Original Article

J Korean Soc Radiol 2023;84(3):676-685
https://doi.org/10.3348/jksr.2022.0029
eISSN 2951-0805

JOURNAL of THE KOREAN SOCIETY of RADIOLOGY

Clustered Microcysts Detected on Breast US in Asymptomatic Women

무증상 여성의 유방초음파에서 발견된 군집 미세낭종

Hyun Jin Kim, MD[1], Jin Hwa Lee, MD[1]*, Young Mi Park, MD[2], Kyungjae Lim, MD[1]

[1]Department of Radiology, Dong-A University Medical Center, Dong-A University College of Medicine, Busan, Korea
[2]Department of Radiology, Busan Paik Hospital, Inje University College of Medicine, Busan, Korea

ORCID iDs
Hyun Jin Kim https://orcid.org/0000-0002-8403-9871
Jin Hwa Lee https://orcid.org/0000-0002-4855-9159
Young Mi Park https://orcid.org/0000-0001-7332-3853
Kyungjae Lim https://orcid.org/0000-0002-7622-2406

Received March 18, 2022
Revised August 13, 2022
Accepted September 20, 2022

***Corresponding author**
Jin Hwa Lee, MD
Department of Radiology,
Dong-A University Medical Center,
Dong-A University
College of Medicine,
26 Daesingongwon-ro, Seo-gu,
Busan 49201, Korea.

Tel 82-51-240-5368
Fax 82-51-253-4931
E-mail jhrad@dau.ac.kr

Purpose To investigate the incidence, outcomes, and imaging characteristics of clustered microcysts detected on breast US in asymptomatic women, and suggest appropriate management guidelines.

Materials and Methods We identified and reviewed the lesions recorded as "clustered microcysts" on breast US performed in asymptomatic women between August 2014 and December 2019. The final diagnosis was based on pathology and imaging follow-up results for at least 12 months.

Results The incidence was 1.5% and 100 patients with 117 lesions were included. Among 117 lesions, 3 (2.6%), 2 (1.7%), and 112 (95.7%) were malignant, high-risk benign, and benign lesions, respectively. The malignant lesions included two cases of ductal carcinoma in situ and one invasive ductal carcinoma. Two of them were assessed as category 4, showing mammographic suspicious microcalcifications and internal vascularity on Doppler US. The remainder was a false negative case and showed echo pattern change on the 12-month follow-up US.

Conclusion The incidence of clustered microcysts on breast US in asymptomatic women was 1.5% and malignancy rate was 2.6% (3 of 117). Knowledge of outcomes and imaging features of benign and malignant clustered microcysts may be helpful for radiologists, thereby aiding categorization and management recommendations.

Index terms Breast; Ultrasonography; Mass Screening; Breast Cyst

INTRODUCTION

Clustered microcysts are relatively common incidental finding detected on breast ultraso-

nography (US) and most often observed in women aged 39 to 50 years (1). According to American College of Radiology Imaging Network (ACRIN) 6666 experience, clustered microcysts were observed in 104 of the 2662 (3.9%) participants who underwent screening breast US (2). It is one form of benign cystic change in the breast and represents the terminal duct lobular unit (TDLU) or a portion of it, in which there is cystic dilatation of individual acini (3). Multiple acini within the TDLU are lined by bland or apocrine metaplastic epithelium (3, 4).

According to the American College of Radiology Breast Imaging Reporting and Data System (ACR BI-RADS) 5th edition, clustered microcysts are defined as clusters of anechoic foci, each less than 2–3 mm, which could have thin (< 0.5 mm) septations; however, they should not contain a discrete solid component and their margins should not be indistinct (2, 5). Nevertheless, individual microcysts can contain debris and manifest as low-level echoes or fluid-debris levels (2, 5). Several prior studies included lesions with individual microcysts of up to 5–7 mm (1, 2, 6, 7).

