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ORIGINAL ARTICLE

Axillary lymph node metastasis detection by magnetic resonance imaging in patients with breast cancer: A meta-analysis

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Keywords
Axillary lymph node metastasis; breast cancer; diagnosis; meta-analysis.

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Abstract

Background: The study was conducted to evaluate the diagnostic performance of magnetic resonance imaging (MRI) for the detection of axillary lymph node metastasis in patients with breast cancer.

Methods: PubMed, Medline, Web of Science, Cochrane Embase, Chinese Biomedical Literature, and China National Knowledge Infrastructure databases were searched for open published studies relevant to the use of MRI for the detection of axillary lymph node metastasis in breast cancer patients. The pooled diagnostic sensitivity, specificity, and the symmetric receiver operating characteristic (SROC) curve was calculated by combining the individual data extracted from 26 included studies.

Results: The pooled diagnostic sensitivity and specificity of MRI to detect axillary lymph node metastasis in patients with breast cancer were 0.77 (95% confidence interval [CI] 0.75–0.80) and 0.90 (95% CI 0.89–0.91), respectively. The pooled positive and negative likelihood ratios were 7.67 (95% CI 5.09–11.53) and 0.23 (95% CI 0.17–0.32), respectively, by random effect method. The area under the SROC curve was 0.93 for MRI to detect axillary lymph node metastasis in breast cancer patients.

Conclusion: With high sensitivity, specificity, and area under the curve, MRI is an effective method to differentiate metastatic axillary lymph node in breast cancer patients, which can provide useful information for surgical procedure selection.

Introduction

Statistical studies of cancer have revealed that breast cancer is one of the most common malignant carcinomas diagnosed and the seconding leading cause of cancer related-death in women.[1–3] Axillary lymph node metastasis is common in breast cancer patients, which also affects the treatment modality and surgical procedure.[4] Axillary lymph node status of patients with breast cancer is usually assessed by sentinel lymph node biopsy (SLNB), core needle biopsy (CNB), or fine needle aspiration cytology (FNAC). However, these procedures are mini-invasive and potentially lead to implantation metastasis. Magnetic resonance imaging (MRI), with high resolution of different tissues, is widely used to diagnose many types of cancers and also affects treatment modality. Previously studies have evaluated its performance for evaluating the axillary lymph node status of patients with breast cancer. However, because of the small sample sizes of previous studies, statistical research is limited. In our present study, we searched open published studies relevant to MRI for the detection of axillary lymph node metastasis in patients with breast cancer and conducted a meta-analysis to further evaluate diagnostic performance.

Methods

Publication searching

PubMed, Medline, Web of Science, Cochrane Embase, Chinese Biomedical Literature, and China National Knowledge

Infrastructure databases were searched for open published studies relevant to the use of MRI to detect axillary lymph node metastasis in patients with breast cancer. The search procedure is demonstrated in Figure 1. The terms "breast cancer" OR "breast carcinoma" OR "breast neoplasm" And "axillary lymph node" And "MRI" OR "magnetic resonance imaging" OR "MR" were used.

Study inclusion and exclusion

Two reviewers drew up the inclusion and exclusion criteria and crosschecked the data. The inclusion criteria were: (i) prospective or retrospective diagnostic studies; (ii) studies relevant to the evaluation of MRI to detect axillary lymph node metastasis in patients with breast cancer; (iii) the axillary lymph node metastasis was confirmed by pathological examination; and (iv) the number of true positive (TP), false positive (FP), false negative (FN), and true negative (TN) results could be extracted from each individual study. The exclusion criteria were: (i) duplicate publications or data; (ii) literature review of case reports; (iii) malignant carcinoma other than breast cancer; and (iv) diagnostic data could not be extracted from individual studies.

Initially, 268 relevant studies were identified. Nineteen duplicated publications or data were excluded. After reading the title and abstract, 204 studies were excluded. After review of the full text, a further 19 studies were excluded. Twenty-six open published studies were finally included in the meta-analysis (Fig 1). The main features of the included 26 studies are listed in Table 1.

