



Surgical approaches for papillary microcarcinomas: Turkey's perspective

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ABSTRACT

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Cite this paper as:

Makay Ö, Özdemir M, Giles Şenyürek Y, Tunca F, Düren M, Uludağ M, et al. Surgical approaches for papillary microcarcinomas: Turkey's perspective. Turk J Surg 2018; 34: 89-93.

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Received 28.08.2016; accepted 02.10.2016.

This study was presented at the "7th National Endocrine Surgery Congress", 2015, Antalya, Turkey.

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Objectives: The incidence of papillary microcarcinomas, which are defined as thyroid cancers of <10mm in size, has been increasing in the last decade. Herein, we present internet-based questionnaire results performed by the Turkish Association of Endocrine Surgery with the aim to evaluate the perspective of the management of papillary microcarcinomas in Turkey.

Material and Methods: The user-friendly questionnaire consisted of 13 questions in total. These questions mainly addressed the surgical management of nodules and cancer of <1 cm in size. Patient management before, during, and after surgical intervention was also included; additionally, the "active surveillance approach" was questioned.

Results: There were 420 responders in total who were of multidisciplinary origin (endocrinologists, surgeons, nuclear medicine specialists, pathologists, and oncologists). Total thyroidectomy was the predominant treatment approach (65%) for the classical type of microcarcinoma limited in one lobe, whereas in cases of microcarcinomas incidentally diagnosed during hemithyroidectomy, complementary surgery approach was advised by 40% of the responders. The responders found capsule invasion (86%) and patient based management (94%) of high importance. The percentage of the responders who recommended radioactive iodine ablation in incidental cancers having no aggressive criteria was 51%. The survey participants that were against routine central dissection in these cases accounted for 73% of the responders. The recommendation of active surveillance (follow-up without any interventional therapy) was limited with 9% responders.

Conclusion: The results of the questionnaire demonstrated that there have been various choices in Turkey for the surgical treatment of the papillary microcarcinomas.

Keywords: Papillary microcarcinoma, Turkey, thyroidectomy

INTRODUCTION

The incidence of 'papillary microcarcinoma' (PTMC), which is defined as papillary thyroid cancer with the diameter smaller than 10 mm, has gradually increased in the last 20 years (1). One of the most important causes of this increase is the detection of nodules in the thyroid gland during ultrasonography, computed tomography, magnetic resonance imaging, or positron emission tomography that are performed for extrathyroidal reasons (2). There are many controversial issues about the clinical importance of papillary microcarcinomas, which are generally found incidentally. The acceptance of PTMC as a subclinical disease, its not displaying progression, and not affecting survival constitute the main cause of these discussions (3). In this study, it was aimed to evaluate the approach to PTMC in our country.

MATERIAL AND METHODS

A questionnaire study was arranged by the Turkish Society of Endocrine Surgery through their website between August 2014 and October 2014. The announcement of the survey with a brief introduction writing was conveyed to all enrolled members by the means of the website of the Turkish Society of Endocrine Surgery. One month after the first electronic announcement, the members were sent a second electronic mail for reminding. The online survey, which would be applied with a computer-assisted questionnaire technique (SurveyMonkey®; Palo Alto, CA, USA), was reached to the members via electronic link address. In this way, the questionnaires were completed electronically and recorded automatically. The questions were prepared by considering the controversial subjects about the approaches to papillary microcarcinomas in literature and scientific meetings. This questionnaire, which was easy-to-use, consisted of 13 questions on nodules with a diameter of <1 cm and cancer management. In addition, the participants were asked about non-surgical monitoring approach in cases of papillary microcarcinoma. Preoperative, intraoperative and postoperative patient management was also included in the questions. The participants to the survey were divided according to their disciplines.

The data collection, protection, and access were provided by the same computer-assisted software (SurveyMonkey®). This study was performed in accordance with the Declaration of Helsinki.

RESULTS

The questionnaire forms were completed by a total of 420 participants from 5 different disciplines including endocrinology, general surgery, nuclear medicine, pathology, and medical oncology. Of the participants, 57% were surgeons, 23% were nuclear medicine specialists, 18% were endocrinologists, 1% were pathologists, and 1% were medical oncologists.

The role of fine needle aspiration biopsy and primary treatment planning in detected cancer

The response to the question 'Do you recommend fine needle biopsy for an ultrasonographically suspected nodule with a diameter of <1cm?' was 'yes' by 89% of the participants and 'no' by 11% of the participants. Considering the study fields of the participants, while all of endocrinologists and nuclear medicine specialists responded as 'yes', 15% of general surgeons responded as 'no'.

