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## Incidence of thyroid papillary cancer in contralateral lobe

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### Abstract

**Background & objectives:** Prognosis of thyroid papillary cancer is quite well long lasting, so a 10- year survival is observed in more than 90% cases. In this study, rate of incidence of thyroid papillary cancer in contralateral lobe was assessed among patients who had a surgical thyroidectomy re-operation.

**Materials & Methods:** In this retrospective study, we examined 82 patients diagnosed with thyroid papillary cancer that had thyroid lobectomy surgery first and thyroidectomy re-operation next from 1997 to 2007.

**Results:** Of 82 patients studied, 33 (40%) were diagnosed with papillary cancer in contralateral lobe. No significant relationship was observed between age, sex, size of the original tumor, intervals between two surgical operations and incidence rate of papillary cancer in contralateral lobe; however, due to tumor's multifocusing and presence of metastasis spread to lymphatic glands, an increase in tumor risk was caused in remaining of the thyroid. Following thyroidectomy re-operation, no complications were common highly, but a few of them included: RLN transient paralysis in six patients (7.3%); RLN permanent paralysis in two patients (2.5%) fleeting hypokalemia in nine patients (11%); and persistent hypoparathyroidism in one patient (1.2%). Following surgical operation, five patients (6%) suffered hematoma two cases of which needed re-operation.

**Conclusions:** Surprisingly, the incidence rate of thyroid papillary cancer was relatively high in the remaining tissue of contralateral lobe. We believe that such patients must undergo treatment of thyroidectomy reoperation which can be performed with acceptable complication rate, maintaining patient's health.

**Keywords:** Thyroid papillary cancer; Thyroidectomy re-operation; Cancer incidence in remaining lobe

### 1. Introduction

Papillary carcinoma is the most common malignancy of thyroid gland seen typically is 30-40 year individuals, being more common in

females. Papillary carcinoma is a potent lymphotropic in nature and causes a multifocal disease within thyroid gland and tends to be metastatic to regional lymphatic glands. Prognosis of thyroid papillary cancer is excellent with appropriate treatment and a 10-

year survival is seen in more than 90% of cases<sup>1</sup>. In many cases, thyroid papillary cancer is diagnosed after thyroid lobectomy to treat its benign diseases and nodules as well as after histopathological examination. There is some disagreement among surgeons over selecting a suitable treatment method under conditions in which thyroid cancer is diagnosed after lobectomy operation and patient is asymptomatic. Although there exists a general consensus over performing total (complementation) thyroidectomy in patients with high level of complications (over 45-year patients with positive lymphatic gland, with large tumors, outside capsule tumor invasion, etc.) it is not the case for selecting such a method for patients with low complications. In thyroid reoperation, resection surgery and determination of vital elements (like RLN, parathyroid glands, etc.) are difficult due to such situations as scar and fibrotic tissue formation as well as bed inflammation; therefore, thyroid re-operation may be accompanied by more post-operation complications than primary ones. For this reason, some surgeons do not agree with the thyroidectomy reoperation, and believe that treating complications caused by thyroid re-operation is more laborious than that of the remaining tumor. They suggest that the residual thyroid tumor can be eliminated by using radioactive iodine. In contrast, most surgeons and endocrinologists agree with total thyroidectomy as a standard therapy for thyroid papillary cancer<sup>2</sup>, and believe that complementation thyroidectomy can be performed with acceptable level of complications with no risk. Moreover, surgical elimination of thyroid tissue completely in patients with papillary carcinoma has some advantages as follows: 1) Removing the entire thyroid gland facilitates diagnosis and treatment of metastatic disease; 2) once the whole normal tissue of the thyroid is removed, the level of serothyroglobulin represents a more useful indicator to diagnose disease recrudescence; 3) removing whole thyroid tissue destroys the chance of anaplastic

transformation of residual tumor; 4) many studies also have shown that removing the thyroid gland entirely is more effective than radioactive iodine treatment in eliminating the tumor and preventing its recrudescence<sup>1</sup>. The objectives of the present study are to examine the incidence rate of thyroid papillary cancer in the contralateral lobe of patients undergone thyroidectomy reoperation, and to determine factors predicting the presence of papillary cancer in the contralateral lobe of thyroid. During this study, the level of complications due to the thyroid re-operation was assessed.

