Gamma probe ^{99m}Tc-pertechnetate assisted completion thyroidectomy vs conventional thyroidectomy in differentiated thyroid carcinoma

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Abstract

Patients undergoing partial thyroidectomy for benign diseases may need re-operation if differentiated thyroid carcinoma (DTC) is detected on histopathology. *The aim* of this study was to determine if using gamma probe during the above surgery in a procedure called: gamma probe completion thyroidectomy (GPCT) could support the diagnosis of DTC tissue and offer an advantage in the surgical treatment of DTC patients. *We have studied* 100 patients who after bilateral subtotal thyroidectomy for benign disease in several hospitals, were found to have DTC histopathologically and referred to our clinic for subsequent re-operation. Of these, 50 underwent conventional completion thyroidectomy (Group I) and 50 underwent GPCT (Group II). We compared retrospectively Group I and Group II in terms of volume of residual thyroid tissue, thyroid stimulating hormone (TSH) values, complication rates and incidence of tumor found in the residual thyroid. *Our results* showed that one month postoperatively, TSH was significantly higher in Group II (P<0.001). Volumes of residual thyroid were also significantly less in Group II (P<0.000). Complications and the incidence of tumor cells found in the residual thyroid tissue between the groups were not statistically different (P>0.05). *In conclusion,* GPCT in patients with DTC significantly increased the success of this operation in localizing and removing residual thyroid tissue.

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Introduction

After partial thyroidectomy in patients with benign thyroid disease, it is common to find differentiated thyroid carcinoma cells (DTC) in the postoperative specimens. The incidence of DTC in these cases is about 10% [1, 2]. When DTC cells are found in histopathology after partial thyroidectomy, recurrence of DTC is more common in patients with large residual thyroid tissue and 50% of these patients will succumb to DTC [3-6]. Other authors have advised total or near-total thyroidectomy on these patients, especially in cases with multinodular goiter, to avoid second operation of a conventional completion thyroidectomy (CCT) [2-4]. Other authors advise CCT in all cases, except for occult papillary carcinoma and for minimally invasive follicular carcinoma [7-10].

In some institutions, it is not always possible during CCT operations, to ablate all thyroid tissue, due to fibrosis arising from the first operation, and the difficulty to identify parathyroid glands and the recurrent nerve [11-13]. Recently, gamma probe has been used inter-operatively in CCT, to detect and dissect cancer recurrence in the lymph nodes and the residual thyroid tissue [3, 14]. The objective of this study was to determine if gamma probe assisted completion thyroidectomy (GPCT) offers an advantage over CCT in patients with DTC as detected in the residual tissue.

Subjects and methods

A total of 100 patients referred to our clinic between January 2002 and January 2008 who initially underwent bilateral subtotal thyroidectomy in several hospitals and found to have DTC on final histopathology. Of these, 50 underwent CCT (Group I) and 50 underwent GPCT (Group II). Mean age for Group I was 40 (18-62 years) and 43.2 (15-72 years) for Group II. Male/female ratio was 6/44 for Group I and 7/43 for Group II. Mean tumor diameter was 19.6±16.4mm (4-90mm) in Group I and 22.0±7.6mm (2-65mm) in Group II (P=0.58). In Group I after the first operation, histopathological evaluation revealed papillary carcinoma in 41 patients, follicular carcinoma in 8 patients and Hürthle cell carcinoma in 1 patient. İn Group

2, histopathological evaluation as above, revealed papillary carcinoma in 44 patients and follicular carcinoma in 6 patients.

Pre-operatively, all patients underwent physical examination, thyroid scintigraphy (TS), neck ultrasonography (USG), indirect laryngoscopy and serum thyroid stimulating hormone (TSH) determinations. All patients and their data were evaluated by our Thyroid Diseases Council, which includes endocrinologists, nuclear medicine physicians and physicians from endocrine surgery and pathology. Patients who had been diagnosed after initial surgery as having DTC and those having after initial surgery: a) serum TSH less than 30mIU/L at 6 weeks or b) 2grams or more of residual thyroid tissue measured by USG or c) one thyroid nodule identified by USG were accepted for CCT.

