in the 60-70 % of autopsy specimens and it is very important to rule out the malignancies in such cases. Incidence of carcinomatous changes is reported in 5-15 % of solitary nodules. We present the results of prospective study on 418 thyroidectomies with the aim to review the experience of our unit, to establish the correlation between clinical presentation and histopathology, to discuss the malignancy rates and surgical complications.

Patients and Methods. Five hundred eighteen consecutive cases of thyroidectomy 419 female (80.8 %), and 99 male (19.2 %) patients. performed between January 2002 and October 2004 were included in this prospective study.

Results. In 71 (13.7 %) cases the malignancy was found by paraffin specimens, the highest prevalence of malignancy being found in patients with nodular goiter (NG – 18 %) followed by 14.6 % in multinodular goiter (MNG). The sensitivity of preoperative fine needle cytology (FNAC) was 83.3 % with false positive rate of 1.3 %. Complications were seen in 5.2 % of cases of which 4 (0.7 %) had hypoparathyroidism and 7 (1.3 %) had recurrent laryngeal nerve injury. All patients observed came from endemic area. Family history nearly doubles the risk of malignancy.

Conclusions. In an endemic area the nodular goiter is the most common. Preoperative cytology, although sensitive, gives a considerable number of false positive results. Results of thyroid surgery at a high volume centre are satisfactory with very low rates of recurrent laryngeal nerve and parathyroid injury. Probability of malignant transformation in a long standing thyroid swelling should always be kept in mind. There appears to be an increase in prevalence of thyroid malignancies in Turkey after Chernobyl disaster.

For details see <www.elis.sk>

Key words: Thyroidectomy – Thyroidectomy complications – Thyroid cancer – Goitre

Goiter is defined as a pathological enlargement of thyroid tissue and can be classified as toxic or nontoxic, diffuse or nodular and nodules can be solitary or multiple. Although controversy about thyroidectomy continues, indications for surgery in nonendemic areas are suspicion of malignancy or hyperthyroidism and in endemic areas are tracheal compression, cosmetic reasons, hyperthyroidism and malignancy (SEDGWICK et al 1974; ROHER et al. 1987; GREENSPAN et al 1991). Of these, suspicion of malignancy is the most important factor as thyroid malignancies can show different presentations especially as an asymptomatic solid nodule(s). The nodules have been found in 60-70 % of autopsy specimens; hence, it is very important to rule out the malignancy in these cases (MAZZAFERRI et al. 1993). Incidence of carcinomatous changes ranges from 5 to 15 % in solitary nodules.

Diagnosis of malignancy in solitary nodule is challenging and most of the cases reported as follicular or Hürthle cell neoplasm require ipsilateral hemithyroidec-

tomy for establishing the diagnosis. Nearly 1490 deaths from thyroid cancer were expected in USA in 2005 (JEMAL et al. 2005). Although the approach to goiter depends on clinical evaluation, histological results obtained by fine needle aspiration cytology or pathological investigations of thyroidectomy materials help in directing the proper intervention. We present the results of a prospective study on thyroidectomies performed between January 2002 and January 2004. By these results we aim to review the experience of our unit which is one of the reference centers in Turkey, to establish the data in an endemic region, to correlate clinical presentation and histopathology as well as to discuss the prevalence of malignant neoplasm and surgical results.

Subjects and Methods

Five hundred and eighteen consecutive cases of thyroidectomy were included in this prospective study. Clinical examination of the cases before surgery was done in endocrine unit and was followed by hormonal assays, routine biochemistry, ultrasonography (US), fine needle aspiration cytology (FNAC) and scintigraphy. Many of our patients came from an endemic region for goiter (CALIK et al. 1996). Patients' history, home town and other risk factors like radiation and family history were also noted. The patients with history of voice change, hoarseness, dysphagia, odynophagia, shortness of breath underwent an additional examination by otolaryngologist. In presence of hyperthyroidism, patients were subjected to medical therapy in order to achieve euthyroid status before surgery. All patients underwent US examination using a 10-15 MHz transducer. Thyroid scintigraphy using Tc^{99m} was carried out and its results were combined with that of power Doppler ultrasonography in order to identify nodules greater than 8 mm and to establish their nature, to investigate general thyroid function, and to search for ectopic gland. Thyroid scintigraphy has the accuracy, specificity and sensitivity of 0.86, 0.91, 0.67 respectively (DEMIREL et al. 2003). Thereafter the goiters were classified as toxic or nontoxic. Toxic goiters were subdivided into nodular goiter (TNG), toxic multinodular goiter (TMNG), or toxic diffuse goiter (TDG).

