Neck dissection in papillary thyroid carcinoma: when and why?

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Background
Papillary thyroid carcinoma (PTC) is the most common histological subtype of thyroid cancer, occurring in about 80% of cases. Ongoing debates on the best treatment strategy for patients with PTC over the last decades have included the extent of lymphadenectomy, the value of radioactive iodine (RAI) ablation, and the impact of each therapy on the patient's life.

The aim
The aim of this study was to compare different surgical procedures with regard to their safety, efficacy, and impact on the patient's life, as well as compare surgery with other treatment modalities such as RAI ablation.

Patients and methods
This study was conducted on 142 patients with PTC. Patients were arranged into three groups according to their clinical presentations: Group I included 34 patients who presented with hidden PTC within multinodular goiter; they were treated with total thyroidectomy (TT). Group II included 52 patients with PTC without palpable lymph nodes; they were treated with TT + prophylactic central neck dissection (pCND). Group III included 56 patients with PTC with palpable lymph nodes; they were treated with TT + central neck dissection (CND) + lateral neck dissection. RAI ablation was given to those patients who showed residual disease in the RAI scan. Completion surgery was performed only in relapsed cases with palpable disease. We compared the results of the three groups regarding complications, recurrence, and impact on patients' life.

Results
There was a statistically significantly higher incidence of most postoperative complications in groups II and III than in group I, although the final outcome was the same in the three groups. RAI therapy showed a good success rate in ablation of residual impalpable disease. At the end of the follow-up period, all patients were tumor free.

Conclusion
pCND should be abandoned because of its considerable risks and limited benefit. RAI ablation is a very good treatment option for residual PTC. Completion surgery should be decided only for relapsed bulky disease.

Keywords:
neck dissection, papillary thyroid carcinoma, radioactive iodine ablation

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Introduction

Papillary thyroid cancer is the most common endocrine malignancy and accounts for the majority of cases of thyroid cancer in iodine-sufficient areas of the world [1].

Lymph node (LN) metastases are a common finding in papillary thyroid carcinoma (PTC), occurring in the central compartment of the neck (level VI) in 20–50% of patients and in the lateral compartment of the neck (levels II–V) in 10–30% [2]. The high rate of metastases to regional lymph nodes is clearly associated with a higher risk for persistent or recurrent disease, although effects on survival remain controversial [3].

The subject of management of the neck has been extensively debated as the prognostic implications of the presence of positive nodes, either in the central compartment or in the lateral neck, were found to be minimal [4]. When there is no suspicion of metastatic disease to lymph nodes on imaging or palpation, prophylactic or elective central neck dissection (pCND) is a matter of debate [5–16].

The combination of surgery, radioactive iodine (RAI) treatment, and thyroid hormone suppression is the mainstay of treatment for PTC. However, because of the overall excellent outcomes in patients with PTC and the lack of prospective randomized controlled trials, many of the current recommendations and guidelines for treatment of PTC are controversial, such as the extent of surgery, the role of RAI treatment in low-risk patients, and the extent and frequency of surveillance [17].

In this research, we aimed at evaluating each surgical procedure with regard to its safety, efficacy, and impact on the patient's life. In addition, we tried to compare

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surgery with other treatment modalities such as RAI ablation.

Patients and methods

This study was conducted on patients with PTC admitted to Zagazig University Hospitals from March 2008 to March 2011. Cases were followed up for at least 3 years up to April 2014.

Inclusion criteria

(1) Age above 10 years and below 80 years.
(2) Histopathologically proven presence of PTC.
(3) Being fit for and willing to undergo surgery.

All patients consented to undergo surgery and join this study. For patients below 18 years of age, consent was given by their parents.

Exclusion criteria

(1) Age below 10 years or above 80 years.
(2) Prior unilateral, subtotal, near-total, or complete thyroidectomy.
(3) Histopathological report of any type of malignancy other than PTC, even the mixed papillary and follicular type.
(4) Being unfit for or refusal to undergo surgery.
(5) Being lost to postoperative evaluation or follow-up.

The plan

Patients were arranged into three groups according to their clinical presentations.

Group I included patients who presented with multinodular goiter (MNG) with clinically impalpable cervical lymph nodes (cN0). After total thyroidectomy (TT), their histopathological specimens showed hidden PTC. Patients whose postoperative RAI scan showed deposits in the cervical LNs received RAI ablation. Only patients who showed relapse [enlarged cervical LNs with elevated serum thyroglobulin (TG)] underwent neck dissection followed by thyroid hormone suppression.

