

Searching of Rational Volume Surgery in Cases of Locally-Invasive Differentiation Thyroid Cancer

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Abstract

Introduction: Surgical intervention is the preferred method for eradicating invasive thyroid carcinoma (TC), but the extent of resection is still controversial.

Materials and Methods: A total of 2593 patients were operated on for differentiated TC between 1973 and 2007. Wide extrathyroid TC spread (T4) was found in 464 (21.9%) cases of 2115 included in that research. We performed 256 combined thyroid and adjacent organ resections, 246 extended neck and mediastinum lymphadenectomy, 146 palliative operations. Transsternal approach have used during 31 operations. Totally were carried out 581 such operation at 441 patients. There were 19.2% males, 80.8% females (1:4.2). Average age made 57.7. Papillary TC was found in 62.9%, follicular - in 24.8% and medullar - in 12.3%. TC extension on muscles of neck and larynx (73.8%), RLN (37.9%), trachea (35.2%), pharynx and esophagus (23.8%), main neck or mediastinal vessels (21.9%) were found.

Results: Seven patients died after 435 operations. No lethal outcomes happened of 97 patients operated on into two stages. Unexpected RLN palsy, temporary HPT observed at 6.2%. Follow up results (median 9.6±0.9) were investigated in 84.9%. The 5-year survival rate made 81.9% and 10-year – 71.1% after combined and 86.7% and 70.6% - after extended operations. The local failure rate after organsparing “shaving” and “wedge” aerodigestive organ resections were not significantly worse than after of those circular resections (9.8% and 3.7%). But quality of life, 5 and 10 years survival rates after organ-sparing were much better (80.5% and 35.7% compared to 76.0% and 7.1%). 5-year follow-up results after palliative operations made 40.7% in papillary and follicular TC cases and 17.1% - in medullary carcinoma. 29.1% of differentiated TC patients were alive after palliative operations, adjuvant therapies during 10 and more years.

Conclusion: “Shave” excision, “wedge” resection procedures in cases of TC aerodigestive organ invasions have produced better results than “sleeve” resection for recovery and improving of patient’s quality life.

Introduction

Locally invasive thyroid carcinomas spread into nearby anatomic structures (T4a) and bilateral regional cervical and mediastinal lymph nodes (N1b). According to the literature, they occur in 8 to 25% of cases [1-6]. Surgical strategy in these cases is often complicated by general severity of the disease due to the advanced tumor stage and the age of the patient. Nevertheless, surgery remains the only means to maintain life-supporting functions in these patients, primarily – breathing [3, 7-9]. This makes the necessity of these surgeries obvious. The major question of surgical aid to the patient with a locally invasive thyroid cancer is the optimal volume and the optimal access, as well as comparison of the efficiency of “shaving”, limited lateral and circular resections of trachea, esophagus, and recurrent nerves.

Materials and Methods

Twenty five hundred and ninety three thyroid cancer (TC) patients have undergone surgery in St. Petersburg Center for Endocrine Oncology between 1973 and 2007. Local invasive TC papillary, follicular and medullar carcinomas of T4 grade were found in 464 cases (21.9%) out of 2115 patients included in this report; of them, 89 (19.2%) were males, and 375 (80.8%) were females. In the total TC group studied, the values were 11.9% and 88.1%, respectively. Male to female ratio made 1:4.2 (1:7.4 in the total group). Mean age was 57.7 ± 2.0 years (ranging from 17 to 83 years), much higher than in the total group (51.6 ± 0.17 years, P<0.05). More than a third (38%) of them were older than 60. In 217 cases, carcinomas were the only pathology, while in 257 other thyroid pathologies were found. Regional metastases were found in 281 (60.6%) cases.

Thus, differentiated TC in males and in older patients was more aggressive since these groups were more represented at the T4 grade (P<0.05).

Patients were examined using traditional laboratory and radioimmune tests, neck and mediastinal X-ray in two dimensions, with esophageal contrasting, computer tomography, and endoscopy in cases when penetration into esophagus and/or trachea were concerned.

Patients in whom an incomplete removal of papillary or follicular TC due to spreading into trachea, esophagus, arterial branches of neck and mediastinum, or to other organs (M1) were treated with radioactive iodine (106 cases), or by external irradiation (211 cases). Patients with a similar spread of medullar TC received external irradiation of the neck or chemotherapy.

In practice, we use the classification of surgical interventions proposed by B. Peterson in 1976 [10]. A combination surgery is called so when, in addition to the tumor-bearing organ, a neighboring affected organ is also removed either partially or completely. An extended surgical removal is the one in which lymphatic nodes are removed beyond typical recommendations. In terms of TC, it is more than just

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a unilateral dissection of the neck when groups 2,3,4,5 and 6 lymph nodes are removed. *Palliative* surgery is the one in which, after TC and lymph nodes removal, tumor still remains in organs' walls, neck lymph nodes, mediastinum, or when there are distant metastatic loci.