Based on the BI-RADS 5th edition in 2013, the guidelines for management of clustered microcysts are as follows: when a microlobulated or oval mass composed of small simple cysts is observed on sonography, category 2 assessment (benign) may be appropriate. When clustered microcysts are small or deep, for which diagnostic certainty is reduced, category 3 (probably benign) assessment and recommendation for short-term imaging surveillance may be appropriate. However, it states "The relatively small number of cases studied limits precision in estimating the likelihood of malignancy to be ≤ 2%; the data would be more convincing if at least 500 cases were studied" (5). Since then, several additional studies have reported the outcomes of clustered microcysts and more than 500 cases across multiple studies have been now published (1, 2, 6-12). However, they were the results from diagnostic breast US, unlike the ACRIN 6666 trial in which all lesions were identified from whole-breast screening US (2).

Therefore, the purpose of this study was to investigate the incidence, outcomes, and imaging characteristics of benign and malignant clustered microcysts that were detected on breast US in asymptomatic women, and to suggest appropriate management guidelines.

MATERIALS AND METHODS

PATIENT SELECTION AND INCLUSION CRITERIA

Between August 2014 and December 2019, bilateral whole-breast US was performed in 8333 asymptomatic women at our hospital. The indications for breast US are as follows. In case of supplemental screening in patients with dense breast tissue at mammography, postoperative screening in patients with personal history of breast cancer, screening which is requested by patients or their physicians for reasons such as family history of breast cancer, routine follow-up for benign breast lesions detected on previous breast US. In the last case, some patients had undergone breast biopsy or surgical excision and the pathology was benign.

In these breast US examinations, we retrospectively identified 141 lesions in 123 patients with a recorded 'clustered microcysts' by the interpreting radiologist using the picture archiving and communication system report search. 'Clustered microcysts' were recorded based on the BI-RADS definition of 'a cluster of anechoic masses, individually, < 2–3 mm, with thin (< 0.5 mm) intervening septations and no discrete solid component' (5).

Among these 123 patients with 141 lesions, 23 patients with 24 lesions who were not followed up for more than 12 months were excluded and 100 patients with 117 lesions were included in the study. Fifteen of these 117 lesions were pathologically confirmed.

The retrospective study was approved by the Institutional Review Board, and the requirement for informed consent was waived (IRB No. DAUHIRB-21-152).

IMAGE ANALYSIS

Breast US examinations were performed by one radiologist with 15 years of experience in breast imaging. Images were obtained using a 7–13-MHz or 5–12-MHz linear-array transducer (Philips iU22, Philips Healthcare, Best, the Netherlands; Logic 9, GE Medical systems, Milwaukee, WI, USA). Bilateral whole-breast and both axillae were scanned in the screening US examinations. For sonographic evaluation of each lesion, gray scale images were first obtained including a minimum of two orthogonal views, both with and without measurements. Following this, power Doppler US images were obtained.

We reviewed the available mammographic reports to document the breast composition and the mammographic assessment categories. And then, we retrospectively reviewed the mammograms to assess the mammographic findings in the area that correlated with the clustered microcysts on US. In each case, the examining radiologist interpreting mammography before performing bilateral breast US examinations. After a US examination, a BB marker was placed on the skin above the clustered microcysts and the patient underwent mammography to assure that the lesion on US was consistent with the finding detected on mammography.

The final assessment given to 'clustered microcysts' was based on an overall assessment, combining both mammographic and sonographic findings. The 'clustered microcysts' were routinely assessed as BI-RADS category 3 and when the lesion was one of multiple bilateral benign appearing nodules, it was classified as BI-RADS category 2. BI-RADS category 4 was given if mammographic suspicious microcalcifications were noted in the expected area of the clustered microcysts on US or internal vascularities were observed on power Doppler US.

ESTABLISHMENT OF FINAL DIAGNOSIS

The final diagnosis was based on pathologic results and imaging follow-up for more than 12 months. We performed US-guided core needle biopsy (CNB) using a 14-gauge semi-automated core biopsy needle (Stericut coaxial needle; TSK Laboratory, Tochigi, Japan) for lesions classified as BI-RADS category 4 and the lesions which increased in the overall size or showed an internal echo pattern change to solid component on follow-up breast US. Biopsy was also performed for BI-RADS category 3 lesions when requested by patients or their physicians. When the pathology results revealed high-risk lesions on CNB, surgical excision or vacuum-assisted removal with an 8-gauge needle (Mammotome; Devicor Medical Products; Cincinnati, OH, USA) was recommended. The histologic results from the pathology report were obtained from the electronic medical record.