Group II included patients who presented with suspicious thyroid swellings that were proved by fine needle aspiration cytology (FNAC) to be PTC; however, their clinical, ultrasonography, and computed tomography (CT) neck examination showed no suspicious cervical LNs (cN0). They underwent TT + pCND. Patients with deposits in the lateral cervical LNs on postoperative RAI scan received RAI ablation and follow-up. Patients showing relapse underwent completion lateral neck dissection (LND) followed by thyroid hormone suppression.

Group III included patients who presented with thyroid swellings with multiple enlarged cervical LNs detected by clinical and/or CT neck examination. These were proved by FNAC to be PTC. They were treated with TT + CND + LND. Patients whose postoperative RAI scan showed active deposits on the contralateral LNs received RAI ablation. Again, only patients who showed relapse with palpable LNs underwent contralateral neck dissection. Finally, all patients received thyroid hormone suppression (Fig. 1).

Neck ultrasonography and CT were performed by an experienced trained radiologist (Figs 2 and 3).

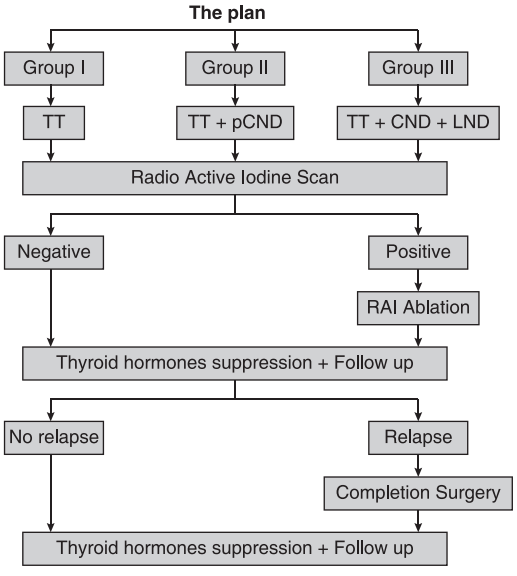
The ultrasound criteria by which LNs were recognized as malignant deposits are as follows:

(1) Size 1 cm or more.
(2) Presence of hyperechoic punctuations.
(3) Loss of corticomedullary differentiation.
(4) Cystic degeneration.
(5) Peripheral vascularization

These criteria were the inclusion criteria in group III.

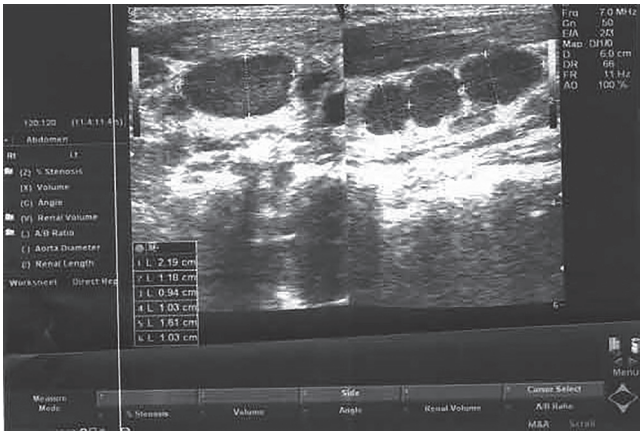
TT indicates removal of the whole thyroid gland aiming at leaving no thyroid tissue but making every effort to preserve the recurrent and external laryngeal nerves and the parathyroid glands (Figs 4 and 5). This cannot be achieved without adequate identification and careful dissection of these structures.

Figure 1



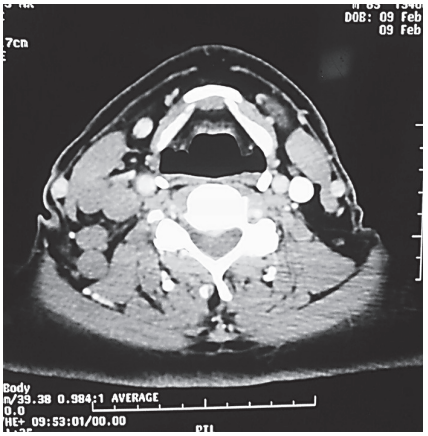
Plan of patients' management

Figure 2



Neck ultrasonography showing multiple enlarged cervical lymph nodes.