Gamma probe (C-Trak System, Care Wise, Morgan Hill, California) was used for GPTC. Firstly, residual thyroid tissue was localized by administering 185MBq of technetium-99m pertechnetate ($^{99m}TcO_4^-$) intravenously into the basilica vein of the forearm 10min prior to surgery and obtaining measurements at 4 quadrants of the thyroid bed. Measurements from the contra-lateral shoulder were considered as background (Bg). After raising the skin flaps and prior to separating the strap muscles, measurements were done over the thyroid region and the residual thyroid tissue was localized. During excision of the residual thyroid tissue, the gamma probe was also used whenever visual distinction between thyroid tissue and muscles was questionable or fibrosis was present. After the residual thyroid tissue was excised, measurements of the thyroid bed were done and recorded as residual thyroid tissue/Bg (T/Bg) and thyroid bed/Bg (Tb/Bg). The ratios of T/Bg and Tb/Bg were calculated pre- and post-operatively. Equal Tb and Bg values were considered to be an indicator of successful removal of the residual thyroid tissue.

TS were performed on the 1rst postoperative day and serum free thyroxine (fT4), free triiodothyronine (fT3) and TSH levels were performed postoperatively on the 6th week in all patients. At least one month after the initial operation, we performed USG of the residual thyroid tissue and calculated its volume by multiplying the three dimensions measured by USG and their product multiplied with π/6, assuming that the tissue is ellipsoid in shape. When referring to this tissue by weight in grams, we presumed 1cm^3 of thyroid tissue to be 0.99gr or approximately 1gr.

Post-operative complications, the presence of tumor in residual tissue, high postoperative serum TSH levels and residual thyroid were compared in the CCT and GPCT Groups retrospectively. The study protocol was approved by our hospital's Ethics Committee, and all patients provided their written informed consent for performing the study.

Statistical analysis

Data were analyzed using SPSS 15.0 for Windows. Results were expressed as mean ± SD. Student's t-test and chi-square were used for comparison. A P<0.05 was accepted as statistically significant.

Results

Among the two Groups, the period between the initial and second operation was not significantly different, 80±37 days in Group I and 76±33 days in Group II (P=0.85). Preoperative and postoperative findings of these Groups are shown in Table 1. Pre-operatively, serum TSH levels were less than 30mIU/L in all patients and their mean values not statistically different between the two Groups (P=0.51). Post-operatively, these values were statistically different between Groups I and II (P=0.001). All patients of Group II had post-operative TSH values over 30mIU/L, whereas in 13 patients of Group I TSH did not exceed 30mIU/L.

Pre-operatively, residual thyroid tissue volume measured by USG was more than 2gr in all patients. The pre-operative mean residual tissue volume was not statistically different while the post-operative volume in Group II was significantly lower than in Group I (P<0.000). On TS, no residual tissue was found in 24/50 (48%) patients of this Group. On the other hand, only 11/50 (22%) patients in Group I had no residual tissue. Pre-and post-operative TS and USG residual tissue measurements in 4 patients in Group I remained unchanged. Their histopathology reports did not show any thyroid tissue either; only striated muscle and granulation tissue.

There was no significant difference in the duration of surgery between Groups (P=0.25). In Group II, the T/BG rate was 9.3±2.3 and the T bed/BG rate 1.3±0.2 (P<0.001).

The number of complications between Groups I and II did not differ (P=0.84). Permanent recurrent laryngeal nerve damage occurred in 1 patient (2%) from Group I and in 2 patients (4%) from Group II. Transient hypocalcemia was seen in 3 patients (6%) from Group I and in 5 patients (10%) from Group II. Permanent hypocalcemia occurred in 1 patient (2%) from Group I, and in 2 patients (4 %) from Group II.

With preoperative USG evaluation, nodular lesions were found in 13 patients from Group I and in 9 patients from Group II. Eleven patients (22%) in Group I and 10 patients (20%) in Group II had tumor in the residual tissue. Preoperative TS of a patient in the GPCT Group is shown in Figure 1 and his postoperative TS in Figure 2. Gamma probe device used in GPCT is shown in Figure 3.

Table 1. *Comparison of preoperative and postoperative findings in CCT and GPCT Groups*

	CCT (n=50)	GPCT (n=50)	P value
Preoperative TSH value (mIU/L)	8.9±5.4	8.3±4.4	NS
Postoperative TSH value (mIU/L)	44.5±24.5	59.2±19.3	P=0.001
Preoperative residual thyroid volume (gr)	6.22±3.29	5.22 ±2.56	NS
Postoperative residual thyroid volume (gr)	0.96±1.25	0.16±0.23	P<0.000
Operation time (min)	78 ± 15	76±11	NS

TSH: Thyroid stimulating hormone, CCT: Conventional completion thyroidectomy, GPCT: Gamma probe assisted completion thyroidectomy, NS: Nonsignificant

