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The relationship clinicopathology differentiated thyroid carcinoma post thyroidectomy on scintigraphy profile

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ABSTRACT

Introduction: Differentiated thyroid carcinoma (DTC) is one of the most frequently found endocrine malignancies. This study was conducted to evaluate the factors responsible for the presence of residual thyroid tissue in scintigraphy.

Methods: Retrospective study of patients with DTC identified from the Medical records. Statistical analysis included standardized differences, P values, and chi-square test was used to compare each difference variables; a P value of < 0.05 was considered to have statistical significance.

Results: 112 patients with DTC who underwent near-total or total thyroidectomy mean age 43,4 ± 16.0 (standard deviation) years, 94 (83,9%) female, 25,18 (16,1%) male. The average tumor size with well-differentiated thyroid carcinoma was 5.5 ± 1.6 cm. All patients were not found to have metastasis. 97 patients showed residual thyroid tissue after surgery on scintigraphy examination. Tumor size ≥ 5 cm, $p = 0.32$. Well differentiated thyroid carcinoma showed residual thyroid tissue after thyroidectomy on scintigraphy, $p = 0.28$. Residual thyroid tissue in group 1 and group 2, $p = 0.98$. Residual thyroid tissue with major capsular invasion, $p = 0.17$. Patients undergoing near total thyroidectomy, $p = 0.65$. Low risk group, $p = 0.002$.

Conclusion: Residual thyroid tissue posts near-total or total thyroidectomy is significantly associated with high-risk groups patients well-differentiated thyroid carcinoma.

Keywords: Thyroidectomy; Scintigraphy; High risk; Ablation.
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INTRODUCTION

Scintigraphy is a diagnostic test where radioisotopes either by themselves or tagged to protein or other molecules are administered intravenously or orally that travel specifically to an organ or tissue and the emitted radiation is captured by specialized scanners known as Gamma Camera to form two-dimensional images. This thyroid scintigraphy will ultimately give you an overview and functional status of the thyroid glandular in vivo[1].

Thyroid carcinoma is one of the world's most endocrine glandular cancer. The prevalence of thyroid cancer in women is as much as 1%-5% and as much as 2% in males. In 2012, it was estimated that women and individuals experienced around 300,000 new cases of thyroid cancer, most of the cases under 65 years.[2,3] Based on data Dr. Cipto Mangunkusumo hospital in Jakarta, thyroid cancer is ranked 9th for the most common cancer prevalence in Indonesia.[4] Meanwhile, epidemiological data in the local Indonesian region, such as at Makassar, South Sulawesi, is still not available until present.

Based on a few literatures, the age of the onset of thyroid cancer seems to resemble the bell-shaped curve, with the highest incidence in the second, third, and fourth decade of life. However, in two decades, there has been an increase in the incidence of thyroid cancer in fourth and fifth decades of life. Increased diagnosis may be affected by the incidental findings of the tumor on radiologic examinations, such as ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI).[5]

Thyroidectomy is considering to be the best curative therapy. When total thyroidectomy is performed, many patients with thyroid cancer are treated with post-operative radioiodine (RAI) therapy for residual thyroid tissue ablation to apply the focus of cancer that is difficult to reach after surgery.[6] RAI ablation lowers the risk of recurrence and improves the lifespan of high-risk thyroid carcinoma patients.

Recently, based on the consensus of the America Thyroid Association (ATA) published in 2009, suggests that regular RAI ablation is no longer a need in patients with low-risk thyroid carcinoma. The adverse outcome of RAI ablation includes decreased fertility and increased risk of secondary malignancy. The improper RAI will also face the patient against the increase in health care costs associated with thyroid cancer therapy.[7] As a result, the prognostic system is important in determining the clinical decisions to be established in the case of thyroid cancer.[8]

The importance of prognostication as a therapeutic determinant has been demonstrated in a number of studies, and several screening systems have been develop by some institutions and validated for use in patients with thyroid carcinomas.[8] AMES scoring system was discovered in 1980 from a cohort of 814 patients with DTC. Prognostic factors in this system are age, metastasis, extrathyroid invasions, and size. Age and size are expressed in categories variable form; 5 cm is a threshold for size, but the threshold point for age is different for both genders (41 years for males and 51 years for females).[9]

