Journal of the Medical Sciences
(Berkala Ilmu Kedokteran)

Volume 51, Number 3, 2019; 237-245
http://dx.doi.org/10.19106/JMedSci005103201907

The accuracy of fine needle aspiration biopsy to diagnose breast neoplasm

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Submited: 2017-02-03
Accepted : 2019-08-20

ABSTRACT

Breast lump is a very common complaint among women, especially during the reproductive year. Fine needle aspiration biopsy (FNAB) is a less invasive procedure. It is usually performed as an initial diagnosis prior to the operative procedure. The accuracy of the FNAB in Indonesia needs to be elaborated. The study aimed to evaluate the sensitivity and specificity of FNAB in diagnosing breast neoplasm. This is a retrospective study with cross sectional design, involving 145 patients with breast lump who underwent FNAB and histopathology examination in Dr. Sardjito General Hospital, Yogyakarta, from 2012 to 2014. Data analysis showed that female to male ratio was 23. 2:1 commonly occurred at 41-50 years old. Forty-one cases (28.28%) diagnosed as a benign lesion with fibrocystic changes as the most frequentcase (11.19%). The malignant case was 104 cases (71.72%) with ductal carcinoma as the highest case (51.49%). FNAB achieved a sensitivity of 85.58%, a specificity of 100% and a total accuracy of 89.66% in determining the benign or malignant breast lump. The accuracy, sensitivity and specificity of FNAB in diagnosing ductal carcinoma were 83.58%, 85.51% and 81.54%, respectively. The accuracy, sensitivity and specificity of FNAB to diagnose fibrocystic changes lesion were 85.82%, 26.67% and 93.28%, respectively. FNAB can be used as an alternative diagnostic tool to diagnose breast neoplasm. It provides rapid, cheaper, effective, valuable, and less invasive procedure in diagnosis of breast lump.

ABSTRAK

Benjolan payudara adalah keluhan yang sangat umum pada wanita, khususnya selama usia reproduktif. Biopsi aspirasi jarum halus (BAJAH) merupakan prosedur yang kurang invasif, biasanya dilakukan sebagi diagnosis awal sebelum prosedur operasi. Keakuratan BAJAH di Indonesia perlu dijabarkan lagi lebih dalam. Penelitian ini bertujuan untuk mengevaluasi sensitivitas dan spesifitas BAJAH dalam mendiagnosis neoplasma payudara. Studi ini menggunakan rancangan penelitian *retrospective cross-sectional*, melibatkan 145 pasien dengan benjolan payudara yang menjalani BAJAH dan pemeriksaan histopatologi di RSUP Dr. Sardjito, Yogyakarta, dari tahun 2012-2014. Analisis data menunjukkan bahwa rasio perempuan disbanding laki-laki adalah 23, 2:1, umumnya terjadi pada usia 41-50 tahun. Empat puluh satu kasus (28,28%) didiagnosis sebagai lesi jinak dengan perubahan fibrokistik sebagai kasus yang paling sering terjadi (11,19%). Kasus ganas sebanyak 104 kasus (71,72%) dengan karsinoma duktus sebagai kasus tertinggi (51, 49%). BAJAH mencapai sensitivitas 85,58%, spesifitas 100% dan akurasi total 89,66% dalam menentukan benjolan payudara jinak atau ganas. Keakuratan, sensitivitas, dan spesifisitas BAJAH dalam mendiagnosis lesi perubahan fibrosistik adalah 85,82%. 26,67%, dan 93,28%. BAJAH dapat digunakan sebagai alat diagnostic alternative untuk mendiagnosis neoplasma payudara. Prosedur ini cepat, murah, efektif, berharga dan kurang invasive dalam diagnosis dari benjolan payudara.