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## 2. Materials and Methods

In this descriptive sectional study, 82 patients were studied who had a total thyroidectomy surgical operation in Imam Khomeini Hospital of Ahvaz, from 1997 to 2007, because of suffering diagnosed papillary thyroid cancer. All patients had already undergone thyroid lobectomy surgery, and histopathological assessment of their removed thyroid specimen reported the existence of papillary thyroid carcinoma. For these patients with pathological assessment of thyroid specimen incidence of papillary cancer in contralateral lobe was studied following total thyroidectomy surgery. Also, we were looking for predictive factors of existence of tumor, based on demographic data, clinical parameters, and pathological findings, through assessing relationship between the presence of papillary cancer in the thyroid contralateral lobe and various factors including age, sex, absence or presence of lymphatic glands; and anatomical and pathological characteristics of original tumor such as its size, its being multifocal, vascular or neural invasion.

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## 3. Results

Among 82 patients studied, 58 (71%) were female and 24 (29%) male. The patient's age range was between 22 and 72 years, with age

mean being 41 years. All patients have already had thyroid lobectomy surgery. Thyroid nodule was the first surgical operation's (lobectomy) indication for nearly all patients. Histopathological assessment of thyroid specimen reported papillary cancer in these patients (Table 1).

After doing an entire thyroidectomy operation, a thyroid specimen of residual lobe was tested histopathologically (Table 2): for 33 (40%) cases papillary cancer was observed in contralateral lobe. Because of the facilitating nature of study analysis, we divided the patients into two groups based on being positive or negative in terms of residual thyroid tissue: for group 1 including 49 (60%) patients, cancer was not observed in residual tissue of the thyroid; for group 2, including 33 (40%) patients, it was observed in contralateral lobe. The mean size of original tumor was 2.6 cm (ranging from 0.5 to 7 cm), being 2.72 cm and 2.54 cm in group 1 (negative contralateral lobe) and for group 2 (positive contralateral lobe), respectively. A total of 11 (13.4%) patients under study had positive cervico-lymphatic gland, six of whom (54.6%) were in group 2 with positive contralateral lobe original tumor was multifocal for 22 (27%) of patients 17 (77.3%) of whom had reported papillary cancer in the thyroid contralateral lobe. In histopathological assessment on primary specimens, the tumor has invaded to thyroid capsule in 14 cases seven of which exhibited thyroid contralateral lobe cancer, but another seven cases did not. Our patients studied, were undergone total thyroidectomy re- operation 3.2mo, on the average, after having primary hemi- thyroidectomy operation, the interval was 3.5 mo for group 1 and 2.8 mo for group 2.

Of 49 patients in group 1, 35 were female and 14 male; and of 33 patients in group 2, 23 were female and 10 male. The age means were 40.5 gr and 42.1 gr for groups 1 and 2, respectively. None of the patients studied had a history of radiation exposure. And all patients were clinically asymptomatic and no evidence was observed suggesting tumor recrudescence.

Prior to performing re-operation (total thyroidectomy), the majority of under- study patients were euthyroid, But 15 (18.3%) patients displayed weak hypothyroid.