In the imaging follow-up group, the lesions were considered benign if they were decreased in size, spontaneously resolved, or unchanged in size, shape, and internal echo pattern for an imaging surveillance period of at least 12 months.

RESULTS

The incidence of clustered microcysts on breast US in asymptomatic women was 1.5% (141 lesions in 123 patients from a total of 8333 women) at our institution. Of the included 100 patients, 89 patients had one clustered microcysts, 8 patients had two lesions, and 3 patients had more than 3 lesions in both breasts. Five of the 100 patients (5%) had past history of breast cancer, and 31 lesions (26.5%) in 27 patients were newly detected during the surveillance period.

The indications for breast US in the study group are summarized in Table 1. The most common indication was supplemental screening examinations in patients with dense breast tissue on mammography.

Among the included 100 patients, mammography was performed in 90 patients and remaining 10 patients who did not perform mammography were all under the age of 40. The mammographic composition and findings are summarized in Table 2. Most of the patients (83 of 90, 92.2%) had dense breast tissue at mammography, and seven patients (7.8%) had suspicious microcalcifications. Four patients (4.5%) had suspicious microcalcifications at the area that correlated with clustered microcysts on breast US.

The overall assessment for "clustered microcysts" determined by combining mammographic and sonographic findings are shown in Table 3. Twenty lesions (17.1%) assessed as category 2 were one of the multiple bilateral benign appearing nodules, and the reasons for category 4 assessment in five lesions (4.3%) were as follows: mammographic suspicious microcalcifications at the area of clustered microcysts on US and internal vascularities on power Doppler US in 4 and 1 lesion, respectively.

A total of 112 lesions assessed as category 2 or category 3 were initially recommended for

Table 1. Indications for Breast US

Indications (*n* = 100)	*n* (%)
Screening for women under 40 years	11 (11)
Follow-up for benign breast lesion found on previous breast US	22 (22)
Supplemental screening	
For dense breast on mammography	57 (57)
Requested by physicians or patients	5 (5)
Routine follow-up after breast cancer surgery	5 (5)

Table 2. Mammographic Composition and Findings

Mammographic Characteristics (*n* = 90)	*n* (%)
Mammographic composition	
Dense breast	83 (92.2)
Fatty breast	7 (7.8)
Mammographic findings	
Negative or benign finding	83 (92.2)
Suspicious microcalcifications	7 (7.8)
At the area of "clustered microcysts" on US	4 (4.5)
At the different area of "clustered microcysts" on US	3 (3.3)

Table 3. Overall Assessment of the Clustered Microcysts

Final Assessment (*n* = 117)	*n* (%)
Category 2	20 (17.1)
Category 3	92 (78.6)
Category 4	5 (4.3)
Suspicious microcalcifications	4 (3.4)
Internal vascularity	1 (0.9)

Table 4. Histopathologic Results of 15 Clustered Microcysts

Histopathologic Diagnosis (*n* = 15)	*n* (%)
Malignant (*n* = 3)	
Ductal carcinoma in situ	2 (13.3)
Invasive ductal carcinoma	1 (6.7)
High risk lesion (*n* = 2)	
Usual ductal hyperplasia with atypia	1 (6.7)
Mucocele-like lesion	1 (6.6)
Benign (*n* = 10)	
Fibrocystic change	6 (40)
Fibroadenoma	1 (6.7)
Fibrosis with chronic inflammation	1 (6.7)
Adenosis with ductal hyperplasia	1 (6.7)
Usual ductal hyperplasia	1 (6.6)

imaging follow-up. Among them, 106 lesions were followed with imaging and 6 lesions underwent CNB on request of the patients or physicians. During the follow-up period, four lesions, which were initially assessed as category 3, showed interval changes. The overall size was increased in one and the internal echo pattern was changed to solid component in three lesions. All of these four lesions underwent subsequent CNB and three were benign and one was malignant; two fibrocystic change, one fibrosis with chronic inflammation, and one invasive ductal carcinoma. The remaining 102 lesions were stable for more than 12 months (mean follow-up period: 33 months, range: 12–73 months). Ten lesions spontaneously resolved, 3 lesions decreased in size, and 89 lesions showed no interval change.

