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Inferior Parathyroid Gland Preservation In Situ during Central Neck Dissection for Thyroid Papillary Carcinoma

Lei Xie, Jianbiao Wang and Liang Zhou

Additional information is available at the end of the chapter

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Abstract

Hypoparathyroidism is the most common and a potentially serious complication of thyroid surgery; therefore, it becomes very important for thyroid surgeons to preserve the parathyroid glands in situ during the thyroid operation. Because of the application of “meticulous capsular dissection,” the problem about how to preserve the parathyroid gland in thyroidectomy has become minor. Because inferior parathyroid glands enjoy a more variable position in the adult neck and they are located in the area of central neck lymph node dissection, how to preserve them in situ during central neck dissection is regarded as a major problem. To solve it, a new operation concept, “a layer of thymus-blood vessel-inferior parathyroid gland,” is mainly introduced in this chapter.

Keywords: inferior parathyroid gland, thyroid papillary carcinoma, thyroidectomy, central neck dissection, hypoparathyroidism

1. Introduction

Prof. Richard Owen firstly identified the parathyroid gland in an Indian rhinoceros in 1850 [1]. Ivar V. Sandström also found this gland in humans and firstly named it as “glandulae parathyroidae” in 1887 [1]. Because Gley observed that animals whose parathyroid glands were removed subsequently developed tetany in the 1890s, the parathyroid gland and their function became widely appreciated [2]. After that, surgeons understood that the parathyroid glands were vital organs to be treated cautiously during thyroidectomy.

Hypoparathyroidism is the most common and a potentially serious complication of thyroid surgery, which can lead to metabolic and physiologic disturbance, prolonged hospitalization and medical supplementation [3–6]. In general, the prevalence of transient and permanent hypoparathyroidism is reported to range from 14–60% and 4–11%, respectively [7]. Total thyroidectomy (TT) with central neck dissection (CND) significantly increases the rate of transient and permanent hypoparathyroidism in comparison with total thyroidectomy.

In this chapter, a new operation concept, “a layer of thymus-blood vessel-inferior parathyroid gland (TBP),” is mainly introduced to preserve the inferior parathyroid gland (IPTG) *in situ* during CND for papillary thyroid carcinoma (PTC).

2. Classification of the IPTG

1. According to the location relationship between the IPTG and thymus, four groups were classified by J. Grisoli in 1979 [8]. Group 1: the parathyroid gland in the usual classic position, in contact with the terminal branches of the inferior thyroid artery, behind or below the inferior poles of the thyroid lobes (65% of cases); Group 2: the parathyroid gland in a thyrothymic position, more or less equidistant from the inferior thyroid lobe and the thymic cornu (17.5% of cases); Group 3: the superior thymic parathyroid gland, situated in the cornua of the thymus or their immediate vicinity (15.5% of cases); Group 4: intrathymic parathyroid (2% of cases) (**Figure 1**).
2. Based on the relationship between the parathyroid gland and the thyroid gland as well as the color change in the parathyroid glands after separation from the thyroid, different categories of parathyroid gland are as follows [9]:

Type A, no dependency on the thyroid, and with adequate blood supply and no color change after thyroidectomy; B1, partial blood supply from the thyroid but retains adequate blood supply after removal of the thyroid; B2, partial blood supply from the thyroid and becomes devascularized after the removal of the thyroid; B3, blood supply mostly from the thyroid; difficult to preserve *in situ* and C, blood supply completely dependent on the thyroid. The classifications were used to decide between *in situ* preservation and auto-transplantation (**Figure 2**).

3. According to the positional relationship between IPTG and the thyroid gland, JQ Zhu classified IPTG into two types [10], namely type A (close contact) and type B (non-close contact). Type A includes A1 (planar attachment), A2 (embedded attachment), and A3 (intra-thyroid); type B includes B1 (around thyroid), B2 (intra-thymus), and B3 (blood supply from thymus or mediastinum) (**Figures 3 and 4**)

During TT and CND, IPTG typically undergoes “dissection” twice. At first instance, the IPTG is exposed and preserved by meticulous capsular dissection during thyroid lobectomy; at second instance, the IPTG is identified and preserved *in situ* while the central neck fibro-fatty tissue with lymph nodes is removed. The first instance is the premise and basis of the second instance, because *in situ* preservation of IPTG in CND becomes impossible if IPTG has been devascularized or resected during thyroid lobectomy. The identification and preservation of IPTG in the first instance of dissection facilitates the preservation of the IPTG *in situ* in CND

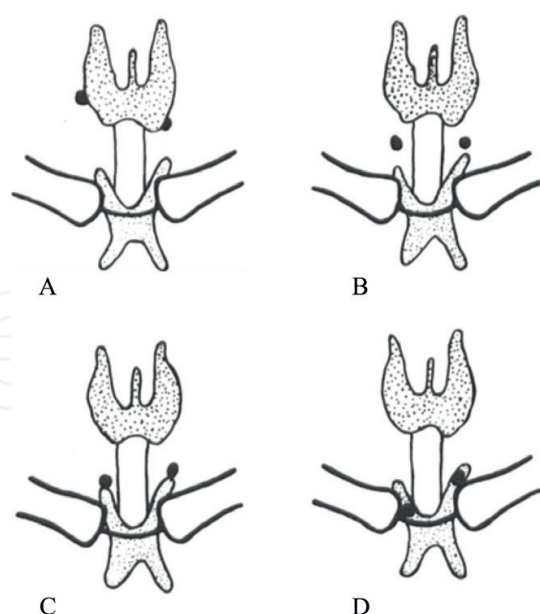


Figure 1. Position of inferior parathyroid gland (by J Grisoli). (A) Usual position; (B) thyro-thymic position; (C) superior thymic position; (D) intrathyroidic.