Figure 3

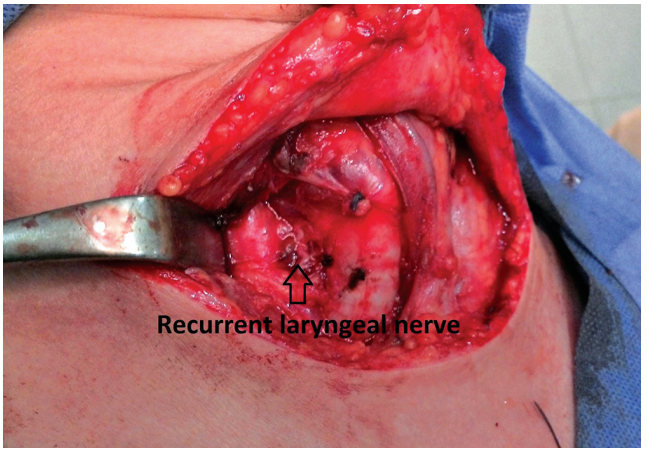


Neck computed tomography showing multiple enlarged cervical lymph nodes.

Figure 4

The neck after total thyroidectomy.

Figure 5



Preservation of the recurrent laryngeal nerve during total thyroidectomy.

CND entails removable of LNs at levels VI and VII – that is, the prelaryngeal, the perithyroid LNs including those around the recurrent and external laryngeal nerves, the pretracheal, bilateral paratracheal LNs, and the superior mediastinal LNs together with the whole fibrofatty tissues from the level of the hyoid bone above to the innominate veins below and from the medial side of the carotid artery on one side to the contralateral one – through a cervical incision.

LND entails removal of the whole LNs at levels II, III, and IV in the ipsilateral side sparing the sternomastoid muscle, accessory nerve, and internal jugular vein from the base of the skull above to the level of the clavicle below.

All patients were admitted to the department of general surgery in Zagazig university hospitals where they were fully investigated and prepared for surgery. Routine laboratory investigations were ordered and basal serum calcium (Ca) levels were ascertained. Indirect laryngoscopy was performed to evaluate vocal cord mobility before surgery. All operations were performed by the same surgical team and following the same surgical principles. Also, all FNAC and paraffin sections of the resected specimen were examined and diagnosed by the same pathologists in the pathology department in Zagazig University Hospitals (Figs 6 and 7). RAI ablation was decided and calculated by radiotherapists at our university hospitals.

Postoperatively, all patients were cared for in the high dependency care unit in our surgical department until they became stable and were discharged when they were surgically free.

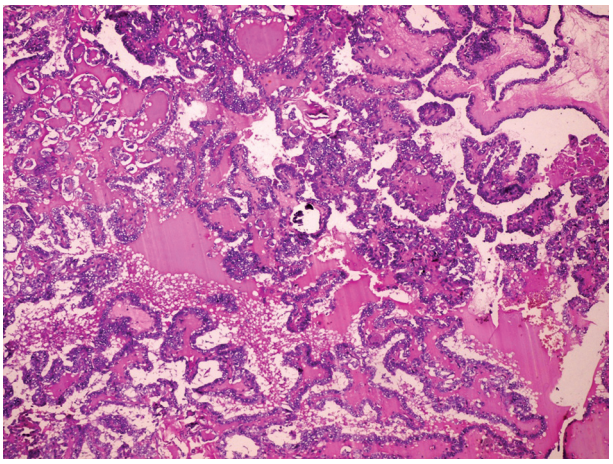
Total serum Ca was measured 24 h after surgery. Medications were started immediately if serum Ca

was less than 10 mg%. No patient developed tetany. Ca salts alone at 3 mg/day were given if total serum Ca was between 8–10 mg%, and calcitriol 1 mg/day was added when it was below 8 mg%. Further, PTH level in the serum was measured 1 month after surgery (normal level 10–65 ng/l); if it was low it was measured every 3 months. Transient hypoparathyroidism was defined as low serum Ca and low PTH that could be corrected within 1 year after surgery; if not corrected, it was defined as permanent hypoparathyroidism.

Indirect laryngoscopy was repeated on the second postoperative day to check for recurrent laryngeal nerve injury (RLNI), which was identified either unilaterally or bilaterally, and patients with RLNI were submitted to regular additional examinations every 3 months until vocal cord mobility was regained. If the mobility remained impaired for more than 1 year postoperatively it was regarded as permanent RLNI.