US-guided CNB was performed on a total of 15 lesions (12.8%), including five lesions of category 4 and ten lesions of category 3. Among them, 10 were benign, 2 were high-risk benign and 3 were malignant (2.6%). And the positive predictive value of biopsy was 20% (3 of 15 lesions). Table 4 summarized the pathology results. In cases of two lesions with high-risk benign results on US-guided CNB, additional US-guided vacuum-assisted removal was performed and the pathology results were the same as those of US-guided CNB. These two lesions were classified as category 4 with suspicious microcalcifications on mammography.

Three malignant lesions included two ductal carcinoma in situ and one invasive ductal carcinoma. All of two ductal carcinoma in situ were detected at supplemental screening US examinations in patients with dense breast tissue and assessed as category 4. In one of the two cases, suspicious microcalcifications were seen on mammography (Fig. 1) and in the other

case, internal vascularities were observed on power Doppler US (Fig. 2). In case of invasive ductal carcinoma, the lesion was initially classified as category 3; however, it showed new solid component within the lesion on follow-up breast US after 12 months. Hence, US-guided CNB was performed. In this patient, ductal carcinoma in situ was concurrently diagnosed in her contralateral breast (Fig. 3). Bilateral breast US was performed even though the age was under 40, because she was a high-risk patient with a family history of breast cancer.

Thirty-one clustered microcysts (26.5%) were newly detected during follow-up and two lesions were assessed as category 4 because of suspicious microcalcifications on mammogram. Biopsy was performed for the four new lesions including two category 4 lesions. One of them was confirmed as usual ductal hyperplasia with atypia and the remainder were benign.

Fig. 1. A 75-year-old woman underwent supplemental screening breast US because of dense breasts on mammography.
A. Left craniocaudal mammogram shows suspicious microcalcifications (arrows) at the upper outer quadrant of the left breast.
B. Breast US shows a clustered microcysts at the 2 o'clock position in the left breast and suspicious microcalcifications are also detected as echogenic dots within the lesion (arrows). It was assessed as category 4 and ductal carcinoma in situ was confirmed by US-guided core needle biopsy.

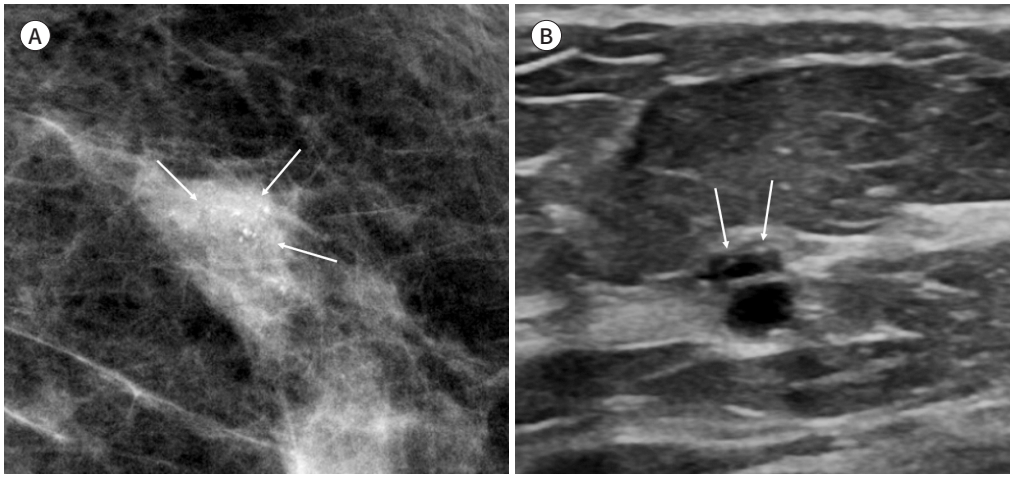


Fig. 2. A 69-year-old woman underwent supplemental screening breast US because of dense breasts on mammography.
A. Breast US shows a clustered microcysts at the 4 o'clock position in the right breast.
B. Power Doppler US shows internal vascularity and it was assessed as category 4. US-guided core needle biopsy was performed, and ductal carcinoma in situ was confirmed.