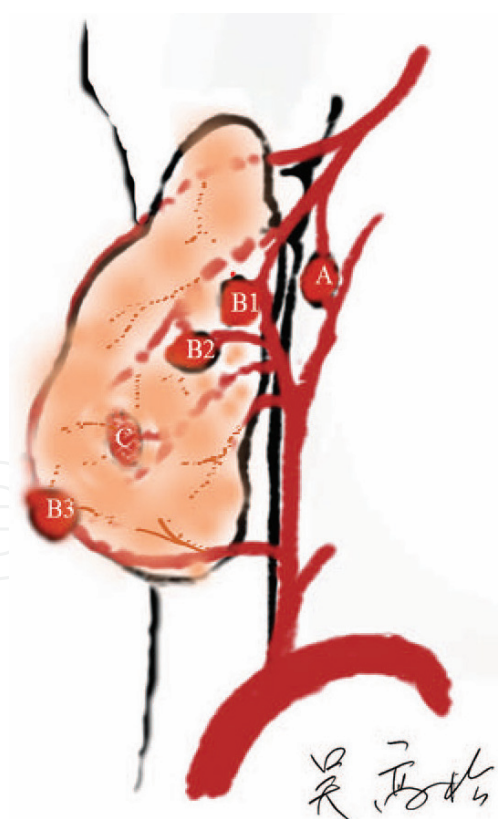


Figure 2. The three main types of parathyroid gland (by GS Wu). Type A, nonattachment to the thyroid and has adequate blood supply; type B1, attached lightly to the thyroid and retains adequate blood supply after thyroid removal; type B2, attached tightly to the thyroid and changes color easily, in which case, the distal tissue is cut in half for autograft; type B3, blood supply is derived mostly from the thyroid gland and may be treated as either type B2 or type C according to the surgeon's skill; type C, under cover of the thyroid capsule and can only be preserved by total auto-transplantation.

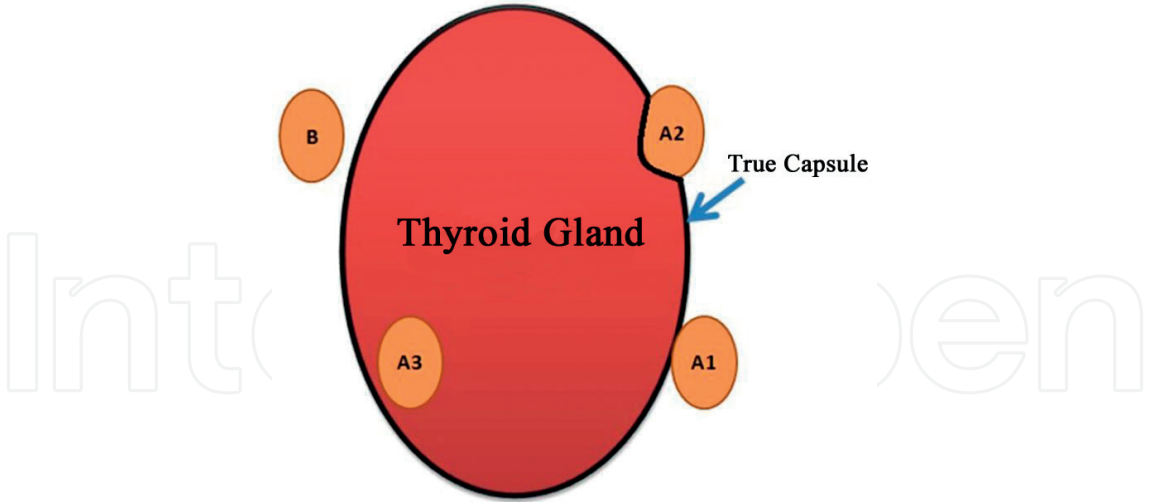


Figure 3. Classification of inferior parathyroid gland (by JQ Zhu). Type A (close contact) includes A1 (planar attachment), A2 (embedded attachment) and A3 (intra-thyroid); type B (non-close contact) includes B1 (around thyroid), B2 (intra-thymus) and B3 (blood supply from thymus or mediastinum).