Keywords:
FNAB,
breast lump,
sensitivity,
specificity,
diagnosis

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INTRODUCTION

Breast lump is a very common complaint among women, especially during the reproductive year.[1] Although breast lumps are often caused by benign (non-cancerous) conditions, however 10-20% of them are cancerous.[2-4] Since 2008, the incidence of breast cancer has increased more than 20% worldwide and its mortality has increased 14%. The incidence rates remain high in developed countries while mortality rate are higher in developing countries due to lack of early detection and access to treatment facilities.[5] If breast cancer can be detected and managed earlier, the chance of being cured will be higher and the mortality will be reduced.[3,6]

Fine needle aspiration biopsy (FNAB) is one of the biopsy procedures known to have the easiest technique and fewer complications.[7,8] It is a procedure in which fine needle used to aspirate cellular material from a mass then the cytological diagnosis is rendered.[9] Moreover, FNAB also can also save time and equipment.[10] However, FNAB has some limitation regarding bad sampling technique, specimen inadequacy, aspirator skills, interpretation error, and overlapping features between lesions.[7] Those diagnostic pit falls may lead to false positive or false negative result.[11] We aimed to show the effectiveness and accuracy of the FNAB in the breast lump diagnosis, in determining benign or malignant lesion, by showing the disparity of the cytological and histopathology result.

MATERIALS AND METHODS

Study design

This study was a descriptive non-experimental study with retrospective cross sectional design. It involved 145 breast lump patients who underwent FNAB and histopathology examination in the Department of Anatomical Pathology, Dr. Sardjito General Hospital, Yogyakarta from January 2012 to December 2014.

Protocol

The secondary data were collected from the medical record of the patient from 1st January 2012 until 31st December 2014. All breast lump patients underwent FNAB and the cytological diagnosis was categorized as benign or malignant lesion according to WHO classification standard. The FNAB result then compared with the histopathology result which was considered as the gold standard.

Data analysis

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy in breast lump diagnosis were calculated. Patients with incomplete data were excluded. Statistical analysis was performed using Microsoft Excel and SPSS software.

RESULTS

There were 145 cases included in this study, 139 cases (95.86%) were female and 6 cases (4.14%) were male, with female to male ratio of 23.2:1. The age ranged from 18 to 74 years, with the peak incidence in age ranged from 41 to 50 years old. From all case, 41 cases (28.28%) were benign and 104 cases (71.72%) were malignant, consisting of 69 cases (51.49%) of ductal carcinoma, 15 cases (11.19%) of fibrocystic changes, 12 cases (8.96%) of lobular carcinoma, 10 cases (7.46%) of fibroadenoma, 6 cases (4.48%) of mastitis granulomatosa, 5 cases (3.73%) of malignant phyllodestumor, 3 cases (2.24%) of ductulo-lobular carcinoma, 3 cases (2.24%) of metaplastic carcinoma, 2 cases (1.49%) of benign phyllodestumor, 2 cases (1.49%) of non-

hodgkin lymphoma, 1 case (0.75%) of atypical lobular hyperplasia, 1 case (0.75%) of paget's disease, 1 case (0.75%) of lactating carcinoma, 1 case (0.75%) of gynecomastia, 1 case (0.75%) of fibrosarcoma, 1case (0.75%) of mucinous carcinoma, and 1 case (0.75%) of fibrosis (TABLE 1).

TABLE 1. Breast lump incidence distribution in Dr. Sardjito General Hospital Yogyakarta 2012-2014 based on age, sex, lesion and pathological diagnosis

Characteristic	Frequency	%
Gender		
• Female	139	95.86
• Male	6	4.14
Age		
• <16 years old	0	0
• 16-20 years old	4	2.84
• 21-30 years old	12	8.51
• 31-40 years old	28	19.86
• 41-50 years old	51	36.17
• 51-60 years old	33	23.4
• 61-70 years old	9	6.38
• >70 years old	4	2.84
Lesion		
• Benign	41	28.28
• Malignant	104	71.72
Pathological diagnosis		
• Ductal carcinoma	69	51.49
• Fibrocystic changes	15	11.19
• Lobular carcinoma	12	8.96
• Fibroadenoma	10	7.46
• Mastitis granulomatosa	6	4.48
• Malignant phyllodes tumor	5	3.73
• Ductulo-lobular carcinoma	3	2.24
• Metaplastic carcinoma	3	2.24
• Benign phyllodes tumor	2	1.49
• Non Hodgkin lymphoma	2	1.49
• Atypical lobular hyperplasia	1	0.75
• Paget's disease	1	0.75
• Lactating carcinoma	1	0.75
• Gynecomastia	1	0.75
• Fibrosarkoma	1	0.75
• Mucinous carcinoma	1	0.75
• Fibrosis	1	0.75