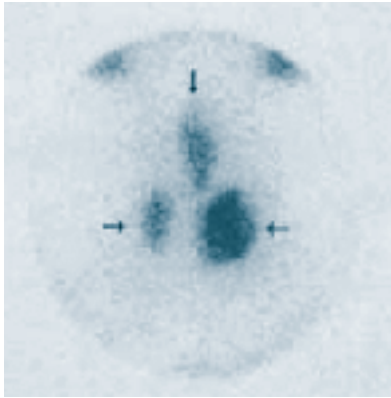

Figure 1. Thyroid scintigraphy with $^{99m}TcO_4^-$ before GPCT. Three distinct activity foci are seen compatible with residual thyroid tissue in the right thyroid lobe, left thyroid lobe and the pyramidal lobe (arrows).

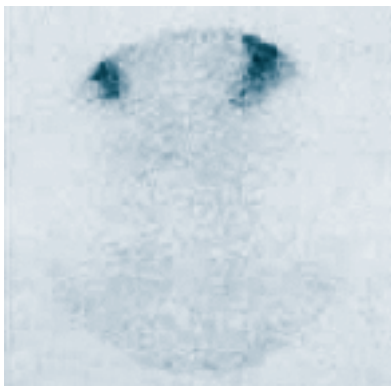

Figure 2. Thyroid scintigraphy with $^{99m}TcO_4^-$, after GPCT. No residual thyroid tissue was detected in the same patient.

Discussion

The mainstay of treatment in DTC patients is surgery, and the ideal procedure is total or near-total thyroidectomy [15-18]. The advantages of total or near-total thyroidectomy are the removal of multifocal disease, lowering the chance of anaplasia in the residual tissue, lowering the rate of local recurrence, discovering and treating metastatic disease and increasing the sensitivity of thyroglobulin (tg) for the follow-up studies [15-16, 19]. Lobectomy or subtotal resection may be adequate for patients, whose tumor is less than 1 cm, is not metastatic and does not show nearly vascular invasion [20-21]. For papillary thyroid carcinomas, the rate of contra-lateral multifocal disease has been reported to be 18%-88% [3, 20, 22-23]. The risk of residual carcinoma is 22%-64% after subtotal thyroidectomy [6]. İn our study, 11 patients from Group I (22%) and 10 patients from Group II (20 %) were found to have tumor in the residual tissue.

Following a limited resection, patients with over 2gr of residual thyroid tissue, a TSH <30 mIU/L and an ^{131}I uptake over 5% are not candidates for radioiodine (RAI) treatment and CCT is advised [24-26]. Among other advantages mentioned above CCT increases the effectiveness of RAI treatment and follow-up, and eliminates side effects of RAI treatment after removing large residual tissue [20, 24, 27-29]. The most important factor affecting the success of RAI treatment is the volume of the residual thyroid tissue; lesser the volume, higher the chance of RAI ablation [26, 30-31].

Laryngeal nerve injury and hypoparathyroidism are higher during CCT compared to primary operations but are strongly associated with the experience of the surgeon [5-6, 32]. After initial surgery subsequent CCT must be performed as soon as possible, to have fewer adhesions and complications [33, 34]. Unfortunately, our patients delayed to refer to our clinic and so early reoperation was impossible. In our study, complication between GPCT and CCT Groups did not differ.

Figure 3. The gamma probe device used in GPCT.

In DTC patients, gamma probe has been recently used to support thyroidectomy and identify regional metastatic lymph nodes [3, 14, 35-38]. Others proposed GPCT for the intraoperative localization and resection of locoregional nonfunctioning DTC recurrences using technetium-99m-methoxyisobutylisonitrile (^{99m} Tc-MIBI) [14, 35, 39]. Others measured by a gamma-probe, the ratio of thyroid activity to background activity ratio (T/Bg) in the residual tissue, with a normal limit of up to 5.1±1.4 [3]. In our study, the T/Bg ratio was 9.3±2.3 and the T bed/Bg-ratio 1.3±0.2.

Tunca et al. (2008) found that GPCT does not offer any benefit over CCT with respect to operation time, complication rates, or completeness of surgery [40]. In our study, we found that gamma probe was very useful intra-operatively in locating and removing the residual thyroid tissue but there was not a significant difference in the duration of surgery between GPCT and CCT Groups. When it was difficult to macroscopically distinguish residual thyroid tissue from muscles and fibroid tissue, we also found it easy to do so using the gamma probe.

In conclusion, our findings suggest that, GPCT compared to CCT showed no difference in the number of complications and in the duration of the operation, but significantly helped in localizing and removing the residual thyroid tissue.

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