Nontoxic goiters were divided into nodular goiter (NG) or multinodular goiter (MNG). Twenty five patients had recurrent nodular goiter and all of them underwent total thyroidectomy. FNAC was performed routinely in all nodular cases under US guidance unless the nodule was palpable at physical examination. Decision to operate was taken according to the following criteria: hypocellular/acellular material in repeated FNAC, malignant lesions on FNAC, follicular lesions on FNAC, cysts that recur on more than two occasions after aspiration, clinical grounds without cytological or radiological evidence, dominant nodule >3 cm diameter, resistance of TSH suppression therapy for 6-12 months, cold nodules on thyroid scintigraphy, MNG with malignancy suspicion; like patients from endemic region, tracheal compression and rapid growth of nodules. Operative procedure was chosen according to results of preoperative investigations, intra-operative findings and frozen pathology results. Being an endemic region and high recurrence rates; we preferred total thyroidectomy in MNG and suspicious cases like radiation history, family history, hoarseness, dysphagia etc.; but if a lesion was predominantly on only one side we chose isthmectomy with unilateral total or subtotal lobectomy (hemithyroidectomy) (CALIK et al. 1996, HISHAM et al 2001). Subtotal thyroidectomy was performed in cases where there was no suspicion of malignancy like Graves or unilateral nodules less than 1.5 cm. TMNG and TDG patients generally underwent total thyroidectomy, because of malignancy suspicion and toxic symptoms. Similarly all patients with preoperative diagnosis of malignancy underwent total thyroidectomy with or without neck dissection depending on presence or absence of lymph node(s). Subtotal thyroidectomy (i.e. surgical excision of 50 % of the gland) was performed either unilaterally or bilaterally; near total thyroidectomy which means surgical excision of more than 90 % of gland retaining less than 2 g of tissue, was performed either unilaterally or bilaterally depending upon the indication. Detailed postoperative record was maintained and all complications were noted.

The patients were discharged after 2 postoperative days in order to control early complication and drainage if exist and then controlled on the first week for wound healing and thyroid function tests; third month for thyroid function tests, physical examination, and then every 6 months for next 2 years. Patients with thyroid malignancies were followed-up by a joint team of endocrinologist, oncologist, nuclear medicine and general surgeon. They are followed by thyroid function test, thyroglobulin level, whole body scan, radiological imaging of chest and thyroid USG after second follow-up. Self limiting complications resolving with in six months after surgery and were recorded as transient whereas those lasting for more then 6 months were

Table 1
Preoperative diagnosis and procedures performed

	NG	TNG	TDG	MNG	RNG	TMNG	Total
Total Thyroidectomy	–	–	26	88	25	20	159
Subtotal Thyroidectomy	–	–	1	120	–	16	137
Neartotal Thyroidectomy	–	–	4	29	–	27	60
Unilateral Neartotal Lobectomy	10	17	–	–	–	–	27
Unilateral Subtotal Lobectomy	8	5	–	–	–	–	13
Unilateral Total Lobectomy	111	5	–	–	–	1	117
Total Thyroidectomy + neck dissection.	4	1	–	–	–	–	5
Total	133	28	31	237	25	64	518

termed permanent. Hypocalcaemia patient were treated with calcium supplementation.

Results

There were 419 female (80.8 %) and 99 male (19.2 %) patients aged 20 to 85 years (mean age of 47.2). Mean age was 46.8 ± 2.23 in female and 48.5 ± 2.54 in male patients. All patients were from endemic areas of Turkey. There were 67 (14.9 %) non malignant thyroid disease patients with family history of benign thyroid disease (BTD), whereas 17 (23.9 %) thyroid cancer patients had family history of BTD. On the other hand, 2 (2.8 %) of papillary thyroid cancer patients had a history of thyroid carcinoma whereas and 4 (0.8 %) patients with non malignant thyroid disease patient had a history of thyroid carcinoma. The risk of developing thyroid malignancy with positive family history was nearly twice that of patients with no family history (OR 1.9). None of the patients had a history of neck radiation. Until the end of October 2004, 98 % of patients have been at least once followed.

According to the preoperative investigations and imaging procedures the study included 133 (25.6 %) cases with nodular goiters (NG), 28 (5.4 %) cases with toxic nodular goiters (TNG), 31 (5.9 %) cases with toxic diffuse goiters (TDG), 237 (45.7 %) cases with multinodular goiters (MNG), 64 (12.6 %) cases with toxic multinodular goiter (TMNG) and 25 (4.8 %) cases with recurrent nodular goiter (RNG) (Table 1).

