Diagnostic value of magnetic resonance and computed tomography colonography for the diagnosis of colorectal cancer

A systematic review and meta-analysis

Yanjun Gao, MS\textsuperscript{a}, Jing Wang, BS\textsuperscript{b}, Hairong Lv, BS\textsuperscript{a}, Yongjie Xue, BS\textsuperscript{a}, Rongrong Jia, MS\textsuperscript{a}, Ge Liu, MS\textsuperscript{a}, Weixian Bai, MS\textsuperscript{a}, Yi Wu, MS\textsuperscript{a}, Lang Zhang, MS\textsuperscript{a}, Junle Yang, MD\textsuperscript{c,\dagger}

Abstract

Background: Surgical resection is the recommended procedure for colorectal cancer (CRC), but majority of the patients were diagnosed with advanced or metastatic CRC. Currently, there were inconsistent results about the diagnostic value of magnetic resonance colonography (MRC) and computed tomography colonography (CTC) in early CRC diagnosis. Our study conducted this meta-analysis to investigate the diagnostic value of MRC and CTC for CRC surveillance.

Methods: A comprehensive literature search was conducted in PubMed, Embase, and the Cochrane library to select relevant studies. The summary sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR), and the area under the receiver operating characteristic curves (AUC) were calculated to evaluate the diagnostic value of MRC and CTC, respectively.

Result: Twenty-five studies including 2985 individuals were selected in the final analysis. Eight studies evaluated the diagnostic value of MRC, and 17 studies assessed CTC. The summary sensitivity, specificity, PLR, NLR, DOR, and AUC in MRC for early detection of CRC were 0.98 (95% confidence interval, CI: 0.80–1.00), 0.94 (95% CI: 0.85–0.97), 15.48 (95% CI: 6.30–38.04), 0.02 (95% CI: 0.00–0.25), 115.09 (95% CI: 15.37–862.01), and 0.98 (95% CI: 0.97–0.99), respectively. In addition, the sensitivity, specificity, PLR, NLR, DOR, and AUC of CTC for diagnosing CRC were 0.97 (95% CI: 0.88–0.99), 0.99 (95% CI: 0.99–1.00), 154.11 (95% CI: 67.81–350.22), 0.03 (95% CI: 0.01–0.13), 642.51 (95% CI: 145.05–2846.02), and 1.00 (95% CI: 0.99–1.00). No significant differences were found between MRC and CTC for DOR in all the subsets.

Conclusion: The findings of meta-analysis indicated that MRC and CTC have higher diagnostic values for early CRC diagnosis. However, the DOR for diagnosing CRC between MRC and CTC showed no significance.

Abbreviations: AUC = the area under the receiver operating characteristic curves, CC = conventional colonoscopy, CIs = confidence intervals, CRC = colorectal cancer, CTC = computed tomography colonography, DOR = diagnostic odds ratio, FOBT = fecal occult blood test, MRC = magnetic resonance colonography, NLR = negative likelihood ratio, PLR = positive likelihood ratio.

Keywords: colorectal cancer, computed tomography colonography, magnetic resonance imaging, meta-analysis

1. Introduction

Colorectal cancer (CRC) is the fourth leading cause of cancer-related mortality in both men and women worldwide, causing a major public health issue.\textsuperscript{[1]} The high morbidity population included patients aged ≥75 years, but the cancer-related mortality rates appear to decline.\textsuperscript{[2]} Mortality in most of the CRC patients occurs due to metastasis, which was consistent with other common cancers. Due to poor diagnosis of clinical symptoms, a relatively high proportion of CRC patients were diagnosed in the advanced stages. According to the data, nearly 25% of CRC patients with metastases were diagnosed initially, and approximately 50% of these patients will develop into metastases stages.\textsuperscript{[3]} Surgical resection remains the mainstay of treatment in nonmetastatic CRC patients, while curative resection was appropriate in a very low percentage of patients.\textsuperscript{[4]} Conventional colonoscopy (CC) is the best method for diagnosis and differentiation of CRC from other lesions. However, CC was considered to be invasive and completely safe in patients undergoing examination.\textsuperscript{[5]} Therefore, additional simpler screening methods should be explored, and compared with colonoscopy, which is a more selective and efficient tool.\textsuperscript{[6]}