When the participants were asked about their treatment suggestions for classical papillary carcinoma that was restricted with a single lobe and detected by fine needle biopsy, and had a diameter of <1cm, the views of 65% were in favor of total thyroidectomy, 33% in favor of hemithyroidectomy, 0.5% in favor of follow-up, and 0.5% in favor of ablation treatment [laser, radiofrequency thermal ablation (RFA), high intensity focused ultrasonography (HI-FU)]. When considered from the view of occupational groups, 78% endocrinologists recommended total thyroidectomy and 22% recommended hemithyroidectomy. Of general surgeons, 58% recommended total thyroidectomy and 40% recommended hemithyroidectomy. 1% of the surgeons presented their views in favor of follow-up and other 1% stated their views as ablation treatment. Of the nuclear medicine specialists who responded the question, while 71% and 24% recommended total thyroidectomy and hemithyroidectomy, respectively, 5% recommended follow-up (Figure 1).

Completion surgery

To the question 'for a patient with a <1cm diameter papillary cancer incidentally detected after hemithyroidectomy, do you recommend completion surgery if residual lobe is ultrasonographically normal?', while 41% of the participants answered as 'yes', 59% answered as 'no'. While 11% of endocrinologists recommended completion surgery, 34% of general surgeons and 48% of nuclear medicine specialists recommended this surgery for a patient having these features.

For the question asking whether they recommended completion surgery even if residual tissues did not include nodule and pathological lymph nodule in patients undergoing subtotal thyroidectomy, while 34% of the participants replied in favor of completion surgery, 66% stated that they did not recommend. 11% of the endocrinologists, 30% of general surgeons, and 50% of nuclear medicine specialists recommended completion surgery (Figure 2).

Management according to the pathological features of specimen and patient

The question 'if you have recommended follow-up, does the presence of capsular invasion change your decision?' was answered as 'yes' by 86% of the participants and as 'no' by 14% of the participants. With regard to the occupational groups,

89% of the endocrinologists, 84% of the general surgeons, and 85% of the nuclear medicine specialists stated their views as 'I change my decision'.

For the question 'do you recommend radioactive iodine (RAI) ablation for a patient with classical papillary carcinoma including more than one foci smaller than 1 cm and without capsular invasion and lymph node metastasis?', 52% of the participants replied as 'yes, I recommend RAI ablation'. The answer was 'yes' by 32% of the endocrinologists, by 52% of the general surgeons, and by 58% of the nuclear medicine specialists.

While 94% of the participants answered as 'yes' for the question 'do you believe in patient-specific management (age, risk factors, pathology result, etc.)?', all of endocrinologists agreed on this view. On the other hand, 92% of the general surgeons and 90% of the nuclear medicine specialists specified that they believed in patient-specific management.

Molecular genetics

For the question 'does the occurrence of preoperative BRAF mutation (+) change your surgical treatment strategy?', the response of 67% was 'yes'. 74% of the endocrinologists, 66% of the general surgeons, and 61% of the nuclear medicine specialists answered as 'yes, I change my surgical strategy' (Figure 3).

Central dissection in papillary microcarcinoma

For the question 'should routine central lymph node dissection be performed intraoperatively in a patient with papillary microcarcinoma?', 27% of the participants said 'yes'. Of the endocrinologists, 78% defended that routine central dissection should be performed in patients with papillary microcarcinoma. However, 86% of general surgeons stated their views in favor of not performing routine central dissection in papillary microcarcinoma cases by answering as 'no'. Of the nuclear medicine specialists, while 50% replied as 'yes', other 50% answered as 'no' (Figure 4).

Active follow-up without treatment and ablation treatments in papillary microcarcinomas

For the question 'do you follow up papillary carcinomas with the diameter of <1cm without any treatment (by not applying surgery and/or RAI ablation)?', the response was 'no' by 91% of the participants and 'yes' by 9%. The response was in favor of follow-up without treatment by 11% of the endocrinologists, 8% of the general surgeons, and 18% of the nuclear medicine specialists.

For the question 'do you include ablation treatments (laser, RF, HI-FU) for microcarcinomas in your practice?', while 88% of the participants responded as 'no', 12% responded as 'yes'. While all of the endocrinologists stated that they did not include ablation treatments in their practices, 91% of general surgeons and 86% of nuclear medicine specialists agreed on the same answer.