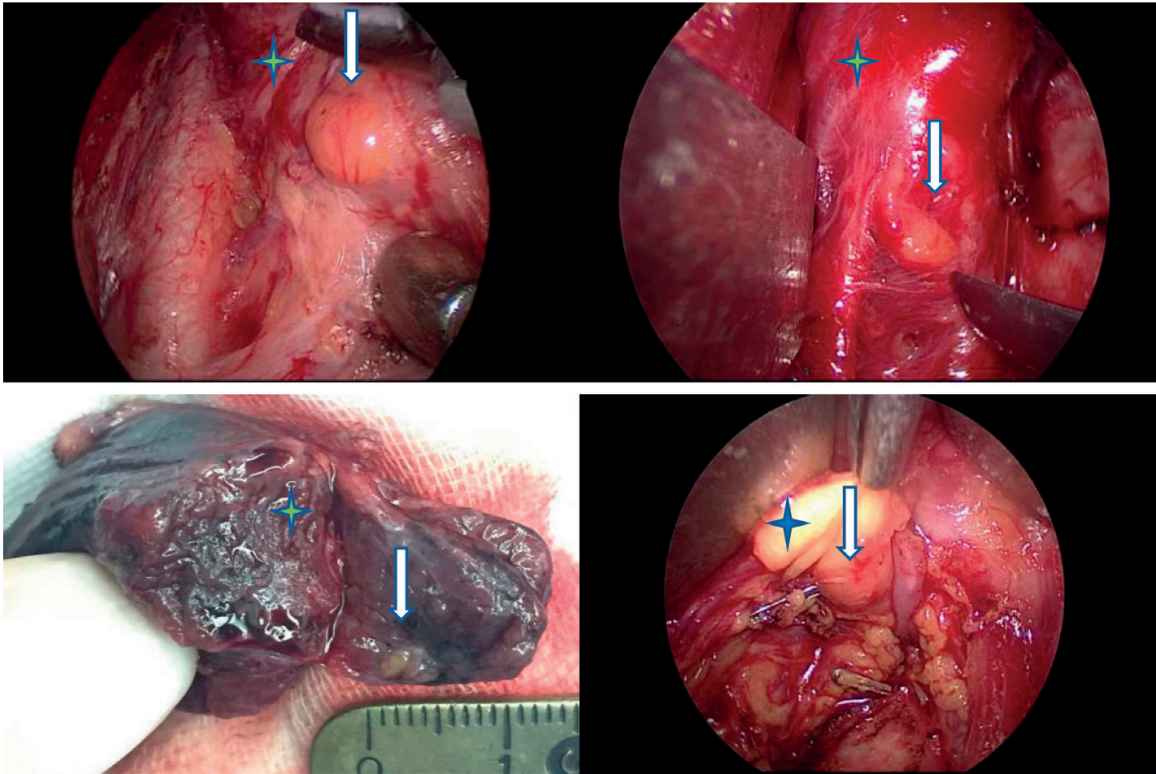


Figure 4. Intraoperative views of inferior parathyroid gland according to Zhu's classification. Type A1 (left upper), A2 (right upper), A3 (left down) and B2 (right down) are included. White arrow: Inferior parathyroid gland; green star: thyroid; blue star: thymus.

(in the second instance of dissection). Therefore, the inferior parathyroid gland can be actually classified into exposure type and unexposure type according to whether the IPTG is identified and preserved during the thyroidectomy (at the first instance). As to the unexposure type, the

in situ preservation of the IPTG in CND could be very difficult. This can be attributed to the fact that IPTGs assume a more variable position in the adult neck, thus making their detection difficult. Moreover, IPTGs are located in the area of central neck lymph node dissection and have to be distinguished from lymph nodes, fatty tissue, and so on.

3. Two operation concepts during TT and CND

3.1. “Meticulous capsular dissection” in thyroid lobectomy

How to preserve the IPTG during the thyroid lobectomy, a concept “meticulous capsular dissection” was put forward by NW Thompson in 1973 [11], and further explanation was given by Attie and other scholars [12]. The protection of the parathyroid glands and to the recurrent laryngeal nerve is achieved by using capsular dissection, hugging the gland and dividing the tertiary branches (i.e., the third order of division) of the vessels while dissecting the parathyroid glands with their vascular pedicles free from the thyroid surface, with minimal exposure of the recurrent laryngeal nerve and disturbance of its blood supply (**Figure 5**).

3.2. “A layer of thymus, blood vessels and inferior parathyroid gland” in CND

Because of the application of “meticulous capsular dissection,” how to preserve the parathyroid gland in thyroidectomy has become a minor problem. Because IPTGs enjoy a more variable position in the adult neck and locate in the area of central neck lymph node dissection, how to preserve IPTG during CND is a major problem.

Some methods are recommended to identify and preserve the IPTG [13, 14]. For example, IPTG is superficial to RLN coronal plane and does not dissect the triangular region in order to protect laterally based blood supply of the IPTG (**Figure 6**). However, actually it is not easy to practice.

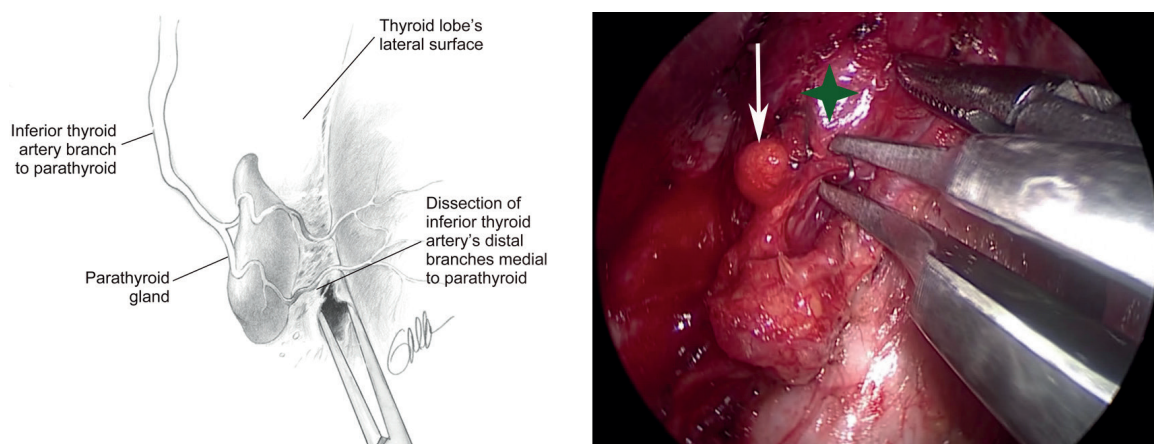


Figure 5. “Meticulous capsular dissection.” The distal branches of the inferior thyroid artery medial to the parathyroid at the level of the thyroid capsule, are identified and controlled. Attie’s drawing (left); intraoperative view (right); white arrow: Inferior parathyroid gland; green star: thyroid.

