The accuracy of fine needle aspiration biopsy to diagnose breast neoplasm

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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 frequent case (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 sebagai 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 dibanding 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 dukus 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 spesifititas 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, 1 case (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     | 89             | 0     | 89    |
|          | 15             | 41    | 56    |
| Total    | 104            | 41    | 145   |

![ROC Curve](image)

**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 positives 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 |            |            |
|----------------|----------------|------------|------------|
|                | Ductal Carcinoma | Others | Total    |
| FNAB           | 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乳状 carcinomas, 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 |            |            |
|-----------------|----------------|------------|------------|
|                 | Lobular Carcinoma | Others | Total    |
| FNAB            | 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 phyllodes tumor, 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 |        |        |        |
|-----------------------|----------------|--------|--------|--------|
|                       | Fibro cystic   | Others | Total  |        |
| FNAB                  | changes        |        |        |        |
| Fibro cystic 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. Histopathologically, 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 |        |        |
|---------------------|----------------|--------|--------|
|                     | Fibro Adenoma  | Others | Total  |
| FNAB                |                |        |        |
| Fibro adenoma       | 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. Biopsy is considered as the only diagnostic procedure that can definitely determine whether the suspicious area is either benign or malignant lesion. FNAB was the first percutaneous needle sampling technique introduced as an alternative for surgical biopsy. This procedure is generally accurate and can prevent patient from having surgical biopsy that is more painful and expensive.

As reported in other literature, age and gender were associated factors of the breast lump. 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.

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. 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%. 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.

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%. Theoretically, ideal diagnostic test has both 100% sensitivity and specificity; however those were not realized in real settings. Sensitivity and specificity are inversely proportional, means when the sensitivity increase then the specificity will decrease and vice versa. The false negative rate (FNR) is defined as percentage of patients with benign cytology which turned out to be malignant after confirmed histopathologically. 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. 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.

The false positive rate (FPR) indicates that a patient with malignant FNAB result was found on histological examination to have benign lesion. False positive diagnosis in aspiration cytology is significantly lower in incidence compared to false negative cases. False positive happened usually because of an interpretation error. In our study, the FPR was 0% which similar to other studies. 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 carcinoma and fibrocystic changes.

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.

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REFERENCES

1. Saunders C. Breast lump and lesions. VMC 2014.
2. Wechter DG, Zieve D. ADAM. Inc. Breast Lump. University of Maryland Medical Center, 2013.
3. Kumar V, Abbas AK, Aster JC. Robbins and Cotran pathologic basis of disease 9th ed. Canada: Elsevier Saunders; 2015.
4. John Hopkins Medicine. What is Breast Biopsy? John Hopkins Medicine, 2015.
5. International Agency for Research on Cancer. Latest world cancer statistics global cancer burden rises to 14.1 million new cases in 2012: marked Increase in Breast Cancers must be addressed. Lyon: WHO, 2013.
6. Infodatin. Stop kanker. Jakarta: Kementerian Kesehatan RI. 2015.
7. American Cancer Society. Breast Cancer. American Cancer Society Inc. 2015.
8. Borecky N. Breast fine needle aspiration biopsy. The Royal Australian and New Zealand College of Radiologist; 2009.
9. Amedee RG & Dhurandhar NR. Fine needle aspiration biopsy. Laryngoscope 2001; 111(9):1551-7. https://doi.org/10.1097/00005537-200109000-00011
10. Millis RR. Needle biopsy of the breast. Monogr Pathol 1984; 1984(25):186-203. https://doi.org/10.1007/978-94-009-6589-8_7
11. Anonim. Breast fine needle aspiration cytology and core biopsy: a Guide for Practice.Camperdown (NSW). USA: National Breast Cancer Centre; 2004.
12. Anonim. How is breast cancer diagnosed? USA: Center for Disease Control and Prevention; 2014.
13. Anonim. Biopsy. USA: National Breast Cancer Foundation Inc.; 2012.
14. Calhoun KE, Anderson BO. Needle biopsy for breast cancer diagnosis: a quality metric for breast surgical practice. J Clin Oncol 2014; 32(21):2191-2. h t t p s : / / d o i . o r g / 1 0 . 1 2 0 0 / J CO.2014.55.6324
15. American Academy of Otolaryngology. Fine needle aspiration biopsy. American Academy of Otolaryngology- Head and Neck Surgery; 2015.
16. Bukhari MH, Arshad M, Jamal S, Niazi S, Bashir S, Bakhshi IM, et al. Use of fine-needle aspiration in the evaluation of breast lumps. Pathol Res Int 2011; 2011:689521. https://doi.org/10.4061/2011/689521
17. Akobeng AK. Understanding diagnostic test 1: sensitivity, specificity and predictive values. Acta Paediatr 2007; 96(3):338-41. h t t p s : / / d o i . o r g / 1 0 . 1 6 5 1 - 2 2 2 7 .2006.00180.x
18. Pradana JA, Sukarya WS. Nilai diagnostik pemeriksaan biopsi aspirasi jarum halus (BAJAH) dalam mendiagnosis kanker payudara yang dikonfirmasi dengan hasil pemeriksaan histopatologi (Suatu uji diagnostik di RSUD. Dr. Soedarso Pontianak Periode 2006-2010 [Program Kreativitas Mahasiswa (PKM)]. Bandung: Universitas Islam Bandung; 2011.
19. Department of Statistics Eberly College of Science. Medical diagnostic testing. Pennsylvania:
The Pennsylvania State University, 2015.
20. Parikh R, Mathai A, Parikh S, Sekhar GC, Thomas R. Understanding and using sensitivity, specificity and predictive value. Indian J Ophthalmol 2008; 56(1):45-50. https://doi.org/10.4103/0301-4738.37595
21. Sastroasmoro S, Ismael S. Dasar-dasar metodologi penelitian klinis. 4th edition. Jakarta: Sagung Seto; 2011.
22. Siswanto, Susila, Suyanto. Metodologi penelitian kesehatan dan kedokteran. 1st ed. Yogyakarta: Bursa Ilmu; 2014.
23. Mendoza P, Lacambra M, Tan PH, Tse GM. Fine needle aspiration cytology of the breast: the nonmalignant categories. Pathol Res Int 2011; 2011:547580. https://doi.org/10.4061/2011/547580
24. Sari K, Sulastri H, Maulani H, Rahadiyanto KY. Keakuratan diagnosis pemeriksaan sitologi aspirasi jarum halus pada tumor payudara di RSUP.Dr. Mohammad Hoesin Palembang. Majalah Patologi 2011; 20(2):1-5.