Disease status is a relevant consideration in making post-operative therapeutic decisions after previously conducting pathological-clinical considerations. Post-operative disease status evaluation can be done through a number of examinations including, serum thyroglobulin, neck ultrasonography, and scintigraphy. Nevertheless, there are no randomized control trial (RCT) designs that compare specific post-operative diagnostic strategies to therapeutic decision making.[10]

Scintigraphy is often used as a diagnostic pre ablation examination and shows an increase in diagnostic information. Information obtained by scintigraphy has the potential for risk stratification, diagnostic decision making, and long-term strategies.[11] Several studies have brought evidence that the examination of scintigraphy pre ablation has Influenced on determining the stage of patients with thyroid cancer, and the information obtained from the scintigraphy of the pre ablation is able to alter the management flow.

The importance of prognostication as a therapeutic determinant has been demonstrated in a number of studies, and the scoring system has been developed by a number of institutions and validated for use in thyroid cancer. In addition, this scoring system is expected to be able to demonstrate the apparent tumor residue of the remnant thyroid tissue in the post-thyroidectomy differentiated thyroid carcinoma patients.[12]

The number of studies comparing post-operative scintigraphy findings to residual thyroid tissue is not yet available, especially in Indonesia. Thus, this research is considered necessary to guide the clinician in determining the type of surgery to be performed.

METHODS

Setting and subjects

A retrospective study of patients with medical records on all cancers diagnosed in Makassar. Data from patients diagnosed with thyroid cancer between 1 January 2019 and 31 December 2019 were extracted from the database. Cases of thyroid carcinoma were identified using the International Classification of Diseases (ICD)-10 diagnosis code C73.

Patients who underwent near-total or total thyroidectomy were identified using the hospital information systems (HIS). All patients who received near-total or total thyroidectomy were included in the analysis. Patients who received RAI were identified using the medical record. The date of diagnosis of thyroid cancer was determined using the ICD-10.

Demographic, clinical variables extracted from medical record based on age at diagnosis, sex, race/ethnicity, tumor size, tumor stage, metastasis (presence of extra thyroidal extension, and lymph node involvement). Prognostic systems for our patients have been assessed based on AMES (Age, Metastasis, Extent, Size) staging system.[12] This is divided into two groups:[12] A. High risk (1) patients with distant metastasis and 2) females ≥ 51 years and males ≥ 41 years with tumors ≥ 5 cm or extra thyroidal extension if it is papillary carcinoma and major capsular invasion if it is follicular carcinoma. B. Low risk (1) females < 51 years and males < 41 years without any distant metastasis and (2) elderly patients with tumors < 5 cm with no extra thyroidal extension of the papillary carcinoma or minor capsular involvement in follicular cancer.

Statistical analysis

Summary statistics were used to describe baseline characteristics. Standardized differences (SD) were used to represent differences in effect sizes when comparing demographics and clinical characteristics. In continuous data, variables are collected in the form of mean ± standard deviation (SD) or median followed by interquartile range. IBM SPSS Statistics version 25.0 (IBM Co., Armonk, NY, USA) was used for statistical analysis. The chi-square test was used to compare each difference variables; a p-value of < 0.05 was considered to have statistical significance.

RESULTS

This study involved 112 patients (18 male patients [16.1%]) with well-differentiated thyroid carcinoma. The mean age of the patients was 43.4 ± 16.0 years. The average tumor size in patients with well-differentiated thyroid carcinoma was 5.5 ± 1.6 cm. All patients were not found to have metastasis, local or distant. In addition, 97 (86.6%) patients showed residual thyroid tissue after surgery on scintigraphy examination (**Table 1**).

A total of 58 (51.8%) patients with well-differentiated thyroid carcinoma after thyroidectomy showed tumor size ≥ 5 cm. There was no statistically significant relationship between tumor size and the presence of residual thyroid tissue on scintigraphy examination (**Table 2**) (P = 0.32). A total of 17 (94.4%) male patients with well-differentiated thyroid carcinoma showed residual thyroid tissue after thyroidectomy on scintigraphy. There was no statistically significant association between sex and the presence of residual thyroid tissue on scintigraphy examination (**Table 2**) (P = 0.28).

