

DIAGNOSTIC VALIDITY OF CYTOLOGICAL IMPRINT IN THYROID FOLLICULAR NEOPLASM

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Background: Preoperative fine needle aspiration biopsy/FNAB examination, imprint cytology and frozen section intraoperative has big implications for diagnosis and surgical strategy of thyroid nodules with follicular neoplasm cytology. FNAB and frozen section has its limitations, it is difficult to detect the presence of capsular and/or vascular invasion of thyroid follicular carcinoma. Whereas imprint cytology can preserve cellular overview (especially the cell nucleus), including the capsular and/or vascular invasion. In addition, imprint cytology is faster than frozen section. Frozen section examination could not indicate the presence of capsular and/or vascular invasion in most cases so that imprint cytology is used to replace frozen section as an alternative. **Method:** This research is a diagnostic test study using a descriptive design. This is a prospective study to assess the sensitivity, specificity, NPV, and PPV of imprint cytology in patients with thyroid follicular neoplasm cytology. **Results:** In our study; sensitivity, specificity, PPV, NPV, and accuracy of imprint cytology for follicular neoplasm was found as 84.21%, 95.45%, 94.12%, 87.50% and 90.24% respectively. The outcome was based on likelihood ratio value of 18.21 and the ROC curve, area under the curve obtained at 0.879 and Kappa value of 0.802. **Conclusion:** Imprint cytology has a value of a good diagnostic validity in the diagnosis of follicular neoplasm of thyroid nodules with sensitivity and specificity values of 84.21% and 95.45%. Imprint cytology is a technique that is simple, inexpensive, and has good reliability so that it can be used instead of frozen section.

Keywords: frozen, section, imprint, cytology, follicular, neoplasm

INTRODUCTION

Thyroid carcinoma is rare, the incidence rate worldwide about 4 per 100,000 population per year, contributing less than 1% of all malignancies and only 0.5% from cancer deaths (1). Although thyroid carcinoma is generally a disease with slow progression, with a mortality rate of about 6 per one million inhabitants, the tumors that are small (diameter <1.5 cm) often show no lymph node involvement and distant metastases can cause death.²

Of all thyroid carcinomas, the most common is papillary thyroid carcinoma, including 70% -80% of all well differentiated thyroid carcinoma. Next, followed by follicular thyroid carcinoma, including

Hürthle cell subtypes, and medullary thyroid and anaplastic thyroid carcinoma (Table 1).³⁻⁵

Table 1
Relative Percentage of Thyroid Carcinoma
Histopathology.³

Histopathological Type	Relative Percentage (%)
Papillary carcinoma	70-80
Follicular carcinoma	10-15
Medullary carcinoma	5-10
Anaplastic carcinoma	2-10
Poorly Differentiated carcinoma	1-10

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Management of thyroid disorders has undergone many changes, ranging from removal of all solitary thyroid nodules to use a selective approach based on clinical assessment and noninvasive cytological examination (fine needle aspiration biopsy, or FNAB).^{6,7} Controversial issues in thyroid carcinoma are diagnostic investigation and the scope of thyroidectomy. This is basically

due to fears of a malignant lesion in solitary thyroid nodules with surrounding benign abnormalities. A more cautious and selective in the diagnosis and management of thyroid nodules has contributed greatly to the increase in diagnosis of thyroid carcinoma in a single thyroid nodules surgery (from approximately 15% to 50%) and reduced unnecessary surgery on a benign thyroid nodules.⁸

Faquin (2008) stated that Fine Needle Aspiration the biopsy (FNAB) cannot distinguish between thyroid follicular carcinoma and thyroid follicular adenoma. Diagnosis of follicular thyroid carcinoma is determined by the presence of capsular invasion overview and / or vascular and cannot be detected by FNAB. Both diagnoses should be distinguished because of different operative management strategies. Thus, it takes an alternative diagnosis by examination of intra operative frozen section and imprint cytology.

Frozen section examination has its disadvantages and are not always able to detect the presence of capsular invasion and/or vascular because of the freezing process can damage the tissue. Whereas imprint cytology can preserve cellular image (especially nucleus), including the capsular invasion and / or vascular (9). In addition, the procedure in making imprint cytology samples faster than frozen section.¹⁰ Despite imprint cytology is better than frozen section, there is currently no consensus on diagnostic use of thyroid follicular neoplasms.