Data extraction

Two reviewers independently reviewed the data of each included study. General information, such as sample size, year of publication, diagnostic gold standard, and patient age, were extracted. The number of TP, FP, FN, and TN results were carefully extracted from each study and crosschecked.

Statistical methods

All analysis was performed using MetaDiSc 1.4 software (http://www.hrc.es/investigacion/metadisc_en.htm). Statistical heterogeneity across the 26 included studies was

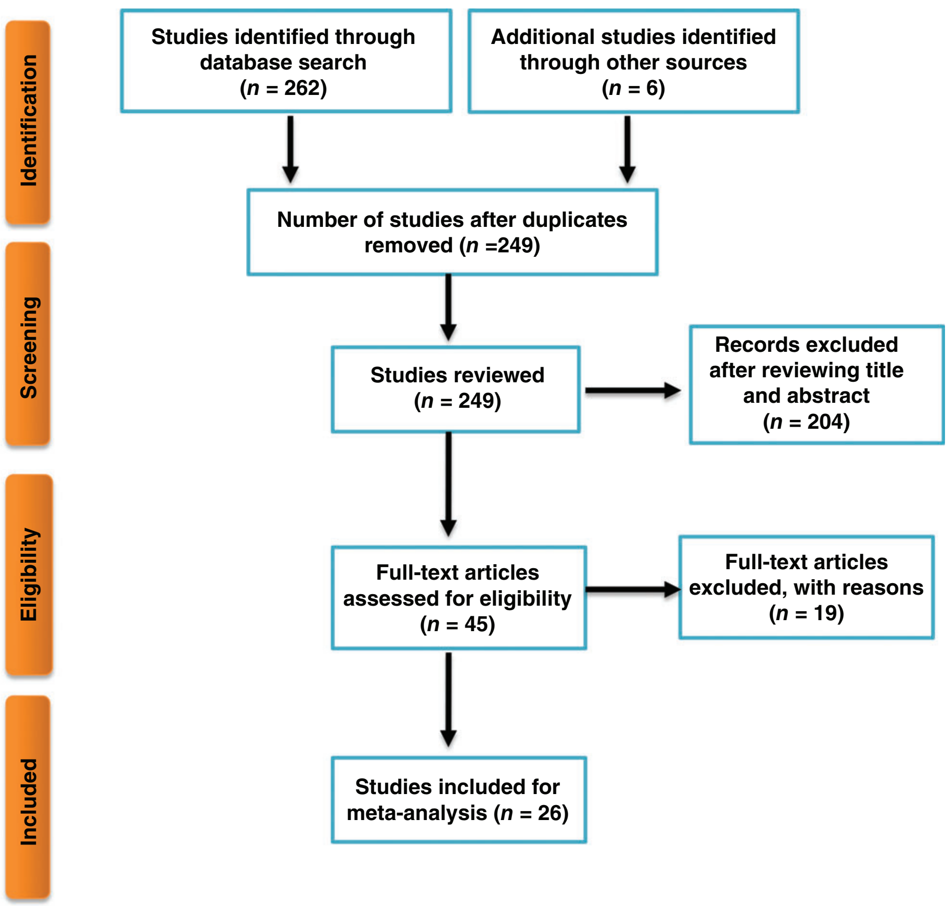


Figure 1 Search procedure.