Based on the patient's age, patients were divided into two groups. Group 1 were female aged <41 or male <51 years old, while group 2 were female aged ≥ 41 years or male aged ≥ 51 years. As much as 45 (86.5%) group 1 patient showed residual thyroid tissue after thyroidectomy. Meanwhile, post-operative residual thyroid tissue was found in 52 (86.7%) patients in group 2. There was no statistically significant association between age groups for the presence of residual thyroid tissue on scintigraphy examination (**Table 2**) (P = 0.98).

Capsular invasion is divided into minor and major invasions based on the results of the pathological examination. Post-operative residual thyroid tissue was found in 26 (96.3%) patients with major capsular invasion of well-differentiated thyroid carcinoma. Although capsule invasion of thyroid carcinoma was not found, 49

(81.7%) patients showed residual thyroid tissue on scintigraphy examination. No statistically significant association was found between capsular invasion and the presence of residual thyroid tissue on scintigraphy examination (Table 2) (P = 0.17).

In patients undergoing near-total thyroidectomy, residual thyroid tissue was still found in 82 (87.3%) patients with well-differentiated thyroid carcinoma. There was no statistically significant association between the surgical technique and the presence of residual thyroid tissue on the scintigraphy examination (Table 2) (P = 0.65). All patients were divided into two groups based on the prognostic stratification of AMES, which is high risk and low risk. A total of 73 (65.2%) patients showed a low risk. Interestingly, all patients who are at high risk indicate the residual thyroid tissue after thyroidectomy. The prognostic stratification is significantly related to the presence of residual thyroid tissue after thyroidectomy (Table 2) (P = 0.002).

DISCUSSION

The incidence of thyroid cancer has significantly increased in recent years. This increase appears to be related to the progress of diagnostic methods.[13,14] A number of researchers and consensus of the American Thyroid Association (ATA) provided the recommendation that the therapeutic strategies of well-differentiated thyroid carcinoma were divided into three stages: total or near-total thyroidectomy, post-operative radioiodine ablation, and thyroid hormone suppression.[14-17] Taking into account the evidence of published research, thyroid carcinoma therapy with a total thyroidectomy is more effective than the near-total thyroidectomy or subtotal thyroidectomy.[18]

Even with a more radical aim, removal of all thyroid tissue using total thyroidectomy still poses a number of residual tissues. The presence of residual thyroid tissue is an important sign of DTC recurrence. There are a number of different views and preferred imaging techniques among surgeons regarding the existence of a number of residual thyroid tissue after thyroidectomy. This difference may be based on the failure to identify

Table 1. Characteristics of patients

Variable	(n = 112)
Age (years ± SD)	43,4 ± 16,0
Male, n (%)	18 (16,1)
Female, n (%)	94 (83,9)
Tumour size (cm)	5,5 ± 1,6
Capsular invasion, n (%)	
Yes	60 (53,6)
No	52 (46,4)
Metastasis	
Yes	0 (0)
No	112 (100)
Scintigraphy (remaining thyroid tissue)	
Yes	97 (86,6)
No	15 (33,4)
Procedure, n (%)	
Near-Total Thyroidectomy	18 (16,0)
Total thyroidectomy	94 (84,0)

Table 2. Comparison of the presence residual thyroid tissue after surgery

Variable	Scintigraphy (residual tissue) n (%)		*p**
	No	Yes	
Tumor size (cm)			
< 5	9 (16,7)	45 (83,3)	**0,32**
≥ 5	6 (10,3)	52 (89,7)	
Gender			
Male	1 (5,6)	17 (94,4)	**0,28**
Female	14 (14,9)	80 (85,1)	
Age (Years)			
Group 1**	7 (13,5)	45 (86,5)	**0,98**
Group 2***	8 (13,3)	52 (86,7)	
Capsular invasion			
No	11 (18,3)	49 (81,7)	
Minor	3 (12,0)	22 (88,0)	**0,17**
Major	1 (3,7)	26 (96,3)	
Thyroidectomy			
Near total	3 (16,7)	15 (83,3)	**0,65**
Total	12 (12,7)	82 (87,3)	
Risk group			***p****
Low risk	15 (20,5)	58 (79,5)	**0,002**
High risk	0 (0)	39 (100)	

