Systematic Review

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The diagnostic performance of magnetic resonance imaging (MRI) in the evaluation of breast ultrasound non-mass lesions: A systematic review

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ABSTRACT

Aim: This study aims to conduct a systematic review of the current knowledge regarding the diagnostic performance of MRI in the investigation of non-mass lesions of the breast.
Method: Up to July 2022, PubMed, Scopus, Web of Science, and Embase were searched comprehensively. All studies examining the diagnostic performance of MRI in non-mass lesions were included except review articles, articles published in a language other than English, and case reports or series of cases. Two independent reviewers performed a literature review and data extraction. A checklist for cross-sectional studies developed by the Joanna Briggs Institute (JBI) was used to assess sources of bias.
Results: The systematic review included two studies. If any enhancement is present on MRI, most ultrasound NMLs exhibit a non-mass-enhancement. We found that the distribution of non-mass enhancement lesions was primarily segmental and regional. The highest number of malignancies is associated with segmental distributions since 81.8% of the cases with segmental enhancement were ductal carcinomas, specifically DCIS.
Conclusion: Non-mass lesions of the US that do not enhance in MRI have a good prognosis. Breast cancer is very unlikely in these cases, so follow-up is acceptable unless there is a suspicion of malignancy on mammography. In cases where regional and segmental enhancement of NMLs occurs on CE-MRI, ductal carcinomas may be present, and a pathological examination is warranted.

Keywords: Non-mass lesion (NML), Breast cancer, Magnetic resonance imaging (MRI), Ultrasound (US)

INTRODUCTION:

Breast cancer is the most common malignancy and the cause of most cancer-related deaths in women. Indeed, one in every eight women suffers from mammary gland malignancy (1). However, timely diagnosis and accurate assessment of breast lesions to determine the appropriate intervention are very important in reducing mortality and improving prognosis (2).

Breast ultrasound is one of the most critical methods for early diagnosing malignant lesions in the breast (3). A non-mass lesion (NML) in breast ultrasound (US) is defined as a lesion that occupies space at two different ultrasound levels but cannot be identified as a mass due to the absence of a visible shape or margin (4).

Identifying breast NMLs is of great importance because not only do some malignant tumors such as ductal carcinoma in situ (DCIS), invasive ductal carcinoma (IDC), and invasive lobular carcinoma (ILC) appear as NMLs, but also many benign lesions such as fibrocystic changes, inflammation, postoperative scars, and biopsy scars (5). When an NML is detected on imaging, open biopsy, core needle biopsy, or fine needle aspiration, cytology is often necessary for diagnosis. However, because the lesion is not visible in form or contour, there is a chance of an inaccurate diagnosis due to insufficient appraisal of the specimen. Furthermore, not all lesions are now subjected to pathological investigation (6).

Although some standard ultrasound features can suggest breast NMLs, accurate diagnosis is difficult due to overlapping malignant and benign NML features. Therefore, it is necessary to improve ultrasound technology to increase the specificity of diagnosis and reduce the number of invasive biopsies. One of the more accurate ways to examine non-mass lesions is to use other imaging methods, including MRI (7).

Breast MRI is an essential technique in breast imaging that can be used in screening women at risk and for investigating ambiguous findings in mammography and ultrasound. When a lesion is suspected to be malignant, a breast MRI can also determine whether a further pathological evaluation is required (6).

Therefore, in the study, we intend to have a systematic review of the current findings on the diagnostic performance of MRI in the investigation of non-mass lesions of breast ultrasound.

Method:

Data sources and searches

A comprehensive search was conducted in PubMed, Scopus, Web of Science, and Embase up to July 2022 to identify relevant articles. Also, the grey literature, including relevant reviews, the references of the references, and the conference abstracts, were searched. Figure 1 shows the search strategy.

Eligibility criteria

Inclusion criteria contain all studies investigating the diagnostic performance of MRI in non-mass lesions.

It was excluded if an article met one of the following criteria: 1- review articles 2- articles published in languages other than English 3- case reports and case series.