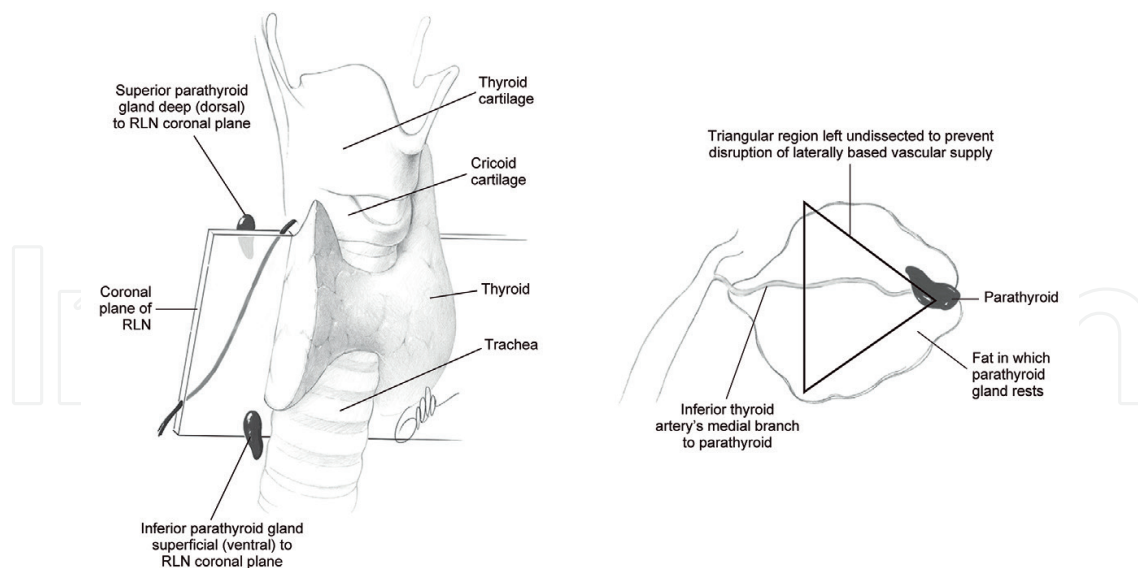


Figure 6. Some methods recommended to identify and preserve the inferior parathyroid gland (IPTG). IPTG superficial to recurrent laryngeal nerve coronal plane (left); triangular region left undissected to prevent disruption of laterally based vascular supply of IPTG (right).

3.2.1. The meanings of “a layer of TBP”

To solve this main problem, “a layer of TBP” was firstly put forward by Lei Xie in 2014 [15]. This new concept has two meanings: (1) the thymus, IPTG and blood vessels connecting them are located in one layer; (2) the layer covers the common carotid artery (innominate artery), the trachea, and the area of paratracheal lymph nodes between them (**Figure 7**).

3.2.2. Theoretical basis of “a layer of TBP”

Embryologically, the IPTGs are derived from the dorsal part of the third pharyngeal pouch, and the thymus arises from the ventral part of the third pharyngeal pouch. As the IPTGs and the thymus migrate together toward the mediastinum, they eventually separate. In most cases, the inferior parathyroid glands become localized near the inferior poles of the thyroid, and the thymus continues to migrate toward the mediastinum (**Figure 8**) [16]. In an anatomical study of the adult thymus, Di Marino et al. [8] described the true sheath of the thymus and its relative structures in detail. In the cervical region, adhesion between the thymic sheaths and thyroid is via the thyrothymic ligaments, in which the superior vascular pedicle of the thymus is contained. The superior vascular pedicle mainly includes the superior thymic artery arising from the ITA as well as the inferior and median thyroid veins, which also supply blood to the IPTG. In addition, from the midline cervicothoracic sagittal section, the thymus, blood vessels within the thyrothymic ligament and the posterior layer of thyroid sheath are in the same plane (**Figure 9**), which could be regarded as an anatomical basis for the TBP layer.

3.2.3. How to practice “a layer of TBP” during CND

According to the ATA guidelines, bilateral CND involves removal of the prelaryngeal, pretracheal, and both the right and left paratracheal nodal basins; and unilateral CND involves