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\textsuperscript{a} Department of Medical Imaging, Xi’an No. 3 Hospital, \textsuperscript{b} Department of Medical Imaging, Xi’an Hospital of TCM, \textsuperscript{c} Department of Medical Imaging, Xi’an Central Hospital, Xi’an, China.

\textsuperscript{\dagger} Correspondence: Junle Yang, Department of Medical Imaging, Xi’an Central Hospital, Xi’an, China (e-mail: yangjie@163.com).

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Currently, virtual colonoscopy including magnetic resonance colonography (MRC) and computed tomography colonography (CTC) have already been studied as alternative methods for the diagnosis of CRC and other colonic pathologies. These 2 approaches have been demonstrated as well tolerated, feasible, and safe methods.\(^{12-15}\) However, the impact of ionizing radiation burden could not be neglected.\(^{10,11}\) Previous meta-analyses studies mainly focused on single virtual colonoscopy compared with CC, and comparison of the diagnostic value between MRC and CTC was not evaluated.\(^{12,13}\) It is particularly important to clarify the best diagnostic procedure in individuals who are at high risk of CRC, as it has not been determined before. Therefore, we systematically examined published studies to evaluate the diagnostic values of MRC and CTC for diagnosing early CRC, and compared their effectiveness.

2. Materials and methods

2.1. Data sources, search strategy, and selection criteria

This review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Statement issued in 2009 (Checklist S1).\(^{14}\) Published studies investigating the diagnostic ability of MRC or CTC in the diagnosis of CRC were eligible for inclusion in this meta-analysis, and there was no language restriction. We searched PubMed, Embase, and Cochrane Library electronic databases for articles published through February 2018 and the following search terms were used (“computed tomography colonography” OR “magnetic resonance colonography” OR “virtual colonoscopy”) AND (“colorectal” OR “colon” OR “rectal”) AND (“cancer” OR “tumor” OR “neoplasm”). Manual search of the reference lists was performed for identifying any potentially eligible studies.

Literature search and study selection process were conducted by 2 reviewers independently, and any disagreement was resolved by group discussion until a consensus was reached. The inclusion criteria of this meta-analysis were as follows: participants: patients with high or moderate risk of progression into CRC; intervention or exposure: patients undergoing MRC/CTC examination; control: studies that employed CC as gold standard; outcomes: the study should report true and false positive, true and false negative, or other data that could transform into the above results; and study design: studies with prospective design.

2.2. Data collection and quality assessment

Two reviewers independently collected the characteristics of the studies and participants who are using a standardized approach, and any inconsistencies were examined and adjudicated independently by an additional author by referring to the original studies. The collected information included the first author’s surname, publication year, region, sample size, mean age, percentage male, inclusion criteria, imaging modality, true and false positive, and true and false negative. For studies that published on similar populations more than once, data from the recently published studies was chosen. Quality assessment was performed by Quality Assessment Tool for Diagnostic Accuracy Studies, version 2.0, which included 14 items that are answered by “yes,” “no,” and “unclear.” The answer “yes” was considered as satisfied with the criteria, while “no” and “unclear” were considered as the study was not satisfied with the criteria or the study was partially satisfied with the criteria or could not provide sufficient information.\(^{115}\)