Study selection and data collection

One researcher removed the duplicate articles. Then, based on inclusion/exclusion criteria, two independent reviewers selected eligible articles by screening article titles and abstracts. Two researchers then reviewed the full texts of the remaining papers. A third reviewer resolved any disagreement between reviewers.

Based on a predefined data extraction table, two independent researchers extracted the following information: author name, publication date, country, study population, demographics, Type of MRI, and significant results.

Evaluating the risk of bias

Two authors performed quality assessments independently based on the Joanna Briggs Institute (JBI) checklist for cross-sectional studies to assess the quality of included articles.

Results:

In the preliminary search, we identified 310 articles investigating the diagnostic performance of MRI in non-mass lesions. After removing duplicates, 160 remained for title/abstract screening. Of those, 18 articles met the

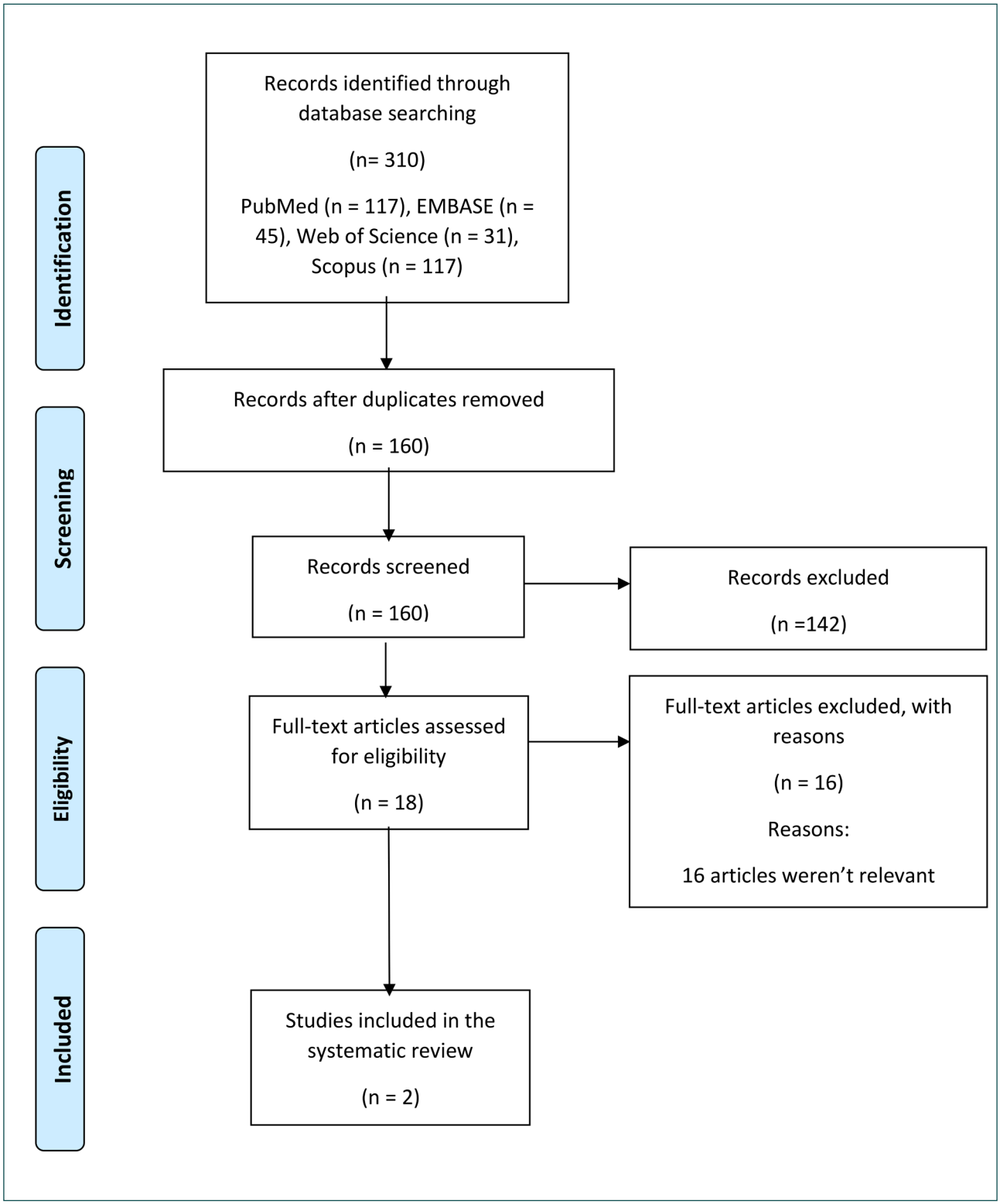

Figure 1. The flow chart of studies inclusion

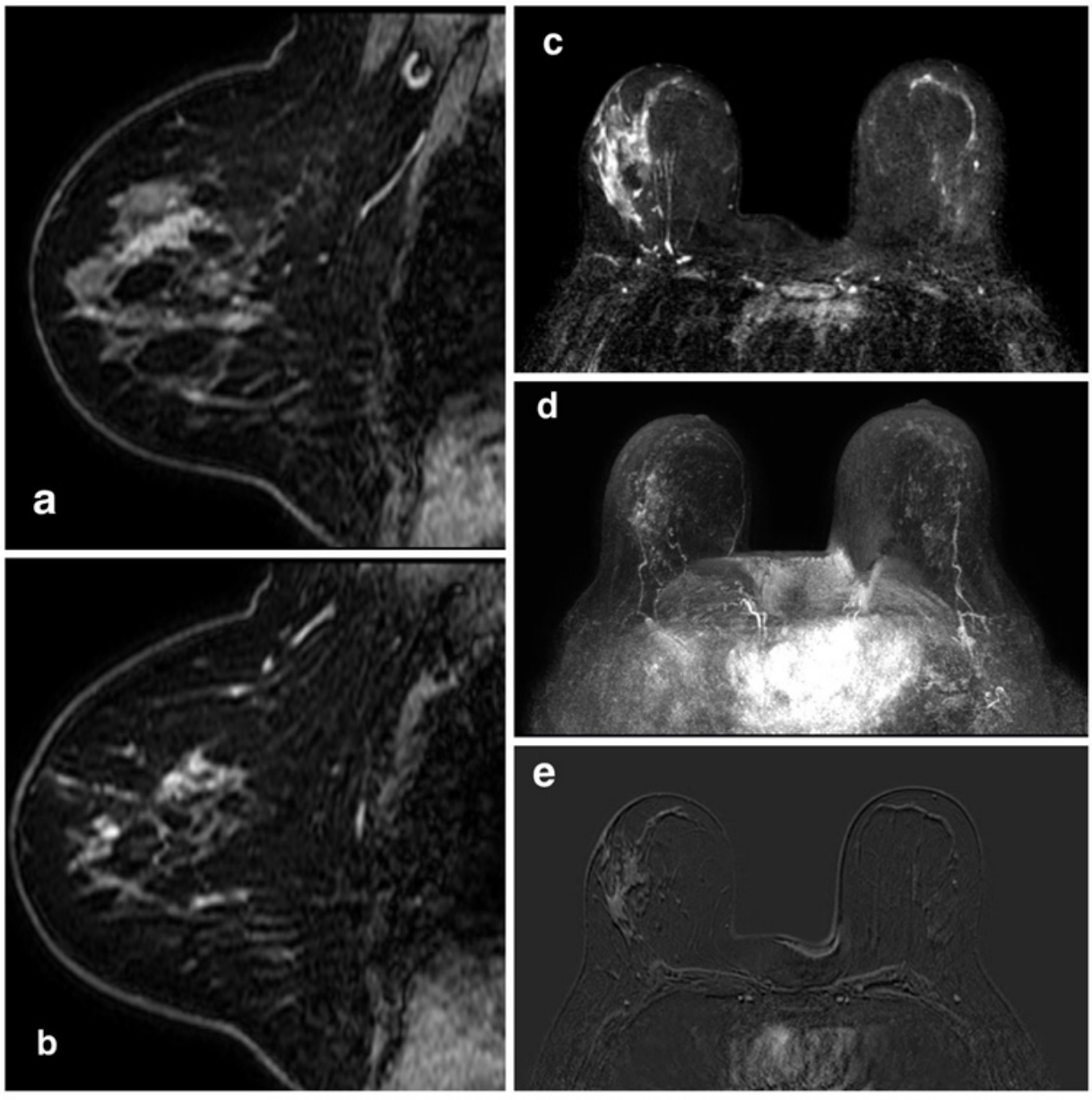

Figure 2. A 62-year-old woman without a positive family history of breast cancer with pathology-proven right breast IDC. On breast MRI a) sagittal fat sat post-contrast b) sagittal fat sat c) STIR d) MIP e) subtraction, in the right breast a clumped segmental nan-mass enhancement is illustrated.