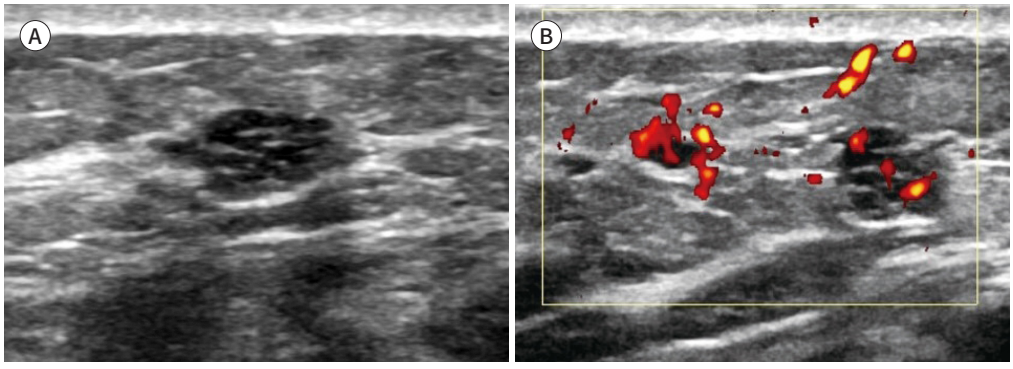
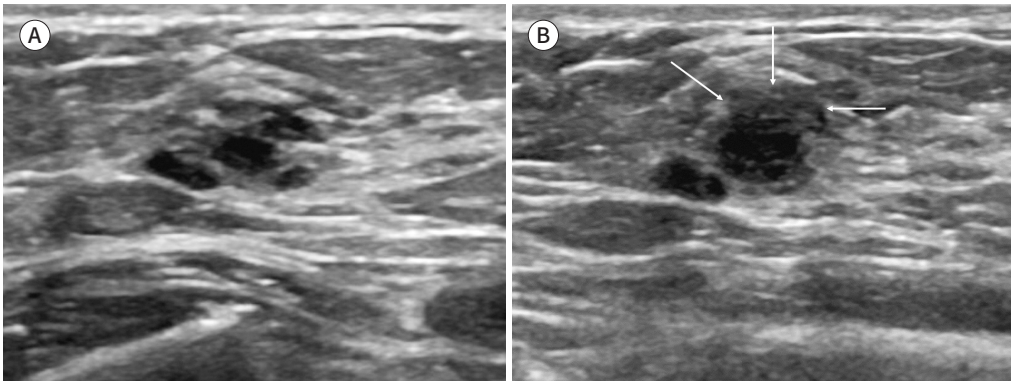


Fig. 3. A 33-year-old high-risk woman with a family history of breast cancer presented for breast cancer screening.
A. Breast US shows a clustered microcysts with debris at the 8 o'clock position in the right breast, and the lesion was assessed as category 3.
B. Follow-up breast US after 1 year shows internal echo pattern change and hypoechoic solid component was suspected within the lesion (arrows). US-guided core needle biopsy was performed and invasive ductal carcinoma was confirmed.



DISCUSSION

Since the 2000s, including the ACRIN 6666 trial, certain early studies reported the outcomes of clustered microcysts with one malignancy (0.4%) among the 235 cases across multiple centers (1, 2, 8-10). The ACR BI-RADS 5th edition in 2013 presented the definition and management recommendations based on some of these data; however, it also stated that further larger studies should be needed for establishing the most appropriate management recommendation for clustered microcysts on breast US (5). There have been several subsequent studies since then, and these studies were mainly derived from diagnostic breast US for screening mammographic recall or clinical symptoms. They reported a variable malignancy rate. While no malignancy was identified in the most representative recent studies, by Greenwood et al. (7) (0%, 0 of 95) and Goldbach et al. (6) (0%, 0 of 196). Tanaka et al. (11) reported a considerably higher malignancy rate of 15.4% (8 of 52). In the latter study, they included only biopsied lesions, and it is thought that more lesions showing suspicious features on mammogram and US might have been included.