Results

This report includes analysis of the data from 581 surgeries performed in 441 patients with papillary, follicular, and medullar TC (T3N1bM0, n=212; T4N0M0, n=91; T4N1aM0, n=115; T4N1bM0, n=23). Among these, 256 (44.1%) surgeries were combination (60 of them appeared palliative); and 246 (42.3) were wide (7 of them appeared palliative). Sternotomy was used in 7 combination and 24 extended surgeries, a total of 31 (5.3%) cases. In 140 cases (24.1%) of T4N1b, surgeries could be considered as both combination and extended; including 5 (3.6%) performed using sternotomy. In addition, 79 (13.6%) palliative surgeries were performed in patients with T4, in which tumor removal was partial and aimed to relieve compression of neck structures, mostly trachea. For the reasons of patients' conditions, and insufficient surgeons experience more advanced combined or extended-combined interventions were not attempted. In 8 patients, after intensive preparations, complete tumor removals were undertaken during repeated surgeries utilizing wide approaches via neck and chest, and were a success. These patients were referred to respective groups, accordingly.

In 71 cases, surgeries were palliative. These patients were combined with 67 patients aimed at more advanced intervention, but in which tumors could not be removed completely, making it a total of 138 patients (146 surgeries). Combination and extended surgeries that ended up as palliative were considered in each group simultaneously. Thus, 146 out of 581 surgeries were palliative (25.1%); the proportion of patients that underwent this type of surgery was 31.3% out of 441 operated. The reason for palliative volume was inability of a complete removal of the tumor or affected lymph nodes (103 cases, 23.4%), or the presence of metastases in distant organs (35 cases, 7.9%).

Histological appearance of the 415 tumors representing T4 consisted of papillary TC in 261 cases (62.9%), follicular TC in 103 cases (24.8%) and medullar carcinoma in 51 cases (12%). Among the total of 1413 patients with papillary TC that underwent surgery during the indicated period, patients with T4 comprised 20.7%; among follicular TC patients (567 cases) the same grade was found in 20.5%; among patients with medullar TC (135 cases) in 41.5%. The proportion of the first two morphological types in the total patients' group and among the patients with T4 was approximately the same (61.6% and 24.8% compared to 62.9% and 24.8%, respectively). However, the proportion of patients with the medullar TC in T4 group was 7 times higher than in the total cohort (41.5% and 5.9%, respectively), reflecting a more aggressive nature of the medullar TC. *Combination surgeries* in patients with advanced TC (T4) were performed in 256 cases (44.1%) either as an emergency aid (21 cases, 8.2%), or planned (235 cases, 98.1%). During clinical and intraoperative assessment of the patients, the TC spreading was found into front and back neck muscles adjacent to the gland in 172 cases (67.2%), laryngeal muscles in 17 cases (6.6%), recurrent nerve in 97 (37.9%), trachea in 90 (35.2%), larynx in 35 (13.7%), pharynx and esophagus in 61 (23.8%), large vessels (mostly neck and mediastinal veins) in 56 cases (21.9%).

Malfunction of vocal cords and abnormal voice prior to the surgery were found in 33 (20.9%) of 158 patients with TC spread on the recurrent nerve. Subjective and objective data were conflicting 10 cases, where malfunction of the vocal cords was detected only by laryngoscopy. The nerve was relatively easily mobilized in 102

cases (64.6%), cut in 43 cases (27.2%), or rejected in 13 (8.2%). After mobilization, the continuity of the nerve was restored by sutures in 9 cases, with positive dynamics in 6 patients observed 6-17 months later. Of 32 cases where recurrent nerve was precisely mobilized from the tumor by a scalpel, nerve function was preserved in 25 cases (78.1%).

Endoscopic evaluation of T4 TC patients prior to the surgery revealed tumor spread to laryngeal, tracheal, pharyngeal, or esophageal mucosa in 14 cases (5.5%). In 10 out of them, surgical or radio approaches had been attempted earlier, however, TC recurred causing obstruction of airways in females (aged between 25 and 60), which required emergency life-saving surgeries. In five of them, a circular resection of tumor-invaded lymph nodes of cervical trachea and esophagus with subsequent skin patching was performed. Local conditions of the neck after left after previous surgeries did not allow using a segment of the colon for this purpose. Post-operative period of two of these patients was complicated by pharyngeal fistula formation. Their removal followed by 2-3 series of radioiodine therapy allowed the patients to continue with their jobs. Survival time of female patients with tracheotomies ranged from 2.5 to 8 years; these patients deceased due to generalization of the TC.