The result of FNAB was compared with histopathology result in determining the type of lesion and the histopathology diagnosis. From the cytological examination, 89 cases (71.72%) diagnosed as the malignant lesion, all of them (100%) confirmed as malignant (confirmed with the histopathology result). From 56 cases (38.62%) benign lesion diagnosed by FNAB, 41 cases (73.21%) proofed to be benign and 15 cases (26.79%) were confirmed as malignant by histopathology analysis. Thus, FNAB achieved a sensitivity of 85.58%, specificity of 100%, positive predictive value of 100%, negative predictive value of 73.21%, and a total accuracy of 89.66% (TABLE 2). Furthermore, sensitivity and specificity of FNAB in determine breast lump histopathology diagnosis respectively 82.5% and 70.3% (FIGURE 1); with a total accuracy of 65.67%.

TABLE 2. Sensitivity and specificity of FNAB for determine the type of lesion

Variable		Histopathology		Total
		Malignant	Benign	
FNAB	Malignant	89	0	89
	Benign	15	41	56
	Total	104	41	145

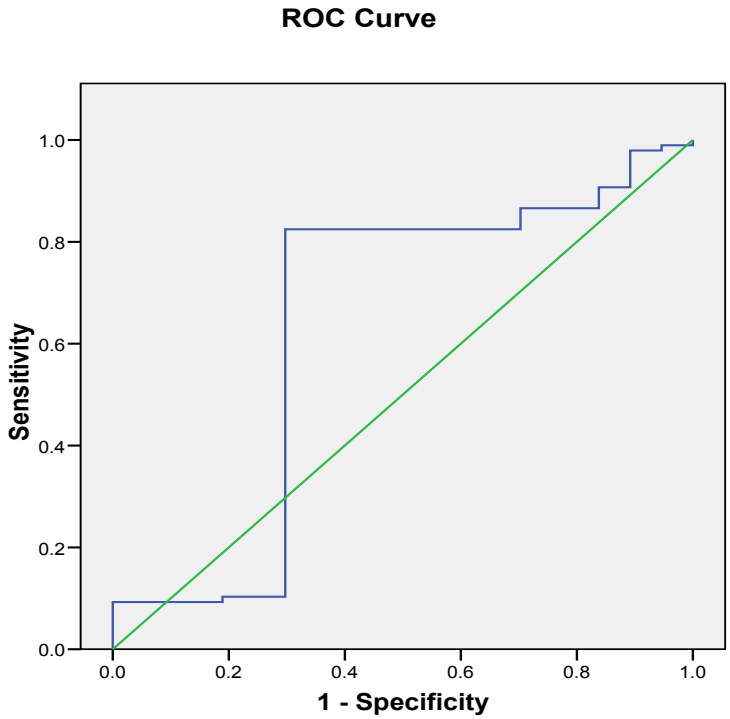

FIGURE 1. Sensitivity and specificity of FNAB for determine breast lump histopathology diagnosis

Ductal carcinoma was the most common case found in this study. Of the included 71 cases cytologically diagnosed as ductal carcinoma, 59 cases (83.1%) confirmed as ductal carcinoma and 12 cases (16.9%) confirmed as other cases by histopathology examination. Those false positive were 7 cases (58.33%) as lobular carcinoma, 2 cases (16.67%) as metaplastic carcinoma, 1 case (8.33%) as atypical lobular hyperplasia, 1 case (8.33%) as mucinous carcinoma and 1 case (8.33%) as ductulo-lobular carcinoma. Hence, in diagnosing ductal carcinoma, FNAB reached a sensitivity of 85.51%, specificity of 81.54%, positive predictive value of 83.1%, negative predictive value of 84.13%, and a total accuracy of 83.35% (TABLE 3).