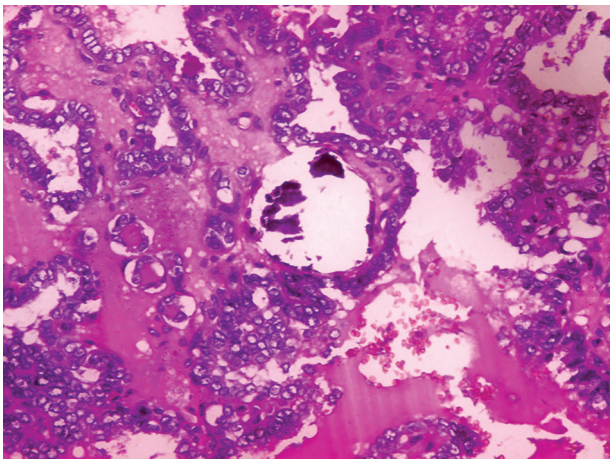
Patients were discharged from the hospital on scheduled follow-up visits every 3 months for the first year and then every 6 months for the next 2 years. At each visit, a full medical examination was carried out and routine laboratory investigations were ordered, including assessment of serum TG and anti-TG antibody. In addition, serum Ca and PTH levels were evaluated in patients with hypothyroidism, and indirect laryngoscopy was performed for patients with RLNI. An RAI scan was carried out 1 month postoperatively and at the end of each year's follow-up to check for any residual or recurrent tumor (Figs 8 and 9). All data were recorded. Immediately after surgery, all patients received the replacement levothyroxine for

Figure 6



Photomicrograph showing complex papillary architecture with vascularized connective tissue cores covered with malignant columnar epithelial cells. H and E, ×100.

Figure 7

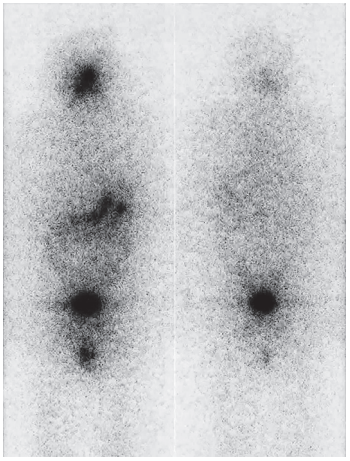


Photomicrograph showing crowded tall columnar epithelium with occasional grooving with large calcified psammoma body at the tip of papillae. H and E, ×400.

Figure 8

Total body scan shows residual tumor (arrow).

Figure 9



Total body scan shows complete ablation of the tumor.

2 weeks; levothyroxine was ceased to prepare the patients for RAI scans, which were taken at 1 month postoperatively. Patients with positive residual tissue were submitted to RAI ablation when their thyroid stimulating hormone level reached above 25 mu/l. Completion radical surgery was performed when there was relapse after RAI ablation in the form of palpable LNs and elevation of serum TG. In such cases, patients received suppressive levothyroxine to keep the thyroid stimulating hormone below 0.1 mu/l.

Statistical analysis

All data were recorded and collected for statistical analysis. The statistical program (SPSS, Chicago, Illinois, USA) for windows, version 13, was used for data entry and analysis. Qualitative data were presented by frequency distribution. The χ^2-test was used to compare between two or more proportions. The lowest accepted level of significance was 0.05.

Table 1 The incidence of postoperative complications among the three groups

Postoperative complications	*N*	Group I (*N* = 34) [*N* (%)]	Group II (*N* = 52) [*N* (%)]	Group III (*N* = 56)
		TT	TT + pCND	TT + CND + LND
Reactionary haemorrhage	5 (3.5)	2 (5.8)	2 (3.8)	1 (1.7)
RLNI				
Unilateral	18 (12.6)	1 (2.9)	7 (13.4)	10 (17.8)
Temporary	13 (9.1)	1 (2.9)	6 (11.5)	6 (10.7)
Permanent	5 (3.5)	0 (0)	1 (1.9)	4 (7.1)
Bilateral	6 (4.2)	0 (0)	3 (5.7)	3 (5.3)
Temporary	4 (2.8)	0 (0)	2 (3.8)	2 (3.5)
Permanent	2 (1.4)	0 (0)	1 (1.9)	1 (1.7)
Total	24 (16.9)	1 (2.9)	10 (19.2)	13 (23.2)
Hypoparathyroidism				
Temporary	26 (18.3)	1 (2.9)	14 (26.9)	11 (19.6)
Permanent	5 (3.5)	1 (2.9)	2 (3.8)	2 (3.5)
Total	31 (21.8)	2 (5.8)	16 (30.7)	13 (23.2)
Other complications				
Accessory nerve injury	7 (4.9)	0 (0)	0 (0)	7 (12.5)
Chyle leak	2 (1.4)	0 (0)	0 (0)	2 (3.5)
Neck stiffness	3 (2.1)	0 (0)	0 (0)	3 (5.3)
Torticollis	1 (0.7)	0 (0)	0 (0)	1 (1.7)
Persistent hypoesthesia	12 (8.4)	0 (0)	0 (0)	12 (21.4)
Total	25 (17.6)	0 (0)	0 (0)	25 (44.6)

LND, lateral neck dissection; pCND, prophylactic central neck dissection; TT, total thyroidectomy.