Three patients aged 44, 52, and 61 diagnosed with papillary TC spreading through the laryngeal wall underwent thyroidectomy with sparing lateral resections of the larynx and lymphadenectomy. Due to the radio negative nature of the tumors, courses of external irradiation were performed. Within 3 years, a recurrent disease was found in the larynx, and laryngectomies were performed. Life span after these surgeries ranged within 5 to 6 years. The younger patient died due to the ovary cancer, the rest from the generalization of TC.

One more patient with a papillary TC underwent a partial resection of the larynx and three tracheal rings due to the spreading of the tumor into all the layers of these organs. This patient remains free of the disease recurrence for more than 10 years with L-thyroxine replacement therapy as the only treatment.

A 57 year old female underwent two surgeries due to a papillary TC of the upper pole spreading into the upper larynx. Organ-saving resection of the upper-right part of the pharynx plus thyroidectomy and central and lateral lymphadenectomy were not efficient, regardless of the postoperative radiation treatment. Laryngectomy was performed for the recurrent TC, but the patient died due to the generalized disease. Overall, large volume circular resections of tumor-invaded recurrent nerves, trachea, larynx, and pharynx, and esophagus were performed in 27 out of 256 (10.5%) patients.

In some patients, TC spread reached submucosa of trachea (88 cases), larynx (32 cases), pharynx and esophagus (57 cases). The surgical volume of these interventions fit to "shave-surgeries" of trachea (62 cases, 70.4%) or larynx (25 cases, 78.2), or lateral (fenestral) tracheal resections (13 cases, 14.8%), laryngeal resections (7 cases, 21.9%), pharyngeal and esophageal resections (15 cases, 26.3%). Defects in the muscular and cartilage tissue after bilateral resections were replaced by local muscular and fascial replacements. In early 80's, in two patients, after lateral resection of three tracheal rings to provide sutural relief, temporary tracheostomies were used. Usually this was accompanied with, in patients with follicular or papillary TC, radio iodine therapy. External irradiation was seldom used (9.8%) compared to medullar carcinomas (37.1%).

A complete tumor removal was achieved in 213 (83.2 %) patients. In 18 (7.0%) patients, remote metastatic disease was found into the bones, lungs, and brain. In 25 (9.8%), there was a continuous growth of

cancer cells in other organs and lymph nodes. Therefore, the surgical volume was considered palliative, in spite of a significant volume of combination resections in these cases of TC. These patients subsequently received thyrotropin-suppressive and chemo/radiotherapy.

In 56 cases (21.9%) TC invaded, in addition to laryngeal and esophageal muscles, into large vessels of the neck and mediastinum, usually into jugular (44 cases, 78.6%), subclavian, and brachiocephalic (6 cases, 10.7%) veins. Real full-depth invasion of sternal walls was very seldom met (2 cases, 3.6%). It was usually possible to partially remove the tumor from the adventitia. Plastic replacement of deep jugular veins, even in bilateral resections or of the brachiocephalic vein, was not needed, since a continuous compression of these vessels by the tumor resulted in appearance of sufficient collateral vasculature, which was sufficient to provide blood flow from head, neck, and hand. Only in two patients (2%) with advanced tumors we had to use partial sternotomy till the 3rd or the 4th intercostals space.

Most of the observations described here deal with the carcinomas verging the stage when their resection is impossible. Surgery included removal of the TC as well as its metastatic outgrowth, therefore 140 (24.1%) of all interventions were both of combination and of wide surgery character.

In 246 (42.3%) cases, extended surgical interventions were used. In 90 (20.4%) of 441 observations, TC was T4N1bM0. Besides, in 49 (13.6%) cases, out of 360 with T1-3N1a-bM0 there were bilateral metastases of papillary, medullar, or follicular TC into neck or mediastinal areas (groups II-V and VII). As a result, spread metastatic TC that required wide surgical approach was found in 49 patients with T1-3 and in 197 patients with T4 grade making a total of 246 cases in 18 (7.3%) of which remote metastases were found, and hence, these wide surgeries were considered palliative.

In 74 out of 441 (16.8%) (i.e., in patients with high risk), wide or wide-combination interventions were divided in two stages. Among those that underwent surgery, mortality during the first stage was 4.84% (4 patients). The causes of death were myocardial infarction, thromboemboly of pulmonary artery, and acute cardiovascular failure. All the 74 patients (an average age 63.9±0.9 years) were dismissed from the hospital after the second stage. Long-term results in these two groups were similar. In analysis of these two groups, a comparison of technical skills and tumor morphology as the most important constituents were taken into consideration.

In the majority of patients, where wide surgical approaches were required, cervical access was used. However, in 25 (10.2%) cases it was not sufficient and we had to use partial L-shaped sternotomy.