TABLE 3. Sensitivity and specificity of FNAB for ductal carcinoma diagnosis

Variable		Histopathology		Total
		Ductal carcinoma	Others	
FNAB	Ductal carcinoma	59	12	71
	Others	10	53	63
	Total	69	65	134

The second most common malignant case found in this study was lobular carcinoma. From cytology diagnosis, 6 cases diagnosed as lobular carcinoma, 2 cases proved as lobular carcinoma by histopathology examination, and 4 remaining cases missed diagnosed. Those remaining cases were 1 case (25%) as diffuse non-Hodgkin lymphoma, 1 case (25%) as ductal carcinoma, 1 case (25%) as lactating carcinoma, and 1 case (25%) as ductulo-lobular carcinoma. Therefore, in diagnosing lobular carcinoma, FNAB had a sensitivity of 16.67%, specificity of 96.72%, positive predictive value of 33.33%, negative predictive value of 92.19%, and a total accuracy of 89.55% (TABLE 4).

TABLE 4. Sensitivity and specificity of FNAB for lobular carcinoma diagnosis

Variable		Histopathology		Total
		Lobular Carcinoma	Others	
FNAB	Lobular carcinoma	2	4	6
	Others	10	118	128
	Total	12	122	134

The most common benign lesion found in this study was fibrocystic changes. Twelve cases were cytologically diagnosed as fibrocystic changes, 4 of them (33.33%) proved histologically, meanwhile 8 of them (66.67%) falsely diagnosed with 5 cases (62.5%) of ductal carcinoma, a case (12.5%) of benign phyllodestumor, a case (12.5%) of gynecomastia, and a case (12.5%) of fibroadenoma. In diagnosing fibrocystic lesion, FNAB showed a sensitivity of 26.67%, specificity of 93.28%, positive predictive value of 33.33%, negative predictive value of 90.98%, and a total accuracy of 85.82% (TABLE 5).

TABLE 5. Sensitivity and specificity of FNAB for fibrocystic changes diagnosis

Variable		Histopathology		Total
		Fibrocystic Changes	Others	
FNAB	Fibrocystic changes	4	8	12
	Others	11	111	122
	Total	15	119	134

Fibroadenoma was the second most frequent benign lesion found in this study. Sixteen cases revealed as fibroadenoma through cytology examination. Histopathologicaly, 9 of them (56.25%) were confirmed as fibroadenoma, and 7 cases (43.75%) were confirmed as non-fibroadenoma lesion. The false positive cases were confirmed 4 cases (57.14%) as fibrocystic lesion, 1 case (14.29%) as lobular carcinoma, 1 case (14.29%) as ductal carcinoma and 1 case (14.29%) as ductulo-lobular carcinoma. In diagnosing fibroadenoma, FNAB attained a sensitivity of 90%, specificity of 94.35%, positive predictive value of 56.25%, negative predictive value of 99.15%, and a total accuracy of 94.03% (TABLE 6).

TABLE 6. Sensitivity and specificity of FNAB for fibroadenoma diagnosis

Variable		Histopathology		Total
Fibro Adenoma		Others		
FNAB	Fibroadenoma	9	7	16
	Others	1	117	118
	Total	10	124	134

DISCUSSION

There are some diagnostic tools that can be used to diagnose the breast lump; such as breast ultrasound, mammogram, magnetic resonance imaging (MRI), histopathology examination and biopsy.[12] Biopsy is considered as the only diagnostic procedure that can definitely determine whether the suspicious area is either benign or malignant lesion.[13] FNAB was the first percutaneous needle sampling technique introduced as in alternative for surgical biopsy.[14] This procedure is generally accurate and can prevent patient from having surgical biopsy that is more painful and expensive.[15]