To date, the Department of Surgical Oncology Sanglah General Hospital Bali-Indonesia use frozen section for intraoperative evaluation in the case of thyroid nodules in FNAB showed thyroid follicular neoplasm. However, from experience, in most the case, frozen section can not indicate the presence of capsular invasion and / or vascular. Therefore, the department attempting to use imprint cytology to replace frozen section as an alternative.

Based on the facts above, the authors are interested to see the diagnostic validity of imprint cytology in thyroid follicular neoplasms.

PATIENTS AND METHOD

This is a descriptive diagnostic test study design of 41 patients with thyroid follicular neoplasm. It is a prospective study to determine the sensitivity, specificity, NPV, PPV of cytological imprint on patients presenting with follicular thyroid neoplasm in Sanglah General Hospital Bali-Indonesia from October 2011 – March 2012. All patients signed informed concern and ethical clearance was obtained from local committee ethic. No mall practice observed in this study.

Patients with follicular neoplasm diagnosis from the fine needle biopsy who came to Oncology Surgery Department of Sanglah Hospital underwent preoperative management according to the protocol

of the Oncology Surgery Department of Sanglah Hospital. Samples were collected prospectively intra-operative using cytology imprint. The thyroid tissue obtained from the surgery was sent to Department of Pathology Anatomy, Sanglah General Hospital. The results from cytological imprint were compared with pathology examination to evaluate the sensitivity, specificity, NPV, PPV.

Collected data were descriptively presented to show sample characteristic. Then analyzed using 2x2 table to obtain accuracy, sensitivity, specificity, NPV, PPV.

RESULTS

There were 41 samples that met the inclusion criteria from 2011 until 2012. 10 samples (24.4%) were male and 31 samples (75.6%) were women. Range of ages ranging from 14 years to 70 years with an average age of 43.88 years (SD ± 11.936 years). Of the 41 samples is distributed into Hashimoto thyroiditis one sample (2.4%), 23 follicular adenoma (56.1%), 9 papillary carcinoma (22.0%), 3 Hurthle Cell carcinoma (7.3%), and 5 follicular variant of papillary carcinoma (12.2%) (Table 2).

Table 2
Cytological Imprint Results

Cytological Imprint Results	n (%)
Hashimoto Thyroiditis	1 (2,4)
Follicular Adenoma	23 (56,1)
Papillary Carcinoma	9 (22,0)
Hurthle Cell Carcinoma	3 (7,3)
Follicular Variant Papillary Carcinoma	5 (12,2)
Total	41 (100)

Table 3 shows the histopathological results of 41 samples. There is 1 sample (2.4%) as Hashimoto thyroiditis, 21 samples (51.2%) as follicular adenomas, one sample (2.4%) follicular carcinomas, eight samples (19.5%) follicular variant of papillary carcinoma, one sample (2.4%) Hurthle Cell carcinoma, and nine samples (22.0%) papillary carcinomas.

Table 3
Histopathological Results

Histopathological Results	n (%)
Hashimoto Thyroiditis	1 (2,4)
Follicular Adenoma	21 (51,2)
Follicular Carcinoma	1 (2,4)
Papillary Carcinoma	9 (22,0)
Hurthle Cell Carcinoma	1 (2,4)
Follicular Variant Papillary Carcinoma	8 (19,5)
Total	41 (100)

Table 4 showed that cytological imprint yields malignant positive result in 16 samples (39.0%), all of which also had malignant positive histopathological result. Therefore the true positive value for cytological imprint was 16 (94.1%) and the false positive value for cytological imprint was 1 (5.9%). Cytological imprint showed 21 samples (51.2%) with benign result, therefore the true negative value for cytological imprint was 21 (87.5%) and the false negative value for cytological imprint was 3 (12.5%). Of 17 samples with malignant imprint cytology results, there is one false positive sample (5.88%). The imprint cytology samples showed Hurthle cell carcinoma with histopathologic results showed follicular adenoma. Of 24 samples with benign imprint cytology results, there were three false-negative samples (12.5%). Of the three false negative samples, two showed histopathological results of follicular variant papillary carcinomas and one sample showed histopathology results of papillary carcinoma.

Table 4
A 2x2 Table Between Cytological Imprint and Histopathological Results

		Histopathology		Total
		Malignant	Benign	
Cytological Imprint	Malignant	16	1	17
	Benign	3	21	24
Total		19	22	41

Based from the previous table, the sensitivity value of cytological imprint was 84.21%, specificity value was 95.45%, positive predictive value was 94.12%, negative predictive value was 87.50%, and cytological imprint accuracy was 90.24%.

Based on the ROC, area under the curve obtained at 0.879 (AUC >0.5) (Figure 1). Kappa value of 2x2 tabulation between imprint cytology and histopathology was 0.802 (Kappa >0.75).

