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REVIEW ARTICLE

Diagnostic accuracy of magnetic resonance imaging and computed tomography for lateral lymph node metastasis in rectal cancer: a systematic review and meta-analysis

Nobuaki Hoshino[1] · Katsuhiro Murakami[1] · Koya Hida[1] · Takashi Sakamoto[1] · Yoshiharu Sakai[1]

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Abstract

Purpose Accurate diagnosis of lateral lymph node metastasis is a major concern in rectal cancer. Metastasis is not only a poor prognostic factor, but it can also affect decisions about treatment options, such as preoperative chemoradiotherapy and lateral lymph node dissection. The purpose of this review was to assess the diagnostic performance of magnetic resonance imaging and computed tomography for lateral lymph node metastasis in rectal cancer.

Methods A literature search was systematically performed using PubMed, Scopus, and the Cochrane Central Register of Controlled Trials. All studies in which preoperative magnetic resonance imaging or computed tomography findings involving the lateral lymph nodes were compared with pathologic findings were included. Two authors independently assessed the literature and extracted the data, and any disagreement was resolved by discussion. Pooled sensitivity, specificity, and diagnostic odds ratios were estimated using hierarchical summary receiver-operating characteristic curve analysis. The methodologic quality of the included studies was assessed using the QUADAS-2 tool.

Results Nine studies were included in the meta-analysis of magnetic resonance imaging. The pooled sensitivity, specificity, and diagnostic odds ratio for magnetic resonance imaging were 0.72 [95% confidence interval (CI) 0.66–0.78], 0.80 (95% CI 0.73–0.85), and 10.2 (95% CI 6.4–16.3), respectively. Pooled analyses were not conducted for computed tomography because of the small number of studies (only three could be identified) and the wide range in diagnostic performance between these studies.

Conclusions Magnetic resonance imaging was useful to diagnose lateral lymph node metastasis in rectal cancer, especially due to high specificity.

Keywords Diagnostic accuracy · Systematic review · Rectal neoplasms · Lateral lymph node · Magnetic resonance imaging

Introduction

Accurate diagnosis of lateral lymph node metastasis (LLNM) is a major concern for specialist colorectal surgeons [1–3]. Many studies have reported that LLNM is a risk factor for local recurrence and is associated with poor prognosis in patients with rectal cancer [3–5]. Management of LLNM differs between Western and Eastern countries [6, 7]. Preoperative treatments, including radiotherapy and chemoradiotherapy, are often used in patients with locally advanced rectal cancer in Western countries, whereas lateral lymph node dissection (LLND) is a typical treatment in Eastern countries [8–11]. The relative merits of these treatments have been widely debated, but as yet there is no consensus regarding the management of LLNM [12–15]. However, there have been recent reports on the usefulness of a combination of these therapies in specific patients [16, 17]. Although the surgical standard of care for locally advanced rectal cancer remains controversial and the indications for preoperative therapies or LLND are debatable because of toxic levels of radiation exposure and adverse events, including urinary and sexual dysfunction [8, 18–20], it is still

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✉ Nobuaki Hoshino
hoshinob@kuhp.kyoto-u.ac.jp

[1] Department of Surgery, Kyoto University Graduate School of Medicine, 54 Shogoin-Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan

important to be able to diagnose LLNM precisely for management purposes [21]. Magnetic resonance imaging (MRI) and/or computed tomography (CT) have been reported to be useful for determining the treatment strategy in rectal cancer [22]. There are currently various standards including size, shape, and border regarding the diagnosis of LLNM [23]. However, there is no consensus on how to diagnose LLNM. In this review, we evaluated the diagnostic accuracy of MRI and CT for LLNM focusing on the size of lateral lymph node in patients with rectal cancer.

Methods

Inclusion criteria

All studies in which detection of LLNM was compared between preoperative MRI/CT and pathologic findings were screened for inclusion in this review, regardless of the type of study. Pathologic findings were set as the reference standard. Rectal cancer patients who underwent radical surgery with LLND were included in the review, regardless of preoperative therapies.