Palliative surgeries in patients with locally invasive TC were performed in 138 (31.8%) out of 441 cases; 146 palliative surgeries were 25.1% of total 581 surgeries done, which was 6.5% of all differentiated TC surgeries (2115) performed in the Center.

During the last 33 years, the proportion of palliative surgeries has been at the decline. At the late 80s, their proportion was 25%, at the early 2000 making it 19%. Between 2004 and 2006, 102 surgeries were performed in patients with T4, but only in 8 (7.8%) they were palliative. In 78 (13.4%) of 581 surgeries residual tumor mass was left on the neck and mediastinal organs, while remote metastases were found in 67 (11.5%) of patients in whom combination or wide surgeries were performed. Only in 32 (5.5%) of patients, the surgical strategy was initially planned as palliative due to serious somatic problems or insufficient technical preparedness of the surgeons. In 8 of 79 observations, there was an attempt to get rid of the remaining

tumor mass during a second surgery. As a result, palliative volume of the intervention was limited to 138 patients.

In 9 out of 78 patients (11%) palliative surgeries were combined with a permanent tracheostomy and the patients were subjected to chemotherapy. In two cases, tracheotomies were temporary, and these patients were decanulated after 3 and 7 months.

As a result, after 502 combination and extended surgeries, the tumor and its regional metastases could be removed completely in 435 (86.6%) observations. Unusual specific complications took place in 31 case (6.2%), including damages to one or both recurrent nerves in 17 (3.4%) and 7 (1.4%) patients, respectively; and temporary hypothyroidism in 7 (1.4%) of patients. Of other postoperative complications, we would like to mention bleeding from the thyroid bed that required wound revision in 10 cases (2%), lymph retraction and wound infection in 10 patients, damage to the sympathetic trunk in 2 patients, and of the right hypoglossal nerve in one patient. In addition, we saw postoperative pharyngeal, esophageal and tracheal fistulas (two cases in each group). With growing experience of the surgeons of this Center, the number of complications dropped by 50-100%. During the last 10 years, the combined incidence of damages to the recurrent nerve and post-operative wound bleedings does not exceed 1.5%.

Long-term results have been followed up in 373 (84.6%) patients with local-invasive TC with a mean follow-up time of 10.3±1.6 years (range 3-30 years). Hematogenic dissemination after combination surgeries were found in 8 new cases (2.1%). Thus, in the operated group of 373 patients, the total number of patients in whom remote metastases were found was 43 (11.5%).

An average longevity of the patients that underwent combination surgeries, at the time this study has been completed, was 10.3±0.7 years. Five year survival was observed in 81.9%, and ten year survival was in 71.1%. After "shaving" resections, 80.5% of patients lived longer than five years. Total number of recurrent diseases observed after "shaving" and lateral resections of the neck was 17 (9.8%), while after circular resections it was found in 1 patient (3.7%). Recurrent TC after 87 of these surgeries in a longer term was the major cause of death in 8 patients (9.2%), while generalized tumor growth caused death in 7 cases (8%). In three cases (7%) out of 43 in which the recurrent nerve was mobilized but not resected, recurrent TC was found after 10 years of follow up. Two of them, both older than 50 died of generalized follicular (radio-iodine negative) and medullar TC.

Only 5 out of 14 patients (35.7%) who underwent wide circular resections of upper regions of gastrointestinal system and airways survived more than 5 years; only one patient (7.1%) lived longer than 10 years after the surgery. Recurrent TC was found in 3.5% of these patients. This type of surgery caused severe disabilities of the patients and a dramatic loss of "quality of life".

Patients with differentiated TC that underwent extended resections had a better prognosis; five year survival in this group was 86.7%, 10 years - in 70.6%.

After palliative surgeries, five year survival was observed in 40.7% patients with differentiated TC and in 17.1% patients with medullar TC. Ten year survival was observed in follicular/papillary group (29.1%), but was not seen in the medullar TC. These results may be, at least partially, explained by intrinsically less aggressive nature of differentiated TC. In addition, radio-iodine therapy in 25.7% patients could also have contributed to better longevity in this group.

Conclusions

Combined, extended and palliative surgeries in cases of advanced differentiated TC provided treatment and significant life prolongation for most of patients, who were considered incurable. The maximum removing of the carcinoma made the better prognosis for life and recovering for most of patients with the TC.

In elderly patients and patients with associated somatic pathology the surgical treatment could be divided in two parts since it improves the close results and not worsens the long-term results of treatment.

In cases of differentiated TC extension beyond the sternum and/or mediastinal lymph nodes metastases the *longitudinal- transverses* sternotomy is recommended for organs resection and mediastinal lymphadenectomy

The sparing of larynx, trachea, esophagus and NLS in combination and extended surgeries in patients with papillary, follicular and medullar TC has obvious advantages over the wide circular resection of these organs in same circumstances according to close and long-term results and life quality of operated patients.

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