As reported in other literature, age and gender were associated factors of the breast lump.[3] In the present study, there was a female predominance with female to male ratio of 23.2:1 and mostly occurred in the age range from 41-50 years old. These factors were related to hormone exposure, other factors than age and gender such as reproductive history, breastfeeding, alcohol, body weight, physical activity, exogenous hormone, endogenous hormone, radiation exposure, and exposure to the chemical with estrogen-like effects.[3,5]

Unlike other literature that states the benign cases presented as the majority of cases, this study showed that most of the cases were malignant lesion.[1-3] This study

was conducted in referral hospital; these might become the main reason why we found more malignant cases. Ductal carcinoma became the most frequent malignant lesion (51.49%), followed by lobular carcinoma with the incidence of 8.96%. Meanwhile, the first and second most common cases for benign lesion were respectively fibrocystic change (11.19%) and fibroadenoma (7.46%). In our series, analysis of data revealed sensitivity of 85.58%, specificity of 100%, positive predictive value of 100%, negative predictive value of 73.21%, and a total accuracy of 89.66%. Our results were comparable with published data where FNAB was reported to have sensitivity of 98%, specificity of 100%, positive predictive value of 97%, negative predictive value of 100% and a total accuracy of 98%.[16] There is a wide range difference in the determinant factor. It might be due to the different number of cases and interpretation error. The diagnostic test is useful to detect a person with the disease or exclude a person without the disease. In this case, the result of the test is high in sensitivity, means will help to rule out malignancy if the result rendered benign. Moreover, the result of the test is high in specificity also, means it will help to rule in the malignancy if the result rendered malignant.[17]

Previous report revealed FNAB sensitivity of 93.6%, specificity of 95%,positive predictive value of 99%, negative predictive value of 73% and a total accuracy of 94%.[18] Theoretically, ideal diagnostic test has both 100% sensitivity and specificity; however those were not realized in real settings.[19] Sensitivity and specificity are inversely proportional, means when the sensitivity increase then the specificity will decrease and vice versa.[20] The false negative rate (FNR) is defined as percentage of patients with benign cytology which turned out to be malignant after confirmed histopathologicaly.[21,22] This is an important point to be concerned since it indicates the potential of miss malignant feature. The false negative FNAB results may occur due to both diagnostic errors and true false negative factors.[23] Diagnostic errors include the skills and experience of aspirator, overload of cases, miscorrelation with the patient's clinical and radiologic findings, and interpretation error. True false negative factors consist of sampling error, missed localization of tumor and cytomorphologic overlapping.[11,23]

The false positive rate (FPR) indicates that a patient with malignant FNAB result was found on histological examination to have benign lesion.[21,22] False positive diagnosis in aspiration cytology is significantly lower in incidence compared to false negative cases.[24] False positive happened usually because of an interpretation error.[11] In our study, the FPR was 0% which similar to other studies.[24] In determining specific diagnosis, FNAB was highly sensitive in diagnosing ductal carcinoma and fibroadenoma (85.51% and 90%). However, we could still find some false positive and false negative result. False positive mostly appeared due to interpretation error such as it was tough to have lesion interpretation. Meanwhile, false negative usually occurred due to sampling and interpretation error, especially when involving types of pathology that known to be difficult such as lobular carcinomaand fibrocystic changes.[11]

CONCLUSION

In conclusion, the result of the study is comparable with the published data and it shows that FNAB is highly sensitive and specific diagnostic tools, thus FNAB can be used as an alternative diagnostic tool. FNAB has high accuracy in determining benign or malignant breast

lump as it provides rapid, economical (cheaper), effective, valuable and less invasive diagnostic tools.

ACKNOWLEDGEMENTS

We would like to thanks and gratitude all the patients who the data used in this study. We would also want to thanks all the parties who give contributions in this study.

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