Literature search

A systematic literature search was conducted on August 24, 2018 using the following electronic databases: PubMed, Scopus, and the Cochrane Central Register of Controlled Trials (CENTRAL; The Cochrane Library). The search terms used were "rectal cancer", "lateral lymph node", "MRI", "CT", and related terms (Online Appendix 1).

Study selection and data collection

The titles and abstracts of the articles identified by the literature search were independently scanned by two of the authors (NH, KM). Duplications were excluded by referring to study titles and author names. The full texts of articles that were deemed to potentially meet the inclusion criteria were obtained and considered for final inclusion in the review. The reference lists of the included studies were examined to identify additional relevant studies. Disagreement between the reviewers regarding assessment of the studies was resolved by discussion. All data were extracted by the same authors and checked for accuracy.

Assessment of methodologic quality

The QUADAS-2 tool was used to assess the quality of the included studies [24]. The quality of the studies was assessed based on two categories: risk of bias and applicability of concerns. The risk of bias category was composed of four domains: patient selection, index test, reference standard, and flow and timing. The applicability of the concerns category was composed of three domains: patient selection, index test, and reference standard. The risk of each domain was judged to be high, low, or unclear.

Statistical analysis

The statistical analysis was performed using Review Manager (Cochrane Collaboration) and STATA 13.0 software (Stata Corporation, College Station, TX, USA). A summary receiver-operating characteristic (ROC) curve was created using Review Manager. In a meta-analysis of diagnostic accuracy studies, heterogeneity among the included studies is usually found because of the diversity in test methods and diagnostic modalities across the studies [25], so the summary ROC curve was adjusted by applying the hierarchical summary ROC model in the STATA software. This model can allow for variability in the included studies and estimates pooled sensitivity, specificity, and diagnostic odds ratios [26, 27].

Results

Study selection

The literature search identified 612 articles. After 208 duplications were excluded, 404 articles were scanned by referring to titles and abstracts. Forty-seven full-text articles were then examined to assess their suitability for inclusion in the review, and 36 of them were excluded (Online Appendix 2). Finally, 11 articles were included in this review (Fig. 1).

Characteristics of included studies

Eight articles reported on the diagnostic performance of MRI [23, 28–34], 3 on that of CT [2, 35, 36]. Eight articles reported diagnostic performance data for MRI, but 1 of them reported on data for the left and right lateral lymph nodes separately [23], so was treated as 2 studies ("Ogawa L" and "Ogawa R") for the purposes of analysis. Therefore, this review finally included 9 MRI studies. Three articles reported on CT data and all were included in the review. The characteristics of the MRI and CT studies are summarized in Table 1.

Methodologic quality

A summary of the methodologic quality of the included studies is shown in Table 2.

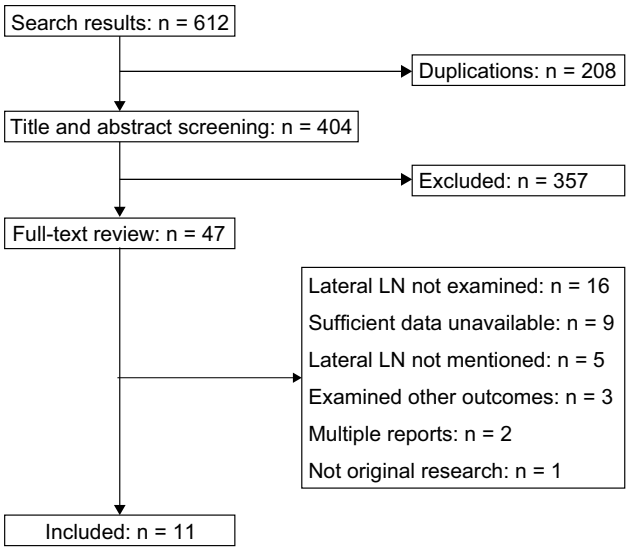

Fig. 1 Flow diagram of showing selection of articles for inclusion in this review. *LN* lymph node, *MRI* magnetic resonance imaging

Risk of bias

Seven studies were judged to be at low risk of bias and 5 to be at unclear risk in the patient selection domain. Three studies were judged to be at low risk, 4 at high risk, and 5 at unclear risk in the index test domain. Eleven studies were judged to be at low risk, and 1 at unclear risk in the reference standard domain. One study was judged to be at low risk, 5 at high risk, and 6 at unclear risk in the flow and timing domain.