Results

Of 148 patients with PTC who fulfilled the inclusion criteria, six patients were excluded (one patient had mixed follicular and papillary carcinoma, two patients refused the second operation of completion neck dissection, and three patients were lost to follow-up) and only 142 patients completed this study. They were 56 male and 86 female patients (male : female = 2 : 3) and their ages ranged from 12 to 53 years, with average age at initial treatment of 32.5 ± 18.25 years.

Group I included 34 patients with hidden PTC in MNG. They underwent TT.

Group II included 52 patients of PTC diagnosed preoperatively with cN0. They underwent TT plus pCND.

Group III included 56 patients with PTC with cervical LN metastasis. They underwent TT + CND + LND.

Postoperative complications

Regarding the immediate postoperative complications, reactionary hemorrhage occurred in five patients (two in group I, two in group II, and one in group III). These patients were re-examined in the operating room and the bleeding sites were identified and managed. All five patients recovered well. There was no statistically significant difference among the three groups regarding hemorrhage (Tables 1 and 2).

RLNI occurred in 24 (16.9%) patients (18 unilateral and six bilateral): 17 were temporary (11.97%) and seven were permanent (4.92%). There was a statistically significantly higher risk of RLNI in groups II and III than in group I, but no statistically significant difference between groups II and III in the incidence of such injury (Table 2). The condition of 13 of the 18 patients with unilateral RLNI improved spontaneously within 3 months, whereas in the remaining five patients hoarseness of voice persisted. With respect

Table 2 The statistical analysis of the incidence of the postoperative complications among the three groups

Complications	Group I vs. group II [*N* (%)]			Group I vs. group III [*N* (%)]			Group II vs. group III [*N* (%)]		
	N = 34	*N* = 52	*P* value	*N* = 34	*N* = 62	*P* value	*N* = 52	*N* = 62	*P* value
Reactionary hage	2 (5.8)	2 (3.8)	0.66	2 (5.8)	1 (1.7)	0.29	2 (3.8)	1 (1.7)	0.51
RLNI	1 (2.9)	10 (19.2)	0.04	1 (2.9)	13 (23.2)	0.02	10 (19.2)	13 (23.2)	0.78
Hypoparathyroidism	2 (11.6)	16 (30.7)	0.01	2 (11.6)	13 (23.2)	0.03	16 (30.7)	13 (23.2)	0.50
Other complications	0	0	–	0	25 (44.6)	0.000	0 (0)	25 (44.6)	0.000

RLNI, recurrent laryngeal nerve injury.

to the bilateral injury four patients showed marked improvement with time but the remaining two cases showed permanent aphonia over the follow-up period.

There were 31 (21.8%) reported cases of hypoparathyroidism: 26 (18.3%) temporary and five (3.5%) permanent. There was a statistically significantly increased incidence of hypoparathyroidism in groups II and III over group I. There was no statistically significant difference between groups II and III regarding this complication (Table 2).

Other complications such as accessory nerve injury, chyle leak, neck stiffness, torticollis, and persistent hypoesthesia were reported only in group III.

Postoperative follow-up

Group I

Histopathology revealed hidden PTC in MNG. There were 18 patients (52.9%) with PTC microcarcinoma (<1 cm) and 16 patients (47.1%) with PTC macrocarcinoma (>1 cm). The postoperative RAI scan showed positive residual tumor in only three patients (8.8%). They were submitted to RAI ablation, which effectively eradicated the residual tumor in all three patients (100%), and RAI scan after 1 year showed full tumor ablation. None of the patients in group I underwent a second operation.

Group II

Histopathology confirmed the diagnosis of PTC and revealed LN deposits in 18 patients (34.6%). The number of cases of LN metastasis is shown in Table 3. RAI scan after 1 month showed only eight patients (15.3%) with lateral LN involvement. These patients were submitted to RAI ablation: six patients (75%) showed marked response with complete disappearance of the residual tumor at the RAI scan after 1 year; two patients (25%) showed relapse and LNs became palpable with elevated serum TG and they were candidates for completion LND performed at 1-year interval. The histopathology showed involvement of 5/18 and 3/21 of the LNs resected in the specimen, respectively. The RAI scan and neck CT 1 month later showed no residual tumor.