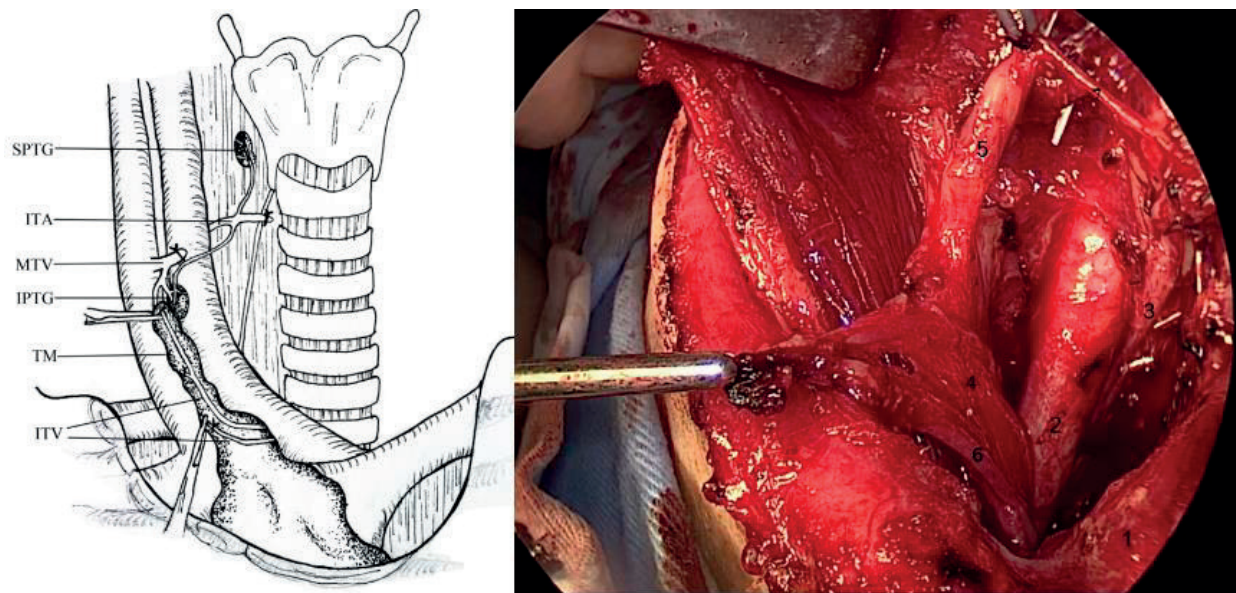


Figure 7. “A layer of thymus-blood vessel-inferior parathyroid gland (TBP).” The thymus, the inferior parathyroid gland, and the blood vessels connecting them are located in one layer. This layer covers the common carotid artery (innominate artery), the trachea, and the area of paratracheal lymph nodes between them. Diagram of this concept (left); intraoperative views of “a TBP layer” preserved after central neck dissection. SPTG, superior parathyroid gland; ITA, inferior thyroid artery; MTV, middle thyroid vein; IPTG, inferior parathyroid gland; TM, thymus; ITV, inferior thyroid vein; 1, trachea; 2, common carotid artery; 3, recurrent laryngeal nerve; 4, Thymus; 5, inferior parathyroid gland; 6, branches of inferior thyroid vein; 7, a branch of inferior thyroid artery.

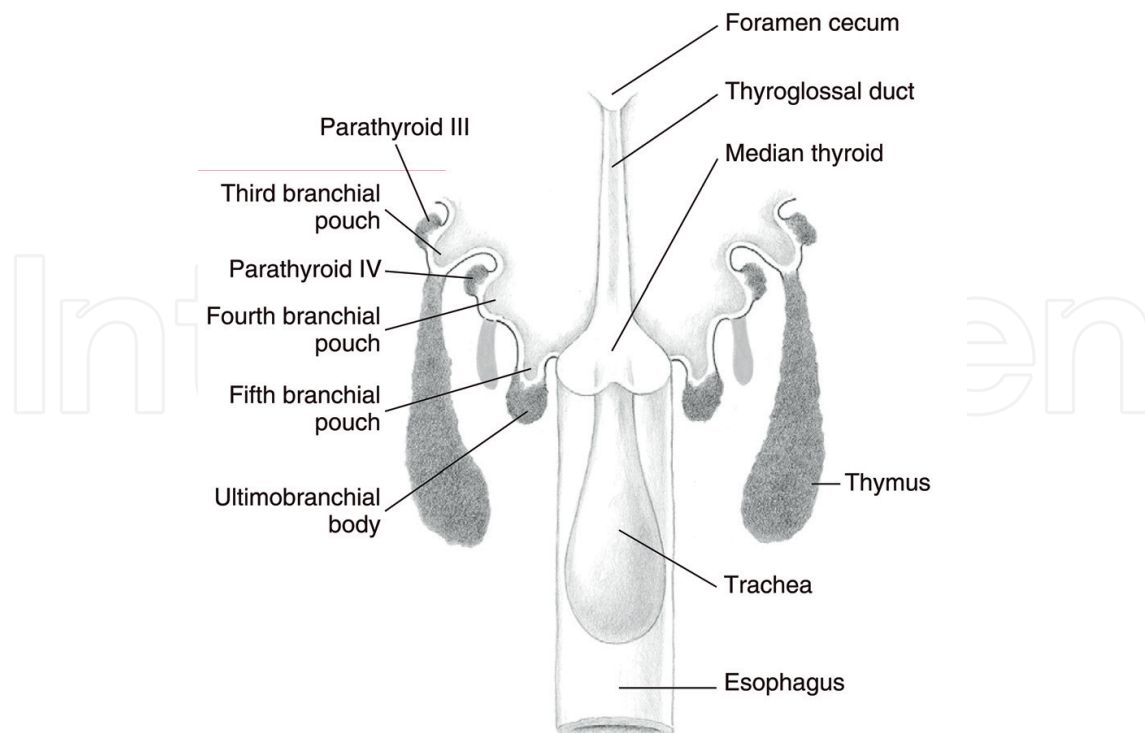


Figure 8. Schematic view of primitive pharynx of an 8- to 10-mm embryo. The inferior parathyroid glands are derived from the dorsal part of the third pharyngeal pouch, and the thymus arises from the ventral part of the third pharyngeal pouch.