**Chi-square test; **Group 1, Male age < 51 years or Female < 41 years; ***Group 2, Male age ≥ 51 years or Females ≥ 41 years*

the superior extension of the thyroid pole or pyramid lobe or the difficulty of dissection on the area surrounding the Berry ligament. Excessive dissection in a number of where there are many nerves will tend to cause nerve damage Thyroid capsules that have decreased integrity in the middle, and lateral ectopic normal thyroid tissue make it difficult to be fully recognized during the surgical process. One factor of the perfection of thyroid resection is the amount of volume raised by the surgeon. Extensive thyroidectomy performed will be much more perfect if removal is performed at a higher volume.[19,20]

In this study, total thyroidectomy was conducted on 94 (84.0%) cases. Cayir D et al. in an observational study conducted in Turkey found that total thyroidectomy was performed in the majority of patients with well-differentiated thyroid carcinoma, which was 91% (169/183 patients).[21] Meanwhile, the remaining thyroid tissue found in our research was found at 97 (86.6%). These results were also found in studies conducted by Silva et al. The researcher found that 62% of patients were found to have residual thyroid tissue after thyroidectomy based on thyroglobulin examination.[15]

Identification of residual thyroid tissue after total thyroidectomy in patients with well-differentiated thyroid carcinoma is very important to estimate the dose of radioiodine ablation.[22] To evaluate the remaining thyroid tissue, iodine (I)-131 or I-123 will be used postoperatively.[21-23]

Several previously published studies have shown that many factors such as age, sex, capsular invasion, tumor degrees, extra thyroid expansion, lymphatic node metastasis, and the number of tumor volume removed will affect the effectiveness of therapy, tumor recurrence, and long-term prognosis.[15,16,24,25]

Well-differentiated thyroid cancer is the only type of cancer in humans that involves age at staging parameters. Shaha reported that age seemed to be the most important factor in patients with well-differentiated thyroid cancer.[24,26] In this study, 60 (53.5%) patients were ≥ 41 years old in females and ≥ 51 years old in men. Although there is a gender disparity, there is no connection between the gender and the presence of thyroid tissue. Many studies have found that the expansion of extra thyroid tumors and capsule invasion without extra thyroid expansion are independent prognostic factors for the presence of residual tissue and/or recurrence. Total thyroidectomy and radioiodine ablation should be performed in cases with these factors.[27,28] In this study, the capsular invasion was found in 52 (46.4%) patients with well-differentiated thyroid carcinoma. These results are slightly more than the study conducted by Husseini, in which 26 (13.2%) patients with well-differentiated thyroid carcinoma.[29] These results were also found by Bai et al. who found capsular invasion in 20 (19%) patients with well-differentiated thyroid carcinoma.[30]

There is a significant correlation between risk groups and the presence of residual thyroid tissue after thyroidectomy. The presence of residual thyroid tissue remains significantly more in patients at high risk. These results are similar to those found by Cayir et al. The study is an observational study conducted in 183 patients with well-differentiated thyroid carcinoma who underwent thyroidectomy.[21] As a result, patients who are at intermediate and high risk significantly more often exhibit the presence of residual thyroid tissue after thyroidectomy. This study also found that capsular invasion, lymph nodes metastatic, and extrathyroidal expansion were not independent prognostic factors against residual thyroid tissue.[18]

However, until now, there is still little literature that makes the same comparison with this study. Therefore, studies with a larger number of samples are needed to determine factors that influence the presence of post-thyroidectomy thyroid residual tissue in patients with well-differentiated thyroid carcinoma.

CONCLUSION

Residual thyroid tissue posts near-total or total thyroidectomy is significantly associated with high-risk groups patients well-differentiated thyroid carcinoma.

COMPETING INTERESTS

The authors declare no competing interest.

AUTHORS' CONTRIBUTIONS

Yufriadi Yunus: study concept. Salman Ardi Syamsu and John Pieter Jr.: Data collection, Writing-Original draft preparation. Rudy Thabry: senior author and the manuscript reviewer.: Indra and Elridho Sampepajung: reviewed the manuscript.: Yufriadi Yunus: Editing, Writing.: Yufriadi Yunus: Data curation.

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ETHICAL APPROVAL

The ethical approval of this study was granted from Ethical Committee, Faculty of Medicine, Hasanuddin University Makassar, Indonesia.

CONSENT

Written informed consent was obtained from the patient for publication of this research

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