Applicability category

All studies were judged to be at low risk in the patient selection, index test, and reference standard domains.

Diagnostic performance

The sensitivity and specificity of the diagnostic performance of each MRI study is shown with 95% confidence intervals (CIs) in Fig. 2. A hierarchical summary ROC curve is shown in Fig. 3. The pooled sensitivity,

Table 1 Characteristics of studies included in this review

Modality	Study	Year	Design	Center	Patients (*n*)	Preoperative therapy	Assessment approach (No. of readers for each MRI/CT)	Cut-off value, basis	Reference standard
MRI	Akasu [28]	2009	Prospective, cohort	Single	104	–	Consensus (2)	3–4 mm, short-axis	Pathologic findings Follow-up CT
	Akiyoshi [29]	2015	Retrospective, cohort	Single	77	+	Consensus (3)	5–8 mm, short-axis	Pathologic findings
	Dev [30]	2018	Prospective, cohort	Single	43	–	NR	8 mm, short-axis	Pathologic findings
	Ishibe [31]	2016	Prospective, cohort	Single	84	–	Independent (2)	10 mm, NR	Pathologic findings
	Kim [32]	2018	Retrospective, cohort	Single	57	+	Consensus (2)	5–8 mm, short-axis	Pathologic findings
	Matsuoka [33]	2007	Prospective, cohort	Single	51	–	Independent (1)	5 mm, short-axis 10 mm, long-axis	Pathologic findings
	Ogawa [34]	2014	Retrospective, cohort	Single	77	–	NR	5 mm, long-axis	Pathologic findings
	Ogawa L [23]	2016	Retrospective, cohort	Multiple	268	–[a]	NR	5–10 mm, short-axis	Pathologic findings
	Ogawa R [23]				280				
CT	Fujita [2]	2009	Retrospective, cohort	Single	210	–[a]	Independent (2)	5 mm, NR	Pathologic findings
	Kobayashi [35]	2015	Retrospective, cohort	Single	40	–	NR	NR	Pathologic findings
	Yano [36]	2007	Prospective, cohort	Single	39	–[a]	Consensus (2)	Any detected	Pathologic findings

CT computed tomography, *MRI* magnetic resonance imaging, *NR* not reported

[a]A small number of patients received preoperative therapy

Table 2 Summary of assessment of methodologic quality of included studies

Modality	Study	Risk of bias				Concerns about applicability		
		Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
MRI	Akasu [28]	+	+	+	−	+	+	+
	Akiyoshi [29]	+	−	+	−	+	+	+
	Dev [30]	+	?	?	?	+	+	+
	Ishibe [31]	+	−	+	−	+	+	+
	Kim [32]	+	+	+	+	+	+	+
	Matsuoka [33]	?	−	+	?	+	+	+
	Ogawa [34]	+	?	+	?	+	+	+
	Ogawa L [23]	?	?	+	−	+	+	+
	Ogawa R [23]	?	?	+	−	+	+	+
CT	Fujita [2]	?	−	+	?	+	+	+
	Kobayashi [35]	?	?	+	?	+	+	+
	Yano [36]	+	+	+	?	+	+	+