In the present study, we investigated the malignancy rate of the 'clustered microcysts' on-breast US in asymptomatic womens. The malignancy rate was 2.6% (3 of 117), which was slightly higher than those of prior studies except that of the study by Tanaka (1, 2, 6-11). The first reason for the higher malignancy rate could be because lesions with suspicious microcalcifications on mammogram were included. Seven patients had suspicious microcalcifications on their screening mammography in this study population. Of them, four clustered microcysts (3.4%) were associated with mammographic suspicious microcalcifications, and one of them was finally confirmed as ductal carcinoma in situ (Fig. 1).

Secondly, we did not retrospectively review the US findings of the collected data, unlike previous studies (6, 7). The definition of 'clustered microcysts' had already been established by the BI-RADS 5th edition when we started to collect the data and we strictly applied the definition to the lesion (5). It could better reflect the outcomes of the lesions identified on breast US

in real clinical practice. There was one false negative case, which was initially categorized as probably benign finding. In the retrospective review, we recognized the misinterpretation of solid components within the clustered microcysts to low echoic debris during real time breast US scanning (Fig. 3). As mentioned in ACRIN 6666 study and BI-RADS 5th edition, individual microcyst can contain fluid-debris levels or low-level internal echoes and these may be difficult to differentiate from a solid component (1, 2, 5). Therefore, radiologists should carefully interpret a cystic mass at US to accurately differentiate septum or debris from solid component.

We also performed Doppler US simultaneously for every lesion and reflected the findings in final assessment. In one malignant case, internal vascularities were observed on power Doppler US and it was assessed as category 4 (Fig. 2). To the best of our knowledge, there have been no reports of malignant clustered microcysts with internal vascularities on Doppler US. It is thought that Doppler US can help distinguish between septum or debris and solid component of clustered microcysts.

According to the results of the present study, we could recommend the following management guidelines for the clustered microcysts detected on breast US. Category 4 could be given if the lesion has a solid component, internal vascularities, or mammographic suspicious microcalcifications. If the lesion does not have discrete solid component but thin septation or debris, it can be assessed as BI-RADS category 3 and short-term imaging follow-up is reasonable. When the lesion shows the classic appearances of clustered microcysts, BI-RADS category 2 assessment may be appropriate.

There were some limitations in our study. First, this study was conducted using a retrospective method. Therefore, selection bias for the study population may be inevitable. Second, a small number of cases with clustered microcysts was analyzed. Third, the mean follow-up period was 33 months in our study, but in some cases, the follow-up period was 12 months, which was quite short. Fourth, the study was performed at a single institution by only one radiologist; therefore, intra- and interobserver variability may affect data acquisition and interpretation.

In conclusion, the incidence of the 'clustered microcysts' on breast US in asymptomatic women was 1.5% at our institution and the malignancy rate was 2.6%. If the clustered microcysts has a solid component, internal vascularities, or mammographic suspicious microcalcifications, there is a possibility of malignancy, so biopsy should be considered.

Author Contributions

Conceptualization, P.Y.M., L.K.; data curation, K.H.J., L.K.; formal analysis, K.H.J., L.J.H., P.Y.M.; funding acquisition, L.J.H.; investigation, all authors; methodology, all authors; project administration, K.H.J.; resources, all authors; supervision, L.J.H., P.Y.M., L.K.; writing—original draft, K.H.J.; and writing—review & editing, K.H.J., L.J.H., P.Y.M.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Funding

This work was supported by the Dong-A University Research Fund.