The operations performed included 13 (2.5 %) unilateral subtotal lobectomy, 27 (5.2 %) unilateral near total lobectomy, 117 (22.6 %) unilateral total lobectomy, 159 (30.7 %) total thyroidectomy, 137 (26.4 %) subtotal thyroidectomy, 60 (11.7 %) neartotal thyroidectomy and 5 (0.9 %) total thyroidectomy + modified radical neck dissection. The details of procedure are given in Table 1.

The paraffin embedded specimen was reported as malignant in 71 (13.7 %) of the case. In our series the incidence of malignancy was the highest in patients with NG (18 %), followed by MNG (14.6 %), TNG (7.1 %), TMNG (9.6 %), and toxic diffuse goiters (6.4 %). The details are given in Table 2.

Table 2
Prevalence of malignancy in various goiters

Malignancy incidence	Number of cases	%
Nodular goiter	24	18.04%
Toxic nodular goiter	2	7.14%
Toxic multinodular goiter	6	9.67%
Toxic diffuse goiter	2	6.45%
Relapse multinodular goiter	2	8.0%
Multinodular goiter	35	14.64%
Total	71	38.71%

Table 3 shows histological type of malignant neoplasms encountered in our series. Papillary carcinoma was the most common in 42 cases (59.1 %), while occult papillary carcinoma was found in 13 (18.3 %) cases. Patients with anaplastic carcinoma and two cases of papillary carcinoma underwent neck dissection. When compared to preoperative fine needle aspiration cytology (FNAC) of nodular goiter and permanent pathological results, the sensitivity of FNAC was 83.3 %. The false negative and false positive rate for FNAC was 9.8 % and 1.3 % respectively.

Table 3
Frequency of various histological types of cancers identified

Malignancies	Number of cases	%
Occult papillary carcinoma	13	18.3%
Papillary carcinoma	42	59.15%
Anaplastic carcinoma	3	4.22%
Medullary carcinoma	2	2.81%
Papillary-follicular carcinoma	3	4.22%
Follicular carcinoma	7	9.85%
Hürthle cell carcinoma	1	1.4%
Total	71	100.0%

The occurrence of postoperative hypocalcaemia was documented in 13 patients. Of these, 9 (1.7 %) had transient hypocalcaemia and 4 (0.7 %) had persistent hypocalcaemia. In addition, the flap edema and hematoma which resolved spontaneously were seen in 3 (0.5 %) patients. Only 1 (0.2 %) patient had keloid formation over the incision.

Changes in voice tone attributable to injury of the external branch of superior laryngeal nerve were revealed in ten cases (1.9 %). Of these, 3 (0.5 %) patients experienced temporary hoarseness while 7 (1.3 %) of them had permanent hoarseness attributed to recurrent laryngeal nerve injury. There were no other complications like infection or bleeding. Overall complication rate was 5.2 %.

During the postoperative follow-up 3 patients with anaplastic carcinoma died. In rest of the benign or malignant case no death was recorded.

Discussion

Turkey is a region of endemic goitre (Erdogan et al. 2002) and a majority of previous reports on thyroid from this region are retrospective. As being a reference center in an endemic area, all the patients seen in this hospital were from endemic areas.

This study provides information on the family history of BTD and confirms association between history of BTD and risk of thyroid cancer and also disease itself. An increased risk was observed with positive family history for both carcinoma and BTD. This relation can be explained by the incidence of the disease in general population, prevalence of BTD, genetic predisposition, exposure or increased susceptibility, or to their sharing the environmental factors (Memon et al. 2004). Absence of radiation history makes the effect of other risk factors more prominent, especially the endemicity or environmental factors like Chernobyl accident.

Although several studies showed a higher incidence of NG compared to MNG (Rojeski et al. 1985; Bapat et al. 1993), our series showed a higher incidence of MNG. The overall incidence of malignancy in patients with NG was the highest at 18 %, while it was 14.6 % with MNG.

The incidence of cancer in MNG was reported in 6.2 – 9.7 % in several studies and its incidence was 14.6 % in Turkish patients in a previous study (Pelizzo et al 1997; Sachmechi et al 2000). The FNA sensitivity of 83 % is in accordance with the literature (Terry et al. 2003). As FNA is a cytopathological examination of individual cells rather than of the architecture of cells in the tissue, the experience of cytopathologist should not be underestimated.