Following the thyroid re- operation( total thyroidectomy), six (7.3%) patients suffered transient paralysis of RLN nerve four of whom recovered gradually, but unilateral paralysis of RLN nerve remained in 2 (2.5%) patients. Also, nine (11%) patients suffered fleeting hypoparathyroidism whose serum calcium level was controlled with medication therapy. Among these nine patients, only one (1.2%) patient remained with permanent hypoparathyroidism. Post operation hemorrhage and hematoma occurred in 5(6%) patients two of whom were taken to surgery room again, and hemorrhage was controlled. Other three patients recovered entirely with conservative treatment. According to data obtained, in our study there was no significant relation between age, sex, size of tumor, interval between two surgical operations, tumor invasion to thyroid capsule and the probability of the existence of papillary carcinoma in the thyroid contralateral lobe. Only for patients with original multifocal tumors, the probability of tumor existence in contralateral lobe was considerably high; and there was a significant relation between multifocusing of the original tumor and incidence of tumor in contralateral lobe. In 54.6% patients with positive lymphatic gland, cancer was observed in thyroid contralateral lobe. This figure is slightly higher than that of the total rate of incidence in our study (which is 40%); and the chance of suffering cancer in contralateral lobe is higher in patients with positive lymphatic glands than in other patients studied.

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#### 4. Discussion:

Thyroid papillary cancer is of an excellent long term prognosis; and a 10-year survival is observed in more than 90% of cases. Based on numerous studies, incidence of bilateral thyroid

papillary cancer is relatively high (reported between 30- 80%)<sup>2-3</sup>. There is some disparity of opinion among surgeons over thyroid re-operation for cases in which thyroid papillary cancer is diagnosed after carrying out hemithyroidectomy during histopathological assessments. Some identify complications of second thyroidectomy considerable and accept radioactive iodine as a treatment for papillary tumor in the remaining tissue of the thyroid. In contrast, many surgeons believe in total thyroidectomy as a standard treatment for thyroid papillary cancer, advocating complementation thyro-idectomy; they think that by doing a thyroidectomy re- operation followed by iodotherapy, rates of tumor recrudescence and distal metastasis are reduced while survival is increased. Similarly, following total thyroidectomy, tumor recrudescence will be diagnosed better; measuring serum immunoglobulin will be more useful; and the chance of transformation will disappear through removing thyroid tissue. In contrast, there will be some difficulties with using radioactive iodine alone, without performing surgical operations, including multiple doses of radioactive iodine necessary to eliminating tumor successfully. Completely removing tumors of large sizes is problematic, and using high doses of radioactive iodine causes pulmonary fibrosis, temporal suppression of bone marrow, and leukemia.

In 2007, a U.S. study, in Washington, 150 patients undergone thyroidectomy re-operation were assessed, showing a 41% incidence of papillary cancer in contralateral lobe. In that study, it was found that the presence of tumor in the contralateral lobe had no considerable relation to size of tumor, age of the patient, and positive lymphatic gland; and performing total thyroidectomy operation was recommended for all patients with papillary cancer with respect to high incidence of tumor in residual thyroids of patients with low risk and complications<sup>1</sup>. In 2001, during a study done by Pacini et al., in Italy, papillary contralateral lobe cancer was observed in 44% of patients who had a

thyroidectomy re- operation. Also, in that study, thyroid contralateral lobe involvement was seen more in patients with positive cervico-lymphatic gland. But a significant difference was not observed between low- and high- risks patients for age<sup>4</sup>. Kim et al.<sup>5</sup> studied 81 Korean patients who received thyroidectomy re-operation to treat thyroid cancer. In that study, multifocusing of cancer in ipsilateral lobe was the only predictive factor. In 2007, another study was done on treating thyroid papillary micro- carcinoma (PMC) in Ankara, Turkey. Based on the results of that study, there must be no distinction between treatment of PMC and that of PTC (papillary thyroid carcinoma), so performing thyroidectomy was recommended<sup>6</sup>. Hand Kiewicz et al. studied 131 children with thyroid differentiated cancer who had thyroidectomy reoperation; the incidence of cancer in contralateral lobe was 35% which had no relation with age and sex. Hand Kiewicz et al. recommended thyroidectomy re- operation. By the way, that study determined that, in thyroid papillary cancer, the risks of tumor in the remaining thyroid tissue, multifocusing of the original tumor, and lymphatic metastasis are higher<sup>7</sup>. In several other studies, the incidence of cancer in thyroid contralateral lobe was reported 39%<sup>8</sup>, 47%<sup>9</sup>, and 43%<sup>2</sup>.