Replacement treatment in the cases of papillary microcarcinomas

For the question 'after surgery, should <3 mm papillary cancer with a single focus be followed up or be given only replacement treatment by accepting it as an incidental cancer?', while 66% of the participants replied as 'routine follow-up', 34% re-

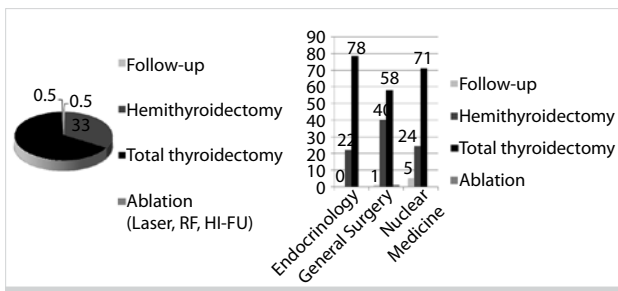


Figure 1. First treatment approach

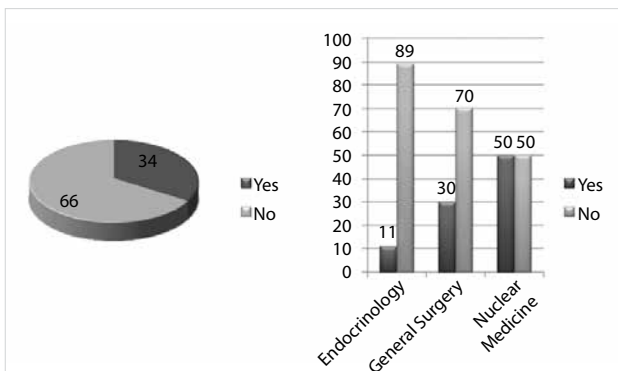


Figure 2. Completion surgery

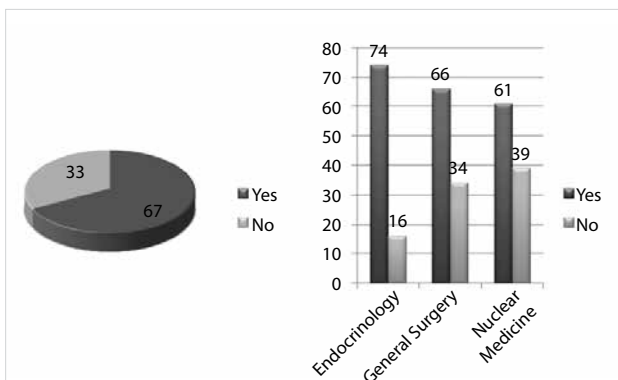


Figure 3. BRAF mutation (+), surgical treatment strategy

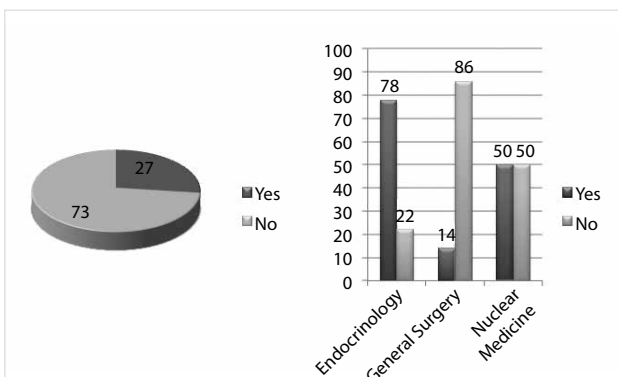


Figure 4. Routine central dissection in papillary microcarcinoma

plied as ‘replacement treatment’. Considering their occupational groups, 89% of the endocrinologists, 69% of the general surgeons, and 67% of the nuclear medicine specialists stated their opinions in favor of performing routine follow-up.

DISCUSSION

The American Thyroid Association (ATA) guidelines, which were published in 2015, make sorting in terms of evidence

value and give some recommendations. One of these recommendations is related to the management of nodules with the diameter of <1 cm. Here, because they only have higher malignancy potential, only nodules having a diameter over 1 cm should be evaluated and they should be performed fine needle aspiration biopsy according to their sonographic features (4). Besides that, the guidelines state that patients having suspected ultrasonographic findings, coexisting lymphadenopathy, history of radiotherapy to the head and neck, and a familial history of thyroid cancer in one of more first-degree relatives should be evaluated if their nodules are smaller than 1 cm. Of the specialists participating in this study, 89% stated that fine needle aspiration biopsy should be applied to ultrasonographically suspected nodules smaller than 1 cm.

Considering treatment suggestions for classical papillary cancer detected through fine needle biopsy and restricted in a single lobe, there is no controversy on that the approach to patients with malignant result of cytology should be surgical. Then, which surgical procedure should be applied? If thyroid cancer is smaller than 1 cm and it does not have extrathyroidal spread, clinically metastatic lymph node, and a clear indication for the removal of the contralateral thyroid lobe, hemithyroidectomy would be sufficient. Hemithyroidectomy is reported to be an adequate treatment for small, unifocal, intrathyroidal carcinomas in patients without a history of radiation therapy on the head and neck, familial thyroid carcinoma, and clinically detected lymph node metastasis (4). While the ATA guideline published in 2015 recommends hemithyroidectomy for these patients, it also emphasizes that there are views defending that these patients can be followed up without any surgery as well as views defending the application of total thyroidectomy. In the hands of experienced surgeons, the rates of complications associated with total thyroidectomy are the same with those associated with hemithyroidectomy (5). In a study conducted by Hay et al. (6), PTMC patients performed hemithyroidectomy and total thyroidectomy were compared. In this study, for total thyroidectomy and hemithyroidectomy, local recurrence rates were reported to be 14% and 19% and lymph node metastasis rates to be 2% and 6%, respectively (6).