The malignancy rates in the patients operated for thyroid diseases in our clinic was found 5 %, 6 % and 11 %, respectively in 1987 (Cifter et al 1987), 1998 (Taneri et al 1998) and 1999 (Ersoy et al 1999).. In this study the malignancy rate was 13.7 % thus suggesting that it is increasing within last two decades. Chernobyl nuclear disaster which occurred on April 26, 1986 has been thought to have a considerable effect on the increase in malignancy rates especially in those of the thyroid.

In the earlier studies the prevalence of thyroid cancer in hyperthyroidism varied from 0.3 to 16.6 % with a higher rate in TNG (Ardito et al 1997). Our findings showed the prevalence rate of 7.1%. Similarly, the type of malignancies resembles that reported in literature (Bapat et al 1993, Taneri et al 1998, Erturk et al 1999, Gregory et al 1999).

Although this is a two-year study, at least 98 % of the patients came for first control and thus the study has long enough follow-up to detect possible complications. Earlier studies reported the permanent or temporary hypocalcaemia rate of zero to 30 % after total or subtotal thyroidectomies (Farrar et al 1983, Marohn et al 1995, Calik et al 1996 Shaha et al 1998). In our case the occurrence of postoperative hypocalcaemia was documented at 2.5 % and transient cases were completely cured in third month. Only 0.7 % patients had permanent hypoparathyroidism.

Although the hemorrhage is a life threatening early complication of thyroid surgery and it's usually caused by inappropriate hemostasis, in our experience we did not encounter it. In various other series, this complication is reported to be in 0.3-1.5 % (Dawson et al 1985, Marohn et al 1995, Shaha et al 1998)..

None of our patients experienced respiratory problems due to edema or injury of the recurrent laryngeal nerve (Weldstein et al 1980) but 10 cases (1.9 %) developed hoarseness. Permanent recurrent laryngeal injury was seen in 4 of which 3 were operated for recurrent TMNG. This shows the difficulty of identifying and preserving recurrent laryngeal nerve in recurrent cases and the importance doing good surgery at first instance.

In the last quarter of this century the mortality rate of thyroidectomies has fallen to 0-0.1 % after the enormous developments in medical practice (Weldstein et al 1980, Farrar et al 1993, Marohn et al 1995, Calik et al 1996).. In our series of 518 cases we have seen no mortality due to surgery. There had been no wound complications less hypocalcaemia no postoperative hemorrhage and less recurrent nerve injury. The operating time too has decreased with increasing experience of our unit.

In this short follow-up period we have seen 3 mortalities only in anaplastic carcinoma patients. The other malignant cases are under control without recurrence or metastasis. This is probably because of our extended surgery and close follow-up or due to shorter follow-up period. It is established that MNG and NG may harbor some occult malignancy or some malignancies may be overlooked in these cases. Because of high MNG incidence in our country and high-risk of cancer we prefer extended operations in nodular cases.

The endocrine surgeons acquired better results with low operational complications, high quality of life, early diagnosis in cancers, etc.- due to increased experience, science and technology in thyroid surgery and thyroid cancer (Coffey et al 1993). However, thyroid cancer rates are still on the rise probably due to genetic, environmental and hormonal factors. Though the prevalence of thyroid malignancies appear to have increased in our area after Chernobyl disaster, an epidemiological investigation is needed to establish its role, if any.

In conclusion, the endemic thyroid diseases must be closely investigated for environmental, family history, genetic factors or other factors like immunological ones – adhesion molecules, cadherins etc.- which can also be affected by environmental factors. The presence of malignancy should be established in order to provide best treatment and to achieve good results. Further studies are needed to establish the cause of apparent rise of thyroid malignancy in Turkey. The need for establishing a familial thyroid registry is re emphasized.

References

Ardito G, Mantovani M, Vincenzoni C: Hyperthyroidism and carcinoma of the thyroid gland. Ann Ital Chir **68,** 23-27, 1997

Bapat RD, Pal P, Shah S, Bhanddarkar SD: Surgery for thyroid goiter in western India. A prospective analysis of 334 cases. J Postgrad Med **39,** 202-204, 1993

Calik A, Kucuktulu U, Cinel A, Bilgin Y, Alhan E, Piskin B: Complications of 867 thyroidectomies performed in a region of endemic goiter in Turkey. Int Surg **81,** 298-301, 1996

Cifter C, Aktan O, Onuk E: Unnecessary thyroidectomies. Mediterranean Surgical Meeting' Abstracts 1987. Istanbul 1987