Table 1 General characteristics of the included publications

First author	Year	Country	Study type	Reference standard	Lymph node	Age (year)	TP	FP	FN	TN
Chen[5]	2014	China	NR	ALND/CNB	154	21–82	70	8	17	59
Meng[6]	2013	China	NR	SLNB	35	35–61	10	0	1	24
Wang[7]	2013	China	Retrospective	ALND/SLNB	136	21–77	55	11	8	62
Xie[8]	2014	China	Retrospective	ALND/SLNB	193	21–73	60	9	20	104
Xu[9]	2004	China	NR	ALND	17	34–70	9	2	2	4
Yin[10]	2013	China	NR	ALND	268	NR	63	52	15	148
Du[11]	2017	China	NR	ALND	229	NR	91	17	11	110
Harada[12]	2007	Japan	Prospective	ALND	506	36–77	42	73	23	368
Kimura[13]	2009	Japan	Prospective	ALND	10	35–79	2	0	0	8
Kvistad[14]	2000	Norway	NR	ALND	65	38–78	6	1	18	40
Memarsadeghi[15]	2006	Australia	Prospective	ALND	22	40–79	6	23	5	99
Michel[16]	2002	Switzerland	Prospective	ALND	18	22–76	25	9	5	243
Mumtaz[17]	1997	UK	NR	ALND	75	29–80	21	5	5	64
García Fernández[18]	2011	Spain	Prospective	ALND	105	52.5	14	3	25	63
Hwang[19]	2013	Korea	Prospective	ALND/SLNB	349	25–79	44	29	48	228
Javid[20]	2010	USA	Prospective	ALND	47	NR	24	2	4	17
Chung[21]	2013	USA	Prospective	ALND	110	NR	68	7	0	35
Fornasa[22]	2012	Italy	Prospective	ALND	43	NR	18	2	1	22
Rautiainen[23]	2015	Finland	Prospective	ALND	32	28–82	22	0	3	7
He[24]	2012	China	Retrospective	ALND	1242	NR	108	26	34	1074
Kamitani[25]	2013	Japan	Retrospective	ALND	110	25–81	24	47	2	37
Kim[26]	2014	Korea	NR	ALND	253	28–82	69	26	22	136
Li[27]	2014	China	Prospective	SLNB	121	30–58	53	1	3	64
Luo[28]	2013	China	NR	ALND	78	30–63	38	4	7	30
Motomura[29]	2011	Japan	Prospective	SLNB	102	57	21	7	4	70
Nakai[30]	2011	Japan	Prospective	ALND	216	36–77	30	4	6	176

ALND, axillary lymph node dissection; FN, false negative; FP, false positive; NR, not reported; SLNB, sentinel lymph node biopsy; TN, true negative; TP, true positive.

assessed by I^2 test. The data was pooled by fixed or random effect method according to the heterogeneity. Publication bias was assessed by line regression test. Diagnostic sensitivity and specificity was calculated using the formula: sensitivity = TP/(TP + FN) and specificity = TN/(TN + FP). $P < 0.05$ was considered statistically significant.

Results

Sensitivity and specificity analysis

The diagnostic sensitivity and specificity of MRI to detect axillary lymph node metastasis in patients with breast cancer were pooled by random effect method because of significant statistical heterogeneity ($I^2 = 86.6\%$ for sensitivity; $I^2 = 92.5\%$ for specificity). The pooled sensitivity and specificity were 0.77 (95% confidence interval [CI] 0.75–0.80) (Fig 2) and 0.90 (95% CI 0.89–0.91) (Fig 3), respectively.

Positive and negative likelihood ratios

The pooled positive and negative likelihood ratios were 7.67 (95% CI 5.09–11.53) (Fig 4) and 0.23 (95% CI 0.17–0.32), respectively, by random effect method (Fig 5).

Diagnostic odds ratio

Because of significant heterogeneity across the included 26 studies ($I^2 = 80.9\%$; $P < 0.05$), the diagnostic odds ratio (DOR) was pooled by random effect method. The pooled DOR was 36.69, with a 95% confidence interval of 22.09–60.92 (Fig 6).

Symmetric receiver operating characteristic curve

The symmetric receiver operating characteristic (SROC) curve was calculated by sensitivity against 1-specificity using MetaDiSc 1.4 software. The area under the SROC curve (AUC) was 0.93 for MRI for the detection of axillary lymph node metastasis in breast cancer patients (Fig 7).