+, low risk; −, high risk; ?, unclear risk

CT computed tomography, *MRI* magnetic resonance imaging

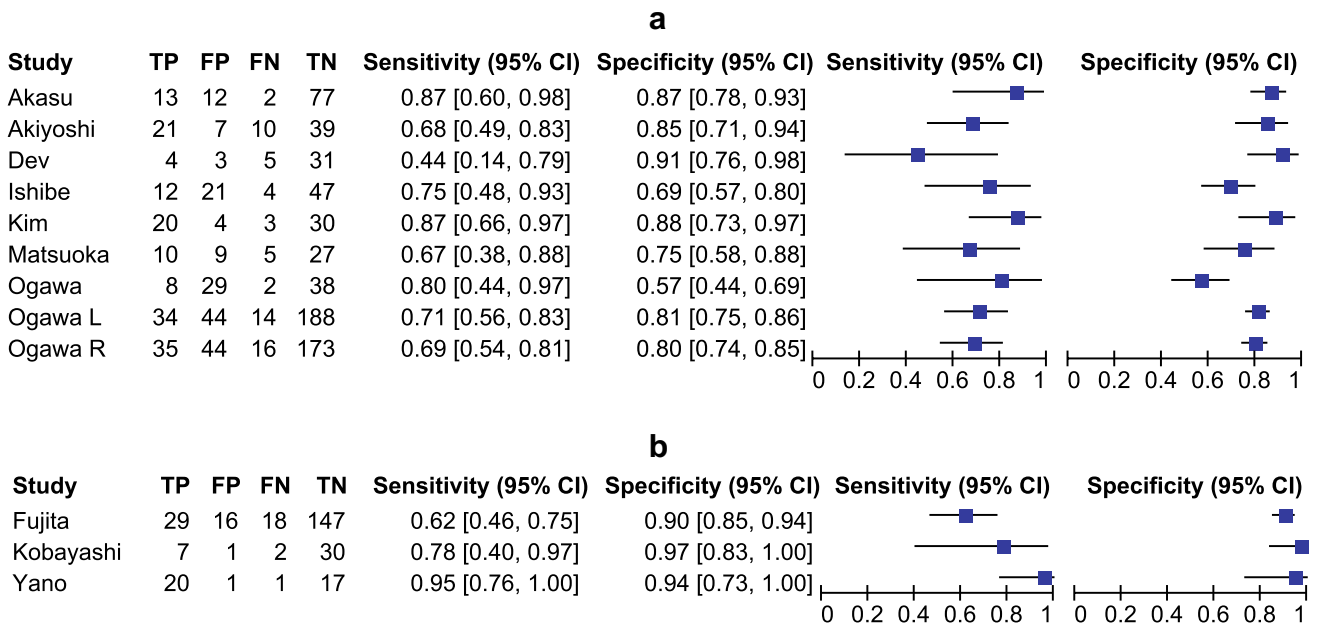

Fig. 2 Sensitivity and specificity with the 95% confidence intervals for each included study. **a** Magnetic resonance imaging. **b** Computed tomography. *CI* confidence interval, *FN* false negative, *FP* false positive, *TN* true negative, *TP* true positive

specificity, and diagnostic odds ratio for preoperative MRI were 0.72 (95% CI 0.66–0.78), 0.80 (95% CI 0.73–0.85), and 10.2 (95% CI 6.4–16.3), respectively, for LLNM. Only 3 studies of the diagnostic performance of CT could be included; the sensitivity and specificity of preoperative CT in each study was plotted, but the plots were scattered (Fig. S1). Therefore, no pooled analysis was undertaken.

Sensitivity analysis

Two studies that analyzed the performance of MRI included patients receiving preoperative chemoradiotherapy, so the sensitivity analysis was performed after excluding the studies [29, 32]. The sensitivity, specificity, and diagnostic odds ratio were 0.71, 0.78, and 8.8, respectively.

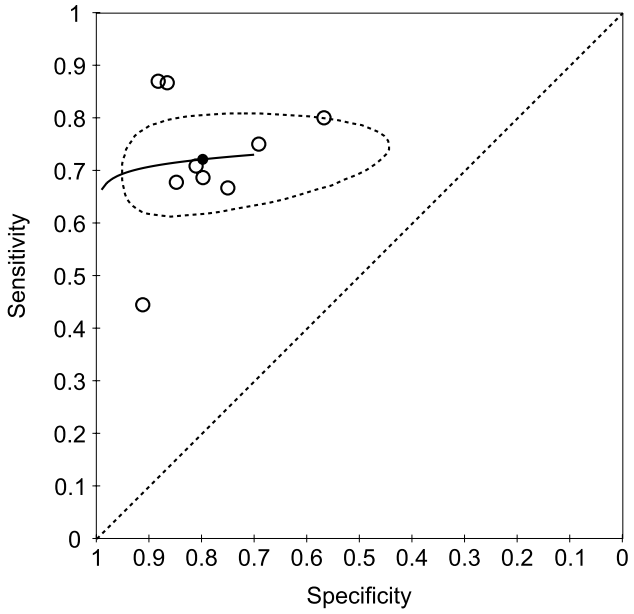

Fig. 3 Summary receiver-operating characteristic curve of the value of magnetic resonance imaging for assessing lateral lymph node metastasis. White spots indicate the points for each study, the black spot indicates the summary point, the solid line indicates the summary curve, and the dotted line outlines the 95% prediction region