Coffey A, Petti G. Endocrinology. In: Head and neck surgery-otolaryngology (B. Bailey, J. Johnson, R. Kohut, H. Pillsbury, M. Tardy M, eds). pp. 135-148. Lippincott, Philadelphia 1993

Dawson PM: The surgical treatment of thyroid disease in a district general hospital. Br J Clin Pract **39,** 220-224, 1985

Demirel K., Kapucu O., Yucel C., Ozdemir H., Ayvaz G., Taneri F: A comparison of radionuclide thyroid angiography, 99mTc-MIBI scintigraphy and power Doppler ultrasonography in the differential diagnosis of solitary cold thyroid nodules. Eur J Nucl Med Mol Imaging 30, 642-650, 2003

Erdogan G, Erdogan MF, Emral R, Bastemir M, Sav H, Haznedaroglu D, Ustundag M, Kose R, Kamel N, Genc Y: Iodine status and goiter prevalence in Turkey before mandatory iodization. J Endocrinol Invest **25,** 224-228, 2002

Ersoy E, Taneri F, Tekin E, Poyraz A, Cihan A, Dursun A, Onuk E: Preoperative fine-needle aspiration cytology versus frozen section in thyroid surgery. Endocr Regul **33,**141-144, 1999

Erturk E, Tuncel E, Yerci O, Gursoy N, Imamoglu S, Koran N, Arinik A: A retrospective analysis of thyroid cancer. J Environ Pathol Toxicol Oncol **15,** 245-249, 1999

Farrar WB: Complications of thyroidectomy. Surg Clin North Am **63,** 1353-1361, 1983

Greenspan FS: The problem of the nodular goiter. Med Clin North Am **75,** 195-209, 1991

Gregory PS, Orlo HC, Jon AV: Thyroid and parathyroid. In: Principles of Surgery (SI Schwartz, GT Shires, FC Spencer, eds), pp. 1681-1689. McGraw Hill, New York 1999

Hisham AN, Azlina AF, Aina EN, Sarojah A: Total thyroidectomy: The procedure for multinodular goiter. Eur J Surg **167,** 403-405, 2001

Jemal A, Murray T, Ward E, Samuels A, Tiwari RC, Ghafoor A, Feuer EJ, Thun MJ: Cancer Statistics, 2005. CA Cancer J Clin **55,** 10-30, 2005

Marohn MR, LaCivita KA: Evaluation of total/near-total thyroidectomy in a short-stay hospitalization: Safe and cost-effective. Surgery **118,** 943-948 ,1995

Mazzaferri EL: Management of a solitary thyroid nodule. N Engl J Med **328,** 553-559, 1993

Memon A, Berrington A, Luqmani Y, Suresh A: Family history of benign thyroid disease and cancer and risk of thyroid cancer. Eur J Cancer **40,** 754-760, 2004

Pelizzo MR, Bernante P, Toniato A, Fassina A: Frequency of thyroid carcinoma in a recent series of 539 consecutive thyroidectomies for multinodular goiter. Tumori **83,** 653-655, 1997

Roher HD, Goretzki PE: Management of goiter and thyroid nodules in an area of endemic goiter. Surg Clin North Am **62,** 233-249, 1987

Rojeski MT, Gharib H: Nodular thyroid disease evaluation and management. N Engl J Med **313,** 428-436, 1985

Sachmechi I, Miller E, Varatharajah R, Chernys A, Carroll Z, Kissin E, Rosner F: Thyroid carcinoma in single cold nodules and in cold nodules of multinodular goiters. Endocr Pract **6,** 5-7, 2000

Sedgwick CE, Filtzer HS: Operative history of goiter. In: Surgery of the thyroid gland,.(CE Sedwig, ed), pp.1-5. WB Saunders, Philadelphia 1974

Shaha A, Jaffe BM: Complications of thyroid surgery performed by residents. Surgery **104**, 1109-1114, 1988

Taneri F, Poyraz A, Tekin E, Ersoy E, Dursun A: Accuracy and significance of fine-needle aspiration cytology and frozen section thyroid surgery. Endocrine Regul **32**, 187-191, 1998

Terry A, Angela C, Khanh G: Multinodular goiter. Otolaryngol Clin N Am **36,** 35-54, 2003

Weldstein SS: Medical complications of thyroid surgery. Otolaryngol Clin North Am **13,** 99-107, 1980

Corresponding author: Osman Kurukahvecioglu
Gazi Üniversitesi Tip Fakültesi
Genel Cerrahi Anabilim Dali
06500 Beşevler – Ankara – Türkiye
Phone: +903122025719
+905326011918
e-mail: okurukahveci@yahoo.com