Evaluation of publication bias

The studies were evaluated by line regression test and no significant publication bias was observed (t = 0.33; $P > 0.05$) (Fig 8).

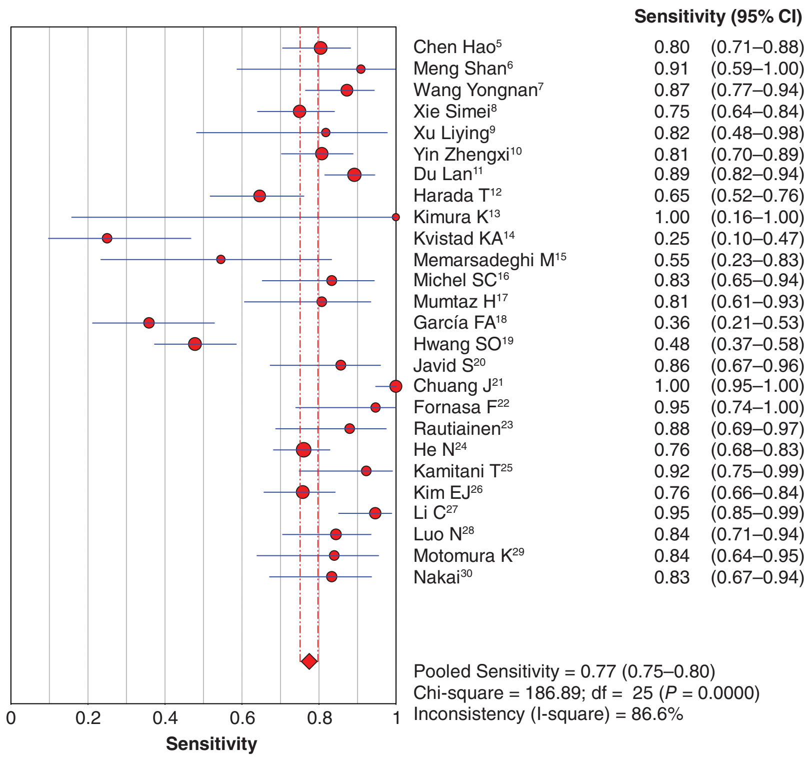


Figure 2 Forest plot of pooled diagnostic sensitivity. CI, confidence interval.