inclusion criteria in the title/abstract screening. Two studies were included in the systematic review after reviewing the full text of eligible articles. Table 1 summarizes the characteristics of the included studies.

Table 2 shows the result of the quality assessment of included studies, in which the score of both studies was 5 (out of 8).

In a cross-sectional study, Kim et al. (5) investigated biopsy-proven breast cancers diagnosed with non-mass lesions in ultrasonography with MRI. Of those, 13 were non-mass enhanced in MRI, and two were mass enhanced.

Table 1. Study characteristics

Study	Year	Country	Study design	Study population	Type of samples	Type of MRI	Reference standard	Significant results
Sotome et al.	2007	Japan	Cross-sectional	82	Non-mass lesions in ultrasonography	Cotrast - enhanced MRI	Needle biopsy	Of non-mass lesions that were non-mass enhanced in MRI, 56.3% were diagnosed as breast cancer. 2.04% of non-mass lesions which were non-mass enhanced in MRI, were diagnosed as breast cancer.
Kim et al.	2018	Korea	Cross-sectional	15	Biopsy-proven breast tumors	MRI	Needle biopsy – surgical excision	86.67% of malignant non-mass lesions were non-mass enhanced in MRI

Table 2. Quality assessment of studies

Authors	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?	Total score
Sotome et al.	*	*	*	*			*	*	6
Kim et al.	*		*	*			*	*	5

In a cross-sectional study, Sotome et al. (6) investigated 82 samples of breast tumors diagnosed as non-mass lesions in ultrasonography. Among lesions that were enhanced in MRI, 56.3% were breast cancer. On the other hand, forty-nine samples were not enhanced in MRI, and only 2.04% were diagnosed with breast cancer, which demonstrated that not enhancing in MRI has a good prognosis for non-mass lesions in US.

Discussion:

A systematic review of the currently available literature was conducted to evaluate the utility of contrast-enhanced magnetic resonance imaging (CE-MRI) in the management of non-mass lesions (NML) of breast ultrasound (US). A total of 118 US non-mass lesions (NMLs) were analyzed in the included studies to determine whether the enhancement pattern in MRI was correlated with the pathological or cytological diagnosis.

In the Kim et al. study, 87% of ultrasound NMLs presented as non-mass enhancements (NMEs) on MRI, while 13% showed mass enhancement (4). The Sotome et al. study also showed that 40.2% of NMLs on ultrasonography appeared as enhanced lesions on contrast-enhanced MRI, of which 97% were NMEs (6). It can be concluded that most ultrasound NMLs exhibit non-mass enhancement on MRI if any enhancement is present. This finding follows the systematic review by Uematsu, which showed that US non-mass lesions should be regarded similarly to MRI non-mass enhancement (8).

Several types of malignant lesions are likely to present as non-mass-like enhancements on contrast-enhanced MRI, such as ductal carcinoma in situ (DCIS) and invasive lobular carcinoma (ILC) (9). Due to the similar appearance of regular tissue enhancement and benign processes, such as fibrocystic change (FCC), it can be challenging to diagnose these lesions.