There are studies that recommend follow-up without any surgery to a patient group with clinically low risk. Particularly two prospective studies with Japanese origin are highly remarkable. In the study conducted by Ito et al. (7) from Kuma Hospital, 1235 patients with PTMC, the presence of which was proven by FNAB, were followed up without surgical treatment. 191 (15%) patients followed for 60 months on average were operated due to tumor growth or newly developed lymph node metastasis and no change was reported during their follow-ups (7). In the other study, Sugitani et al. (8) followed up 230 PTMC patients diagnosed with FNAB for about 5 years and they reported that surgery was required during follow-up only in 7% of these patients. Although the results are striking, further studies on larger series and with high evidence level are needed for the choice of follow-up to come into prominence.

If residual lobe is ultrasonographically normal in a patient with <1cm papillary cancer detected incidentally after hemithyroidectomy, should completion surgery be recommended? The conducted studies have shown that the rate of complica-

tions of completion surgery after hemithyroidectomy is the same with the rates in total or near-total thyroidectomy (9). Besides that, what is recommended for completion surgery in the guidelines is that: completion surgery is needed for cases whose first indication for surgery requires bilateral surgery (4). These cases are those having one of features including extrathyroidal invasion, multifocality, clinically positive central lymph node, history of radiation therapy to the head and neck region, and familial history of thyroid cancer.

In patients with clinically metastatic lymph node, the role of therapeutic lymph node dissection in the treatment of thyroid cancer is apparent. However, the value of routine prophylactic central lymph node dissection is controversial in patients without clinically proven metastasis in the lymph nodes (4). In the hands of experienced endocrine surgeons, central lymph node dissection has a course with low morbidity (10). Despite the applicability of prophylactic central dissection in T3 and T4 tumors, prophylactic central lymph node dissection is not recommended for T1 and T2 tumors by the updated ATA guideline (4).

An increase in the rates of extrathyroidal invasion, multicentricity, and nodal metastasis is known to occur in the presence of BRAF mutation (11). Although BRAF mutation is encountered at the rates between 30% and 67% in PTMCs, its effect on recurrence is low as 1-6% (12). While there are views suggesting that surgical choice in the presence of BRAF mutation should be total thyroidectomy, some researchers defend that it should not be a single criterion for the decision of surgery (4, 13).

For multifocal or unifocal PTMCs, postoperative RAI treatment is not routinely recommended. In a multicenter study including 1298 patients with low-risk differentiated thyroid cancer, 911 patients undergoing RAI ablation treatment and 387 patients not undergoing RAI ablation treatment were followed up for about 10 years and it was demonstrated that RAI ablation treatment had no effect on disease-free survival (14). Moreover, in another study including 704 patients diagnosed with low and moderate-risk PTMC, 578 patients receiving RAI ablation therapy and 126 patients not receiving RAI ablation treatment were followed up for 64 months on average and it was found that RAI ablation treatment did not affect recurrence (15). Postoperative follow-up varies depending on the surgical procedures. Patients who have been treated with only lobectomy or total thyroidectomy without receiving radioactive ablation treatment should be followed with annual neck examination, ultrasonography, and serum thyroglobuline analysis. Similar method is used for patients undergoing total thyroidectomy and RAI ablation treatment. However, the sensitivity of serum thyroglobuline measurements becomes higher in such cases (16).

CONCLUSION

In this questionnaire study, it was aimed to evaluate the approaches of our colleagues to papillary microcarcinomas, the rate of which has increased with the development and more usage of diagnostic methods. In conclusion, it was observed that there were various views about the surgical management of papillary microcarcinomas and postoperative treatment in our country, as across the World. We suggest that more clear

approaches to the treatment of this cancer will appear with further qualified studies on papillary microcarcinomas, as well as increasing number of patients and prolonged follow-ups.

Ethics Committee Approval: Not required in this study.

Informed Consent: Not required in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - Ö.M., Y.G.Ş., M.U.; Design - F.T., M.D., M.U.; Supervision - M.H., G.İ., A.İ., S.Ö., Z.Ö., S.T.; Resource - G.İ., A.İ., S.Ö.; Materials - Ö.M., M.Ö.; Data Collection and/or Processing - Ö.M., M.Ö.; Analysis and/or Interpretation - A.İ., S.Ö., Z.Ö., S.T.; Literature Search - Ö.M., M.Ö., M.H.; Writing Manuscript - Ö.M., M.Ö.; Critical Reviews - Ö.M., Y.G.Ş., M.U., F.T., M.D.

Conflict of Interest: The authors has no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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