Discussion

In this review, we investigated the diagnostic accuracy of preoperative MRI/CT for LLNM using sensitivity, specificity, and the diagnostic odds ratio. For accurate detection of LLNM, we included only studies in which lateral lymph node dissection was performed and pathologic findings could be used as a reference standard. Our results indicate that the diagnostic performance of MRI was not particularly good, and that of CT was not estimated at all because of the small number of studies available and the variable diagnostic performance of CT across the studies.

MRI is often used for preoperative evaluation in patients with rectal cancer, including for tumor depth and lymph node metastasis. The pooled sensitivity and specificity was reported to be 0.71–0.97 and 0.58–0.93, respectively, for diagnosis of *T* category and 0.77–0.78 and 0.93–0.94 for evaluation of the circumferential resection margin [37, 38]; the performance of MRI for both applications was considered to be good. However, the pooled sensitivity and specificity values were reported to be 0.77 and 0.71, respectively, for the diagnosis of lymph node metastasis, which was not considered acceptable [37]. MRI might be useful for diagnosing tumor depth in rectal cancer, but less so for diagnosing lymph node metastasis. However, almost all the lymph nodes were "mesorectal" and the diagnostic performance of MRI for LLNM remains unclear. Total mesorectal excision or tumor-specific mesorectal excision is currently the surgical standard care in patients with rectal cancer, so preoperative diagnosis of mesorectal lymph node metastasis is not crucial, although this type of metastasis is considered to be a potential risk factor for LLNM [1, 2, 39]. However, preoperative diagnosis of LLNM is as important as diagnosing tumor depth because it could influence the treatment strategy, and there may not be any alternatives to MRI available for diagnosis of LLNM.

There have been several investigations of the value of preoperative imaging for detection of LLNM, and recent studies have reported that MRI is often used to diagnose LLNM [23, 29, 32]. In assessment using MRI, several diagnostic criteria for LLNM have been suggested, including the maximum size on the short or long axis of the lymph node, its shape, and its signal intensity [33, 40]. However, use of multiple criteria may be confusing, and results vary between investigators [33]. The size on imaging was reported to be the best indicator of LLNM [40], and pathologic examination also revealed a significant association between the size of the specimen and LLNM [41, 42]. There has been an attempt to diagnose LLNM on the basis of size alone [23]. Therefore, studies that reported data for the size of lateral lymph nodes were included in this review.

The cut-off values ranged widely from "any detected" to 10 mm in the studies included in this review, and it was impossible to determine the optimal cut-off value of lymph node size for diagnosis of LLNM. However, the hierarchical summary ROC model combined the studies despite their variety, and created a hierarchical summary ROC curve indicating that MRI had high specificity but not high sensitivity (Fig. 3). In the clinical setting, a higher cut-off value, such as 8 mm or 10 mm, was preferred when LLNM was diagnosed by MRI alone, and lymph nodes smaller than the cut-off value were evaluated by a combination of MRI and other features, including differentiation and tumor depth [1].

The strength of this review is that it included only studies comparing MRI/CT findings with pathologic findings. This restrictive inclusion criterion allowed accurate assessment of the diagnostic performance of MRI. However, this research has some limitations. There was diversity in the functional ability of MRI/CT, measurement of lymph node size, and cut-off values for LLNM, so the heterogeneity among the included studies was inevitable. Moreover, most of the included studies in this review were performed in Japan, where LLND is often performed for locally advanced rectal cancer.

In conclusion, MRI was useful in the diagnosis of LLNM in rectal cancer, and especially its specificity was high.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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