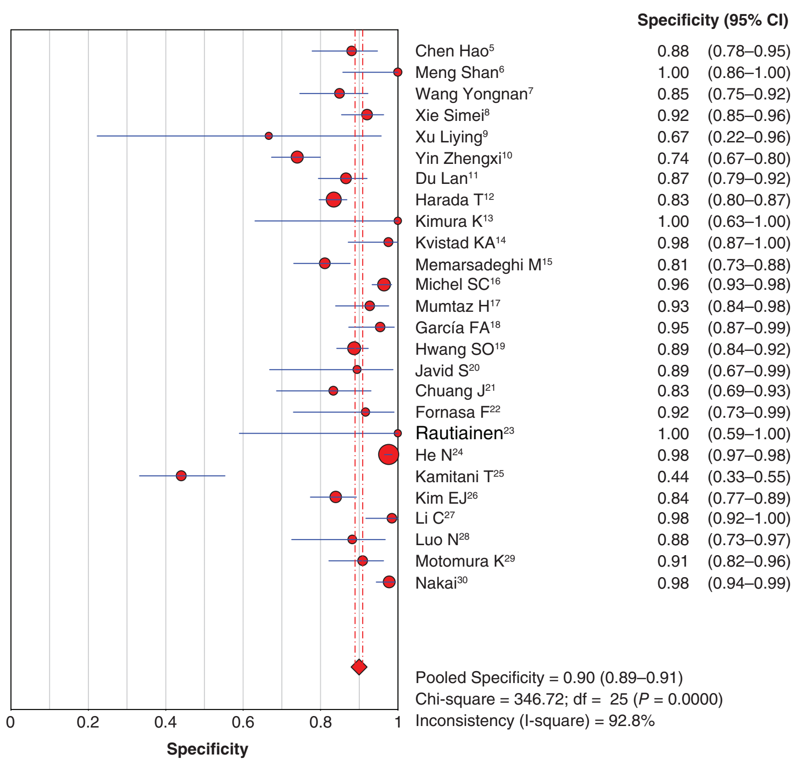
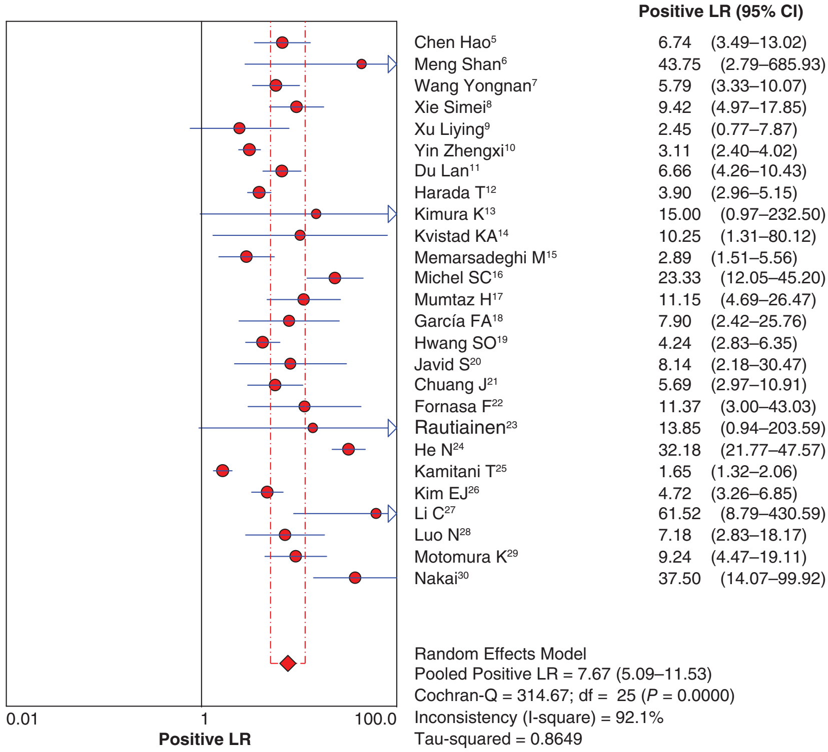


Figure 3 Forest plot of pooled diagnostic specificity. CI, confidence interval.

Discussion

Recent studies have shown that breast cancer has become one of the leading causes of cancer-related death worldwide. It is estimated that 266 120 new breast cancer patients will be diagnosed in the United States in 2018.[31] Breast cancer is the most commonly diagnosed malignant carcinoma in women. Fortunately, the long-