Table 3 Shows the number of lymph nodes involvement in group II and III

Number of LNs	Group II (%)	Group III (%)
First operation	*N* = 52	*N* = 56
Negative cases	34 (65.4)	0 (0.0)
Positive cases	18 (34.6)	56 (100)
1–3 + LNs	12	2
4–5 + LNs	6	15
6–7 + LNs	0	27
>7 + LNs	0	12
Second operation	*N* = 2	*N* = 3
Negative cases	0 (0)	0 (0)
Positive cases	2 (100)	3 (100)
1–3 + LNs	1	1
4–5 + LNs	1	1
6–7 + LNs	0	1
>7 + LNs	0	0

LN, lymph node.

Group III

In group II, histopathology revealed PTC with LN metastasis in all cases. The number and pattern of LN involvement are shown in Table 3. RAI scan after 1 month showed tumor metastasis to the contralateral LNs in 16 cases (28.5%). They received RAI ablation. Thirteen of them (81.2%) showed complete tumor ablation but the other three cases (18.7%) showed progressive disease that necessitated completion contralateral neck dissection. The histopathology reported metastasis in 3/19, 5/22, and 6/24 of the resected LNs in the specimen, respectively. RAI scan at 1 month postoperatively was tumor-free.

All patients were followed up for at least 3 years. The follow-up period ranged from 3 to 5.5 years with an average of 4.1 years. We had no perioperative mortality in the three groups and all patients at the end of the follow-up period were tumor-free – that is, the 3-year cure rate was 100%.

Discussion

There is a big debate around the best way to manage cases of PTC. Treatment should be individually tailored to each case, usually according to the patient's preference and/or surgeon's experience. Radical neck dissection is associated with complications, even with meticulous surgery in the best hands.

In this study, the overall incidence of postoperative complications such as RLNI and hypoparathyroidism were comparable to other studies [4,6,8,13,14,17].

It was not surprising that we found that the nodal recurrence was much higher in group III than in groups I and II, because patients of group III already had palpable LNs and certainly more LN involvement than those in groups I and II and consequently a higher incidence of nodal recurrence.

In cN0 patients, the addition of pCND to TT was associated with much higher incidence of postoperative complications such as RLNI and hypoparathyroidism compared with those with TT alone. These complications outweigh the benefits

of the surgical radicality because most of these complications are incurable and handicapping. The treatment appears to be more hazardous than the disease and this remind us of the dictum 'Let punishment fit the crime'.

RAI ablation gave very good results (100% in group I, 75% in group II, and 81% in group III), which are comparable to the surgical radicality; both groups I and II had cN0; patients of group I did not undergo neck dissection but only RAI ablation in patients with positive RAI scans; in contrast, patients of group II underwent pCND, and in most of them histopathology showed no LN metastasis. Both groups achieved the same final excellent results at the end of the follow-up period but many patients of group II paid the price of surgical radicality.

In our study, the addition of LDN to TT + CND did not increase the risk of RLNI or hypoparathyroidism. This disagrees with the Roh *et al*. [8] who stated that the extension of nodal dissection to the lateral cervical compartment in addition to the central compartment increases the vascular compromise in the dissected central neck and the parathyroid glands, which causes a high rate of hypoparathyroidism during the early postoperative weeks. However, we agree with many studies [18-20] that LND added many other complications not recorded in TT plus CND such as accessory nerve injury, chyle leak, neck stiffness and neck deformity.

Again, RAI ablation achieved a very good cure rate in patients with subclinical LN metastasis from PTC, which is supported by the results of many studies [1,21,22]. This should be taken into consideration before rushing into redo surgery.

Administration of RAI ablation before resorting to radical surgery achieved a highly accepted cure rate and eradication of residual tumor cells, and even in those who relapsed after RAI therapy delay of completion surgery did not disprove the prognosis or hinder cure.

Conclusion

The highly significant increase in the postoperative complications associated with pCND without significant improve in prognosis may preclude its use.

RAI ablation succeeds in eradicating residual subclinical tumor deposits in a good percentage of patients and should be attempted before resorting to completion radical surgery. Neck re-exploration for completion or redo surgery should be reserved only for patients who develop relapse with palpable disease and elevated TG.

Acknowledgements

Conflicts of interest

None declared.

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