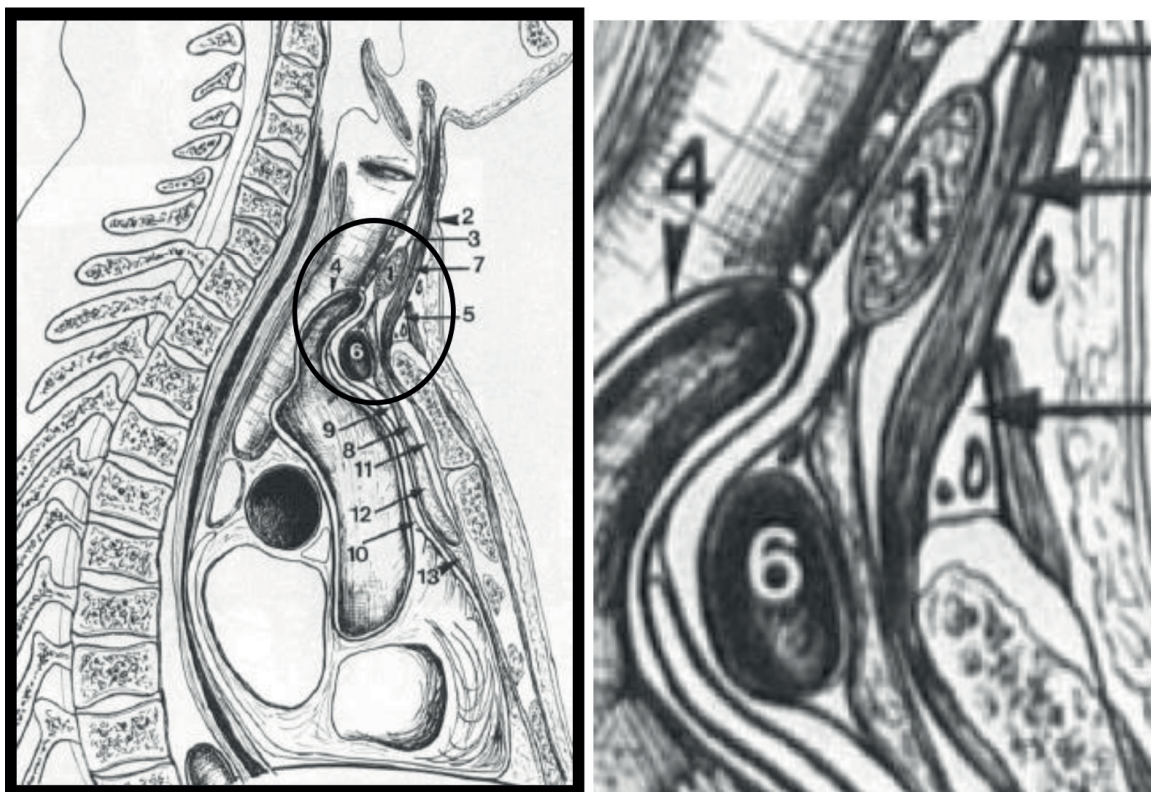


Figure 9. Midline cervicothoracic sagittal section. The thymus, blood vessels within the thyrothymic ligament and the posterior layer of thyroid sheath are in the same plane, which could be regarded as an anatomic basis of the “TBP layer”. 1, thyroid isthmus; 2, superficial layer of cervical fascia; 3, pretracheal cervical fascia; 4, brachiocephalic trunk; 5, pretracheal space; 6, left brachiocephalic vein; 7, sternothyroid muscle; 8, anterior wall of thymic sheath; 9, thyropericardial layer; 10, serous pericardium; 11, anterior interpleural ligament; 12, thymus; 13, subthymic fatty tissue.

removal of the prelaryngeal, pretracheal and one paratracheal nodal basins. In addition, “a layer of TBP” is mainly applied in lateral margin dissection of paratracheal nodal basin.

During the paratracheal lymph node dissection, the medial dissection margin is defined using electrocautery along the tracheal lateral wall from Berry’s ligament to the brachiocephalic vessels. Lateral margin dissection aims to identify and preserve the TBP layer first (**Figure 10**) rather than directly exposing the common carotid artery. The thymus, inferior thyroid blood vessels and their branch stumps are regarded as reference points, with the fibrofatty tissue removed by electrocautery. During this process, the TBP layer is slowly identified and lifted upwards; the common carotid artery (innominate artery) beneath the layer is exposed. The medial border of the common carotid artery is dissected down to the prevertebral fascia. The TBP layer and the common carotid artery are retracted laterally, whereas the trachea is retracted medially, exposing the paratracheal compartment. The recurrent laryngeal nerve (RLN) is freed from the fibrofatty tissue and retracted laterally. The envelope of level VI lymph nodes is then retracted medially and excised en bloc [17].

The relationship between the TBP layer, inferior thyroid artery (ITA) and RLN can be further clarified. Because the TBP layer is superficial to the common carotid artery, whereas the ITA

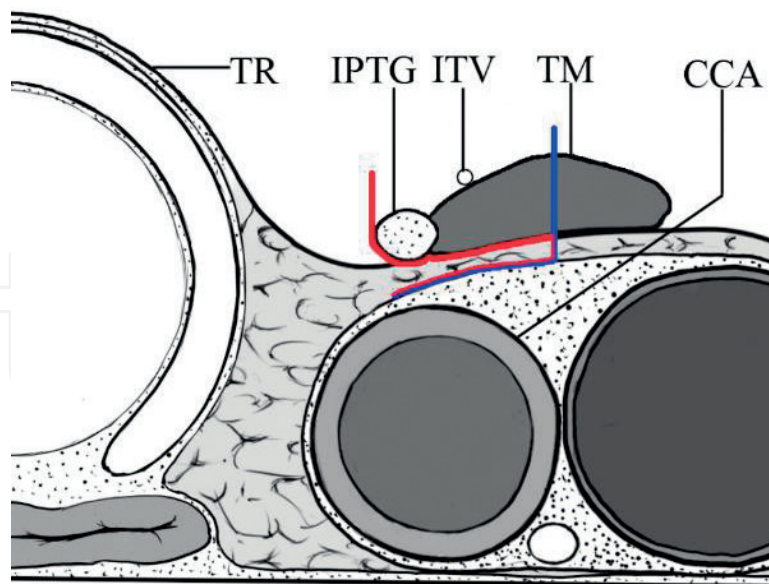


Figure 10. Lateral margin dissection approaches in paratracheal lymph node dissection. The blue line shows the traditional approach to directly expose the common carotid artery (CCA), which could lead to the inferior parathyroid gland injury due to the destruction of the TBP layer. The blue line shows the new dissection approach based on the TBP layer (layer of thymus-blood vessel-inferior parathyroid gland) concept. The thymus (TM), inferior thyroid blood vessels and inferior parathyroid gland (IPTG) are lifted upwards and laterally, exposing the CCA (innominate artery) underneath. TR, trachea; ITV, inferior thyroid vein.