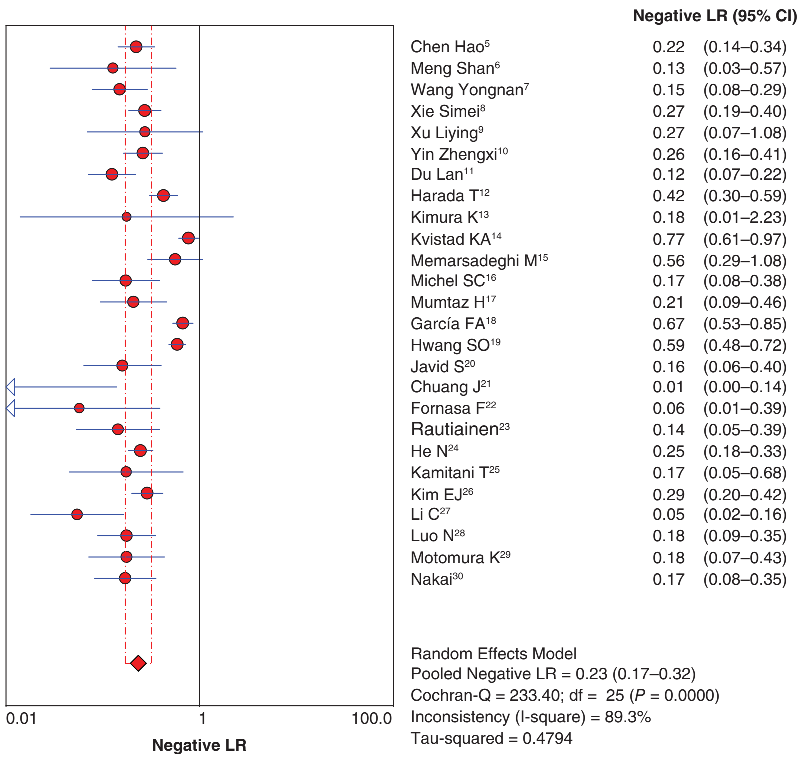
Figure 4 Forest plot of pooled positive likelihood ratio (LR). CI, confidence interval.



term (five-year) survival rate of breast cancer in women is approximately 90%.

As described in previous studies, axillary lymph node involvement is one the key factors relevant to prognosis in breast cancer patients. A clear understanding of the status of axillary lymph nodes in breast cancer patients is important not only for prognosis but also to select treatment modality or surgical method. Axillary lymph node

Figure 5 Forest plot of pooled negative likelihood ratio (LR). CI, confidence interval.



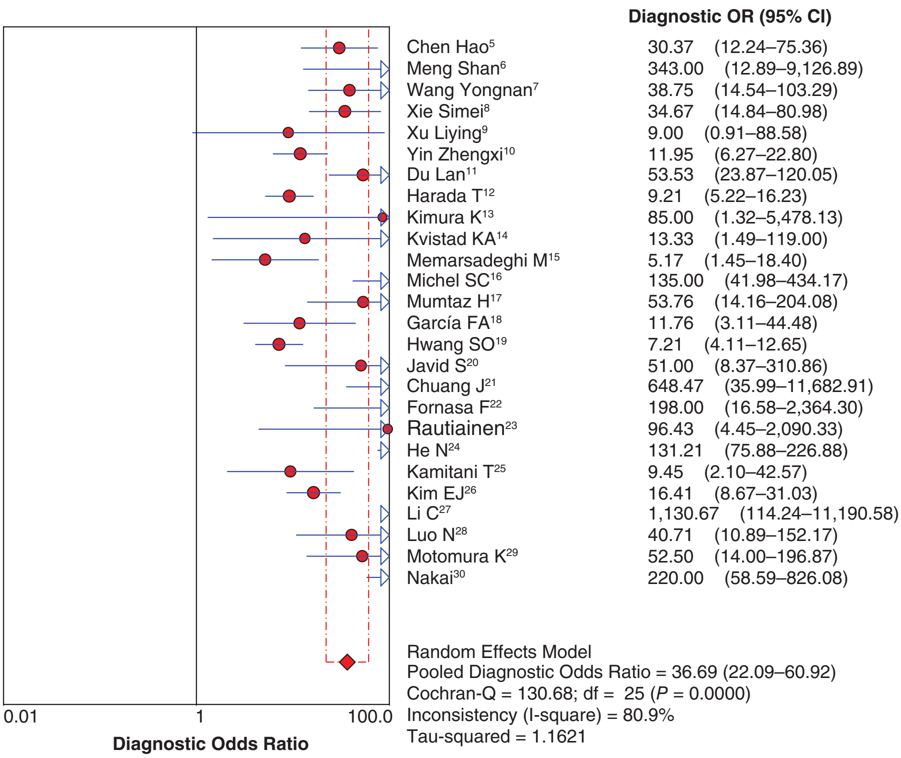


Figure 6 Forest plot of diagnostic odds ratio (OR). CI, confidence interval.

dissection (ALND) is the reference standard for evaluating lymph node involvement. However, approximately 40–70% of breast cancer patients have histopathologically negative axillary lymph nodes[32] indicating that 40–70% of breast cancer patients undergo unnecessary invasive examinations. Determining axillary lymph node involvement before treatment or dissection is important to reduce such examinations.