CE-MRI helped detect breast cancer efficiently by demonstrating a specific pattern of enhancement since the type and frequency of breast cancer varied among groups and subgroups of US non-mass lesions. A standard set of radiological descriptors defined in the BI-RADS lexicon can be used to diagnose these non-mass-like enhancement lesions (10)

In general, the distribution patterns of lesions can be classified into three categories: single-quadrant/solitary lesions (linear), single-quadrant/grouped lesions (focal, regional, segmental), and multi-quadrant lesions (multiple regions, diffuse). It is difficult to define boundaries between these lesions due to fat or normal glandular tissues interspersed between the enhancing malignant tissue (9,10). In our review, non-mass enhancement lesions revealed a mainly segmental and regional distribution. It was reported by Sotome et al. that in cases of duct dilatation with internal echoes in the US, ductal carcinoma in situ (DCIS) or invasive ductal carcinoma (IDC) were frequently found and had segmental enhancement. In lesions that display spotted or low-mottled echo and geographic low echo areas in US, DCIS or IDC with a predominant intraductal component was found and enhanced on MRI either in a ductal or segmental manner (Figure 2). However, there were differences in the frequency of detecting breast cancer. As indicated by the enhancement patterns, there were two main types of breast cancer in lesions that displayed low echo areas with indistinct margins. If a regional enhancement was present, the lesion was likely an invasive lobular carcinoma (ILC). Whenever segmental enhancement is current, the lesion is believed to be ductal carcinoma (DCIS, invasive ductal carcinoma with a predominant intra-ductal component, papillo-tubular carcinoma, or invasive lobular carcinoma)

Previous studies (11–13) indicate that segmental distributions are associated with the most malignancies. We can also make the same conclusion about the included studies since in those cases with segmental enhancement, 81.8% were ductal carcinomas, namely DCIS.

ILC is another common finding in NME. ILC comprises non-cohesive cells individually dispersed or arranged in a single-file linear fashion inside a fibrous stroma. On US and MRI, non-mass-like lesions can mirror the histological characteristics. Mann et al.'s review of the MRI manifestation of ILC indicates that most ILCs are mass lesions with apparent malignant features. The more diffuse tumors, however, are characterized by unexpected enhancements and are much more challenging to diagnose. MRI images of ILC correlate well with histopathological findings, and ILC can present in a non-mass-like manner when the cells grow in a linear pattern along the ductules rather than in a mass; hence, there may only be an indication of tumor asymmetry

in the form of ductal, segmental, regional, or diffuse enhancement (14). All cancer cases with MRI regional enhancement in the Sotome study were ILC; 18% of patients with segmental distribution were also ILC. It is consistent with their ultrasound pattern, which showed a low echo area with indistinct margins.

Moreover, benign breast lesions, such as focal adenosis or fibrocystic and inflammatory changes, may also appear as non-mass-like enhancements, which are frequent findings on MRI. In the Sotome et al. study, 50% of the fibrocystic difference (FCC) cases had enhancement on MRI, and all were regionally distributed. A low echo area within the mammary glands in the US characterized it. Breast fibrocystic change encompasses a wide range of morphological and kinetic characteristics on magnetic resonance imaging (MRI); however, when a non-mass type lesion was present, especially a regional enhancement, the enhancement kinetics were benign, and the enhancement magnitude was low (15). We couldn't discuss the differences in MR enhancement patterns between breast cancers and other benign lesions in our study since the kinetic features of contrast-enhanced MR were not evaluated. It is known that several non-mass image-forming lesions on ultrasonography do not have an enhanced area CE-MRI. Unless there is a suspicion of malignancy following mammography, it is acceptable to follow up since the likelihood of breast cancer is very small in these cases.

Our included studies revealed some limitations. First, the kinetic characteristics of CE-MRI were not evaluated, so a comparison of the peak enhancement time, enhancement intensity, and washout kinetics between breast cancers and other benign lesions was not possible in this review.

The second aspect is that the internal enhancement modes of the NMEs based on the fifth edition of BI-RADS, which comprise homogeneous, heterogeneous, clumped, and clustered rings, have yet to be covered in our study. Further research is required to review and clarify the features of US non-mass lesions on MRI studies in greater detail and to determine whether the detection of additional findings on MRI results in improved survival.

Conclusion:

A favorable prognosis can be expected for non-mass lesions of the US that do not enhance on MRI. Follow-up is acceptable unless there is a suspicion of malignancy on mammography, which is extremely unlikely in these situations due to the low risk of breast cancer. When there is the regional and segmental enhancement of NMLs on CE-MRI, ductal carcinomas may be present; therefore, it is necessary to perform a pathological examination.

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