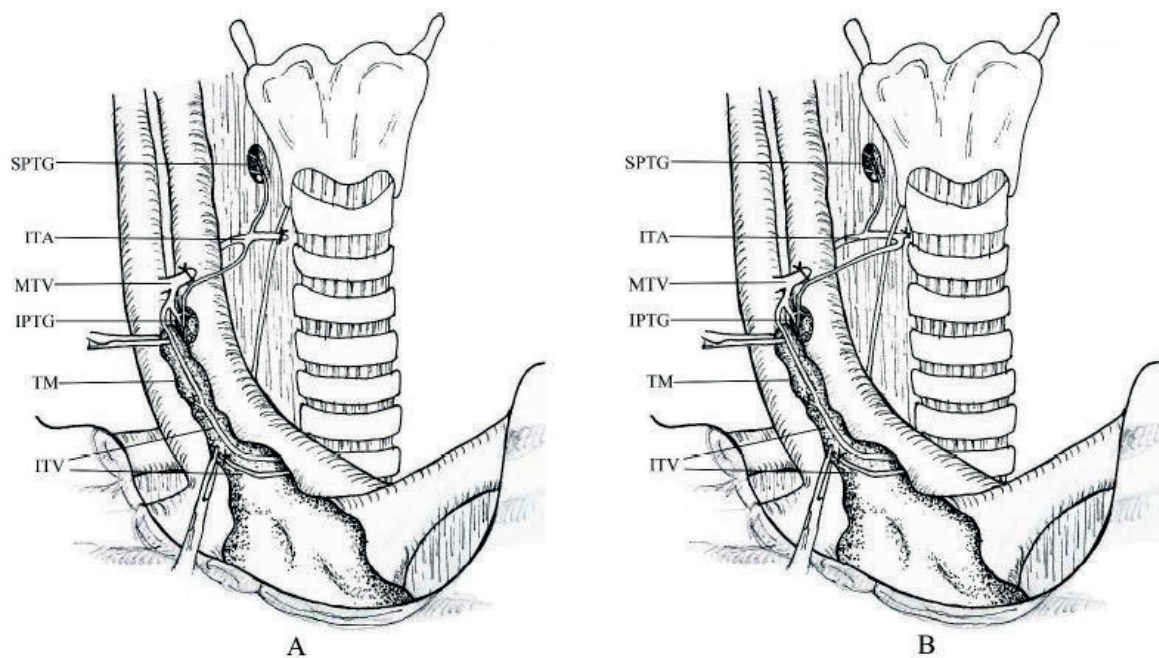


Figure 11. The relationship between the TBP layer, inferior thyroid artery (ITA) and recurrent laryngeal nerve (RLN). A is ITA branches lateral to RLN; B is ITA branches medial to RLN. MTV, middle thyroid vein; IPTG, inferior parathyroid gland; TM, thymus; ITV, inferior thyroid vein. Red circle means that the dissection in this region (between the cricoid cartilage and ITA level) should be emphasized, especially when the concept of “a layer of TBP” is performed.

enters the central neck compartment posterior to the carotid sheath, branches of the ITA need to traverse paratracheal fibrofatty tissue anteriorly to the TBP layer. In general, these branches of the ITA abut against the carotid artery medially and run into the TBP layer; therefore, the TBP layer, carotid artery and ITA branches can easily be retracted laterally, allowing en bloc excision of the paratracheal fibrofatty tissue (**Figure 11A**). The alternative situation is that the ITA branches are not very close to the carotid artery, and the RLN traverses between them (**Figure 11B**). For completeness of dissection and RLN preservation, it is suggested that the paratracheal dissection should be divided into two parts according to the level of the ITA: a dissection cranial to the ITA (between the cricoid cartilage and ITA level) and one caudal to the ITA (between the innominate artery and ITA level).

4. Clinical application results of “a layer of TBP”

A retrospective chart review was authorized and drawn from all 487 patients with PTC who underwent TT with ipsilateral or bilateral CND or plus lateral neck dissection between January 1, 2012 and December 31, 2014 [15]. The study group consisted of 181 patients with using the new surgical concept “a layer of TBP,” from January 2014 to December 2014, whereas the control group included 306 sex- and age-matched patients who underwent conventional method from January 2012 to December 2013. There were no significant differences between the groups in tumor size, multifocality, extrathyroidal extension, and number of harvested and metastatic central lymph nodes. The rate of inferior parathyroid gland preservation in situ was significantly improved from 37.9 to 76.3% on the left side ($P < 0.001$), and from 52.0 to 77.9% on the right side ($P < 0.001$), in the study group compared with the control group (**Figure 12**). The incidence of transient hypoparathyroidism decreased

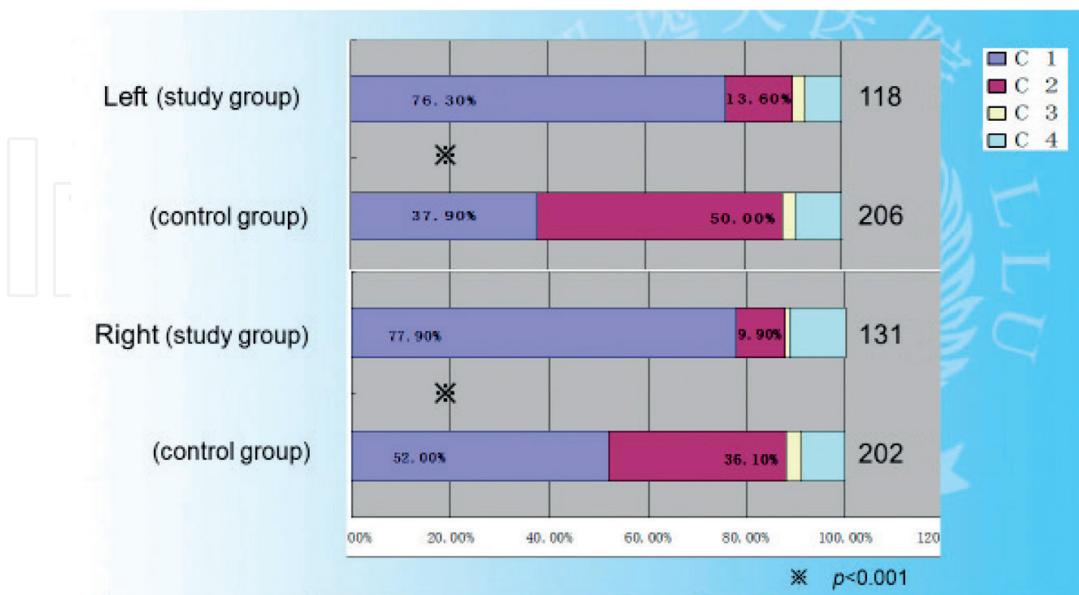


Figure 12. The status of inferior parathyroid glands after TT and CND. It was classified into four categories: C1, preserved in situ (vascularized); C2, autotransplanted (devascularized); C3, removed owing to infiltration by the tumor; and C4, not identified. The rate of inferior parathyroid gland preservation in situ was significantly improved on both sides ($P < 0.001$) in the study group compared with the control group.