The diagnostic performance of MRI to detect axillary lymph node metastasis in patients with breast cancer has been widely discussed. However, the exact diagnostic performance of MRI for discriminating axillary lymph node involvement is not fully understood because of the inconsistent results reported by previous studies.[25,26,28] These inconsistencies may be the result of: (i) small sample sizes with limited statistical power; (ii) patient inclusion criteria; (iii) MRI examination technology; (iv) types of MRI instruments used; and (v) different reference standards for axillary lymph node involvement.

In our present study, we included 26 studies that evaluated the diagnostic performance of MRI to determine

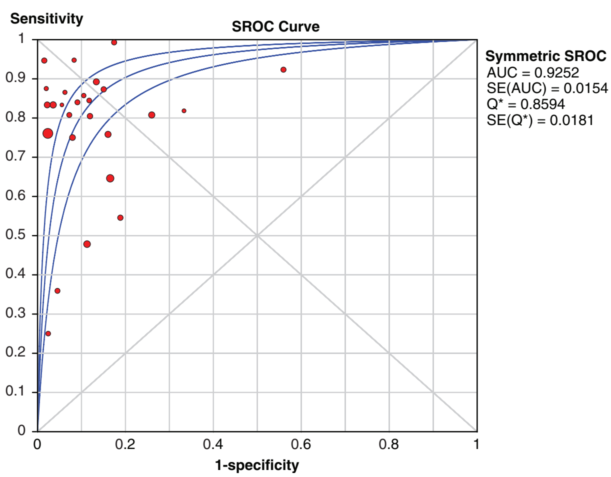


Figure 7 Pooled symmetric receiver operating characteristic (SROC) curves. AUC, area under the curve; SE, standard error.

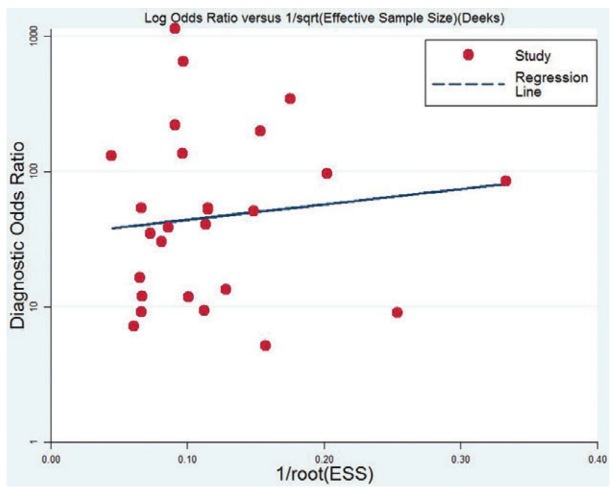


Figure 8 Egger's line regression test to evaluate publication bias.

axillary lymph node involvement in breast cancer and pooled the diagnostic sensitivity (0.77, 95% CI 0.75–0.80), specificity (0.90, 95% CI 0.89–0.91), and SROC (0.92) to further assess its value in clinical application. However, there are some limitations to our meta-analysis. Firstly, we only searched for studies published in English or Chinese, which may have led to publication selection bias. Secondly, significant statistical heterogeneity existed in the sensitivity, specificity, positive and negative likelihood ratios, and ROC effect sizes. Thirdly, not all of the included studies were prospective, reducing the reliability of our results.

Our results show that MRI is an effective method for differentiating metastatic axillary lymph nodes in breast cancer patients because of high sensitivity, specificity, and AUC, and thus can provide useful information for surgical procedure selection.

Disclosure

No authors report any conflict of interest.

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