In our study, the incidence of papillary contralateral lobe tumor was observed in 33 (40%) patients, indicating high risk of the existence of papillary cancer in the remaining thyroid tissue of patients who had a thyroid lobectomy surgical operation. Our study showed there was no significant and noticeable relation between demographic factors like age, sex, and incidence rate of existence of tumor in contralateral lobe. In the present study, the interval between two surgical operations, tumor invasion of thyroid capsule, and size of original tumor had no effect on the rate of cancer incidence in the thyroid contralateral lobe. Twenty- two patients (27% of total patients studied) had original multifocal tumor in 17(77.3%) of whom contralateral lobe cancer was observed. In our study, 11 patients had

positive cervical (nodule) in six of whom cancer was observed in contralateral lobe. Considering this information, it seems that the risk of cancer in contralateral lobe is higher for patients having original multifocal tumor- as well- as those having positive cervical (nodule) the most important reason for opponents of doing thyroidectomy reoperation on patients with thyroid papillary cancer is fear of complications due to the thyroid re- operation. But many studies have shown that complications of thyroid reoperation are not much more than those of primary thyroid surgery. In one study performed by Eden, in 2003, incidence of permanent RLN- nerve paralysis was 3.3% for primary thyroid surgery, of permanent hypoparathyroidism was 4.3%; and for thyroidectomy reoperation, incidence of permanent RLN paralysis and hypoparathyroidism was 3.5% and 4.2%, respectively<sup>10</sup>. In another study by Micheal in the US, Pennsylvania University, in 2002, the results from complications following a thyroidectomy re- operation were reported as follows:

RLN paralysis was 0.00%, temporal hypoparathyroidism account for 13.9%, and no patient with hemorrhage or hematoma following performing surgery was reported<sup>11</sup>. In a study by Lefevrej et al., done in France in 2007, 685 patients who had thyroidectomy operation were studied. Surgical operation's complications included: transient hypoparathyroidism, 5%; permanent hypoparathyroidism 2.5%; permanent RLN paralysis, 1.5%; post operation hematoma, 0.9%; wound infection, 0.2%<sup>12</sup>. In our study, complications

due to total thyroidectomy re- operation were: temporal RLN paralysis, 7.3%; permanent RLN (unilateral) paralysis, 2.5%; temporal hypoparathyroidism, 11%; permanent hypoparathyroidism, 1.2%; post-operation hemorrhage and hematoma, 6%. Comparing these results with data and results of other studies indicates that the incidences of complications in our study are equal to those of other research centers; and the level of such complication is not considerable generally.

## 5. Conclusion

The incidence of papillary thyroid cancer is high and remarkable in contralateral lobe, and its rate is not different significantly in patients with high risk and those with low risk. Age, sex, size of the original tumor, and invasion to capsule had no relation with the incidence of cancer in the thyroid contralateral lobe, but this rate was higher for patients with original multifocal tumor as well as for those with positive cervical lymphatic glands. In addition, our study shows that thyroidectomy reoperation can be performed safely with minimal complications. We suggest that making decisions on doing thyroidectomy reoperation on such patients should be based on the patient general conditions and risk of certain factors, especially in case of latent and microscopic cancers in the contralateral lobe; and fear of reoperation's complications should not affect the surgeon's decisions on treatment and control of disease.

**Table 1. Statistics Histological data**

	total	Positive contralateral lobe	Negative contralateral lobe
N (of patients)	82	33	49
Male,%	24.29	10	14
Female, %	58.71	23	35
Mean age	41	42.1	40.5
Age range	22-72	30-68	32-72

**Table 2. clinical data**

	total	Positive contralateral lobe	Negative contralateral lobe
N	82	33	49
Mean size of tumor	2.6	2.25	1.72
Positive cervico-lymphatic nodule	11	6	5
Invasion to thyroid capsule	14	7	7

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