Variables	Control group (n = 306)	Study group (n = 181)	P
No. retrieved lymph nodes	12.74 ± 6.16 (1-30)	13.83 ± 7.07 (3-43)	0.186
No. metastatic lymph nodes	1.94 ± 2.83 (0-14)	1.95 ± 2.75 (0-13)	0.826
No. retrieved lymph nodes in unilateral CND	11.08 ± 5.71	11.33 ± 5.89	0.756
No. metastatic lymph nodes in unilateral CND	1.52 ± 2.20	1.67 ± 2.28	0.393
No. retrieved lymph nodes in bilateral CND	16.04 ± 5.70	18.10 ± 7.00	0.036
No. metastatic lymph nodes in bilateral CND	2.79 ± 3.66	2.41 ± 3.37	0.342

Table 1. The excised lymph nodes in the unilateral and bilateral central neck dissections.

significantly from 35.0 to 7.2% ($P < 0.001$). In addition, the excised lymph nodes in the unilateral and bilateral CNDs were compared between the groups. The result showed that significantly more lymph nodes were removed in bilateral CND in the study group than in the control group; however, there was no difference in lymph nodes in unilateral CND between the groups (**Table 1**). Therefore, applying the proposed surgical concept improved the rate of inferior parathyroid gland preservation in situ and decreased the incidence of transient postoperative hypoparathyroidism, along with ensuring the completeness of lymph node dissection.

1. Some special considerations relative to “a layer of TBP.”
2. Although the success rate of IPTG preservation in situ can be considerably improved using the concept “a layer of TBP” in CND, it is important that the surgeons have the abilities to identify the parathyroid glands and evaluate their blood supply. Some techniques such as no black stain in parathyroid gland by carbon nanoparticles [18] and the intraoperative near-infrared autofluorescence imaging of parathyroid gland [19] are recommended, but we suggest that it is necessary to clinically train the identification of the parathyroid gland by the naked eyes.
3. Parathyroid autotransplantation has been considered a salvage method to avoid permanent hypoparathyroidism. Although the incidence of IPTG preservation in situ was increased greatly after using the concept of “a TBP layer,” still about 10% of IPTGs were removed inadvertently or devascularized during thyroid surgery. Therefore, the technique of parathyroid autotransplantation should be mastered by thyroid surgeons.
4. The IPTG and its blood supply are frequently involved in the dorsal extrathyroidal invasion of primary tumor or extranodal metastasis of paratracheal lymph nodes; therefore, the preservation of IPTG in situ is unsuitable, and en bloc resection of the thyroid and central neck lymph nodes is recommended. In addition, although the paratracheal area is full of excessive fatty tissue in obese patients, it is also possible to identify and build up “a layer of TBP” by clinical training.
5. Preservation of the IPTG in situ using the approach “a layer of TBP” requires meticulous manipulation during the operation. The requirements for meticulous manipulation include good operation vision, wide operation space, antagonistic traction (the first assistant’s), and

refined operational instruments. In this study, TT and CND were mostly performed under direct vision with the operator's headlight (mPack LL, HEINE Optometrik, Germany), and the first assistant's coordinated traction was emphasized; in addition, the use of a high-frequency electric knife with a needle-shaped head (Changzhou Yanling Electronic Equipment Co. Ltd., Jiangsu, China) and a small titanium ligating clip (Horizon; Weck Drive, Research Triangle Park, NC 27709, USA) are strongly recommended to preserve the parathyroid gland and its blood supply.

6. As mentioned earlier, when the RLN traverses between the ITA branches and the carotid artery, the paratracheal dissection can be divided into two parts according to the level of the ITA: a dissection cranial to the ITA (between the cricoid cartilage and ITA level) and one caudal to the ITA (between the innominate artery and ITA level), for completeness of dissection and RLN preservation (**Figure 11B**). Actually, the dissection between the cricoid cartilage and ITA level is a challenge because superior parathyroid gland and its blood supply from ITA and RLN are on this area. Although some surgeons declare that performing the dissection inferiorly from the trunk of ITA could achieve the equal completion of the dissection in safety [20, 21] because the metastatic lymph nodes are rarely found above the ITA trunk, the recurrence can be observed in this region between the cricoid cartilage and the ITA trunk. Therefore, the dissection in this region (between the cricoid cartilage and ITA level) should be emphasized, especially when the concept of "a layer of TBP" is performed. In addition, the usage of carbon nanoparticles, as a lymph tracer, can facilitate this procedure (not published).

5. Conclusion

The prevention of postoperative hypoparathyroidism entails several issues, including the concept of meticulous operation, the ability of parathyroid gland identification, the technique of parathyroid gland autotransplantation, and the principle of "the preservation of at least one vascularized parathyroid gland" [10, 22]. This chapter shows that the concept of "a layer of TBP" during CND can greatly improve the success rate of IPTG preservation in situ, thereby efficiently decreasing the incidence of temporary postoperative hypoparathyroidism, along with ensuring the completeness of lymph node dissection.

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Disclosure

The author declares no conflict of interest.

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