REFERENCES

1. Berg WA. Sonographically depicted breast clustered microcysts: is follow-up appropriate? *AJR Am J Roentgenol* 2005;185:952-959
2. Berg WA, Sechtin AG, Marques H, Zhang Z. Cystic breast masses and the ACRIN 6666 experience. *Radiol Clin North Am* 2010;48:931-987
3. Warner JK, Kumar D, Berg WA. Apocrine metaplasia: mammographic and sonographic appearances. *AJR Am J Roentgenol* 1998;170:1375-1379
4. Wellings SR, Jensen HM, Marcum RG. An atlas of subgross pathology of the human breast with special reference to possible precancerous lesions. *J Natl Cancer Inst* 1975;55:231-273
5. D'Orsi CJ, Sickles EA, Mendelson EB, Morris EA. *ACR BI-RADS® atlas, breast imaging reporting and data system.* Reston, VA: American College of Radiology 2013
6. Goldbach AR, Tuite CM, Ross E. Clustered microcysts at breast US: outcomes and updates for appropriate management recommendations. *Radiology* 2020;295:44-51
7. Greenwood HI, Lee AY, Lobach IV, Carpentier BM, Freimanis RI, Strachowski LM. Clustered microcysts on breast ultrasound: what is an appropriate management recommendation? *AJR Am J Roentgenol* 2017;209:W395-W399
8. Berg WA, Campassi CI, Ioffe OB. Cystic lesions of the breast: sonographic-pathologic correlation. *Radiology* 2003;227:183-191
9. Chang YW, Kwon KH, Goo DE, Choi DL, Lee HK, Yang SB. Sonographic differentiation of benign and malignant cystic lesions of the breast. *J Ultrasound Med* 2007;26:47-53
10. Daly CP, Bailey JE, Klein KA, Helvie MA. Complicated breast cysts on sonography: is aspiration necessary to exclude malignancy? *Acad Radiol* 2008;15:610-617
11. Tanaka A, Imai A, Goto M, Konishi E, Shinkura N. Which patients require or can skip biopsy for breast clustered microcysts? Predictive findings of breast cancer and mucocele-like tumor. *Breast Cancer* 2016;23:590-596
12. Berg WA. Reducing unnecessary biopsy and follow-up of benign cystic breast lesions. *Radiology* 2020;295:52-53

J Korean Soc Radiol 2023;84(3):676-685

JOURNAL of THE KOREAN SOCIETY of RADIOLOGY

무증상 여성의 유방초음파에서 발견된 군집 미세낭종

김현진[1] · 이진화[1]* · 박영미[2] · 임경재[1]

목적 본 연구는 무증상 여성의 유방 초음파에서 발견된 군집 미세낭종의 발생률, 임상적 결과 및 영상 소견을 알아보고, 적절한 조치 가이드라인을 제시하고자 한다.

대상과 방법 2014년 8월부터 2019년 12월까지 무증상 여성에서 시행한 유방 초음파에서 발견된 군집 미세낭종 병변에 대해 분석하였다. 최종 진단은 병리학적 결과 및 12개월 이상의 추적관찰로 하였다.

결과 100명의 환자에서 117개 병변이 후향적으로 연구되었으며, 군집 미세낭종의 발생률은 1.5%였다. 총 117개의 병변 중, 3개(2.6%)는 악성, 2개(1.7%)는 고위험 병변, 112개(95.7%)는 양성이었다. 악성 병변 중 2개는 관상피내암이었고, 1개는 침윤성 유관암이었다. 이중, 유방촬영술에서 의심스러운 미세석회화 또는 초음파에서 내부 혈류를 보인 2개의 병변은 category 4로 분류되었다. 나머지는 12개월 뒤 시행한 초음파에서 echo pattern의 변화를 보인 위 음성의 증례였다.

결론 무증상 여성에서 시행한 유방 초음파에서 군집 미세낭종의 유병률은 1.5%였으며, 악성률은 2.6%였다. 군집 미세낭종의 악성률과 양성 및 악성 영상 소견을 아는 것은 영상의학과 의사들이 병변을 분류하고 적절한 조치를 권유하는 데 도움이 될 것이다.

[1]동아대학교 의과대학 동아대학교의료원 영상의학과,
[2]인제대학교 의과대학 부산백병원 영상의학과