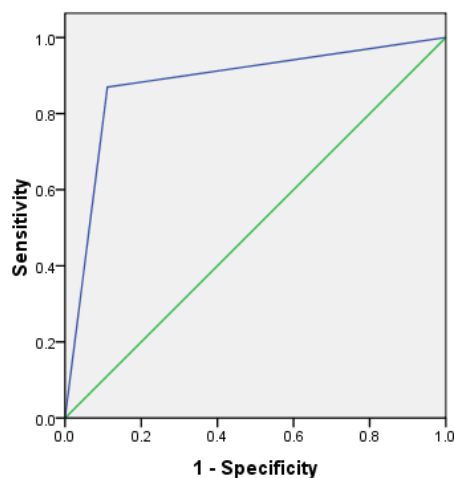


Figure 1

ROC with AUC of 0,879 (area under curve > 0,5).

DISCUSSION

Preoperative FNAB, imprint cytology and intraoperative frozen section has major implications for diagnosis and surgical strategies cytology of thyroid nodules with follicular neoplasm. FNAB has a major limitation. It is difficult to determine capsular and / or vascular invasion of follicular thyroid carcinoma.¹¹

While intraoperative frozen section examination has a low sensitivity due to tissue coagulation process can damage cell nucleus organelles,¹² are not always able to detect the presence of capsular and / or vascular invasion (13), and the making of prepare is time consuming and relatively expensive. Frozen section that is conducted Department of Surgical Oncology, Sanglah General Hospital cannot demonstrate that capsular and / or vascular invasion in most cases.

Intraoperative imprint cytology has several advantages. It can describe the size and forms of the cell, detect the presence of capsular and / or vascular invasion and procedures to make prepare is faster than frozen section.¹⁰

In this research, 41 samples met the inclusion criteria. Of 23 samples of follicular adenoma on imprint cytology, three samples showed a carcinoma (Table 5.3.). Two of the three samples was a follicular variant of papillary carcinoma and one papillary carcinoma. Three imprint cytology samples are Hurthle cell carcinoma and only one sample that demonstrate histopathologic results Hurthle cell carcinoma. Other two samples are follicular carcinoma and follicular adenoma. This is due to the difficulty of detecting the invasion of capsular and / or vascular. Sensitivity, specificity, PPV, NPV, and accuracy of imprint cytology was 84.21%, 95.45%, 94.12%, 87.50%, and 90.24% respectively. Numerous studies also get the sensitivity, specificity, and accuracy of imprint cytology were high (Table 5).

Table 5
Sensitivity, Specificity, and Accuracy of Cytological Imprint

Author	Accuracy	Sensitivity	Specificity
Taneri et al. (2001)	96%	83.3%	97.7%
Mutaharra et al. (2001)	96%	84.0%	93.07%
Tworek et al. (1998)	82.55%	94.11%	71%
Das et al. (1999)	71.15%	85.0%	100%
Pustaka et al (2011)	90,24%	84,21%	95,45%

Author obtained accuracy of imprint cytology was 90.24%, this value is lower than those obtained by Taneri et al. (2001) and Mutaharra et al. (2001). But author obtained accuracy value was higher than those obtained by Das et al. (1999) and Tworek et al. (1998). Sensitivity of imprint cytology is 84.21%, a similar result was also obtained Taneri et al. (2001), Mutaharra et al. (2001), and Das et al. (1999). Specificity of imprint cytology in this study is 95.45%, which is higher than result obtained Tworek et al. (1998), and Mutaharra et al. (2001). PPV and NPV results in this study is 94.12% and 87.50% respectively. Taneri et al. (2001) obtained PPV and NPV of 83.3% and 97.7%.

The difference of accuracy, sensitivity, and specificity in this research are most likely caused by differences in total sample size and inclusion criteria. In this study, we only used patients with follicular neoplasm from fine needle biopsy while other studies included all patients with thyroid nodule, irrespective of the fine needle biopsy results.

CONCLUSION

Diagnostic validity of imprint cytology in follicular neoplasm had a high value with the sensitivity and specificity of 84.21%, and 95.45%. It can be seen from the results of likelihood ratio 18.21 and the ROC curve shows the results of area under the curve of 0.879, Kappa value of 0.802.

Imprint cytology is simple, inexpensive, and has good reliability so that it can be used as a substitute for frozen section. This is a preliminary study, further research is required in which the imprint cytology compared with frozen section on follicular neoplasm.

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