2.3. Statistical analysis

The summary sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR), and the area under the receiver operating characteristic curves (AUC) with their 95% confidence intervals (CIs) were calculated based on true positive, false positive, false negative, and true negative. The summary sensitivity, specificity, PLR, NLR, and DOR were calculated by using bivariate random effects, and the AUC was calculated by hierarchical regression.\(^{16,17}\) Heterogeneity between studies was investigated by using \(I^2\) and Q statistic, and we considered \(P<.10\) as indicative of significant heterogeneity.\(^{18,19}\) Subgroup analyses were performed for DOR in MRC and CTC diagnosis of CRC based on sample size, mean age, and percentage male. Furthermore, \(P\) values between subgroups were also calculated by using chi-squared test and meta-regression.\(^{20}\) Funnel plots and Deeks asymmetry tests were employed to evaluate publication biases for MRC and CTC.\(^{21}\) The significant level (\(\alpha\)) was 0.05 for pooled diagnostic parameters. The meta-analysis was performed by using STATA software (version 10.0; Stata Corporation, College Station, TX).

3. Results

3.1. Literature search

A flowchart of literature selection process was shown in Figure 1. Based on the predefined search strategy, 690 studies (443 from PubMed, 193 from Embase, and 54 from the Cochrane library) were identified during the initial electronic search, and 51 studies were excluded due to duplications. Furthermore, 571 articles were excluded due to irrelevant, reviews, letters, and meta-analysis studies. A total of 68 potentially eligible studies were selected, and after detailed evaluations, 25 prospective studies were selected for...
No additional eligible study was observed by manual searching of the reference lists. Table 1 summarized the baseline characteristics of the studies and participants.

### 3.2. Study characteristics

Twenty-five prospective studies including a total of 2985 individuals were enrolled in this meta-analysis, where 8 studies evaluated the diagnostic value of MRC, and the remaining 17 studies evaluated the diagnostic value of CTC. The published studies ranged from 1999 to 2017, while 6 to 600 patients were included in each study. Seven studies were conducted in the United States or Australia, 15 in Europe, and the remaining 3 studies were conducted in Asia. The details of study quality assessment are presented in Table 2.

### 3.3. Magnetic resonance colonography

Eight studies reported the diagnostic value of MRC for detecting CRC. The summary sensitivity and specificity of MRC were 0.98
| References                  | Question about study design characteristic |
|----------------------------|--------------------------------------------|
|                            | Representative patient spectrum | Reporting of selection criteria | Reference standard | Absence of disease progression bias | Absence of partial verification bias | Absence of differential verification bias | Absence of incorporation bias | Description of index text execution | Description of reference standard execution | Reference standard blinded | Index test blinded | Absence of clinical review bias | Reporting of uninterpretable/intermediate results | Withdrawal |
| [22]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [23]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [24]                       | No  | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [25]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [26]                       | No  | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [27]                       | No  | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [28]                       | No  | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [29]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [30]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [31]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [32]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [33]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [34]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [35]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [36]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [37]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [38]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [39]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [40]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [41]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [42]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [43]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [44]                       | No  | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [45]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| [46]                       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |

Table 2: Quality evaluation of the included studies using the Quality Assessment of Diagnostic Accuracy Studies tool.
(95% CI: 0.80–1.00), and 0.94 (95% CI: 0.85–0.97), respectively (Fig. 2). Furthermore, the PLR and NLR in patients who received MRC were 15.48 (95% CI: 6.30–38.04), and 0.02 (95% CI: 0.00–0.25), respectively (Fig. 3). The DOR of MRC for diagnosing early CRC was 115.09 (95% CI: 15.37–862.01; Fig. 4). Finally, the summary AUC in MRC for diagnosing CRC was 0.98 (95% CI: 0.97–0.99; Fig. 5).

3.4. Computed tomography colonography

Seventeen studies reported the diagnostic value of MRC for detecting CRC. The summary sensitivity and specificity of MRC were 0.97 (95% CI: 0.88–0.99), and 0.99 (95% CI: 0.99–1.00), respectively (Fig. 6). Furthermore, the PLR and NLR in patients who received MRC were 154.11 (95% CI: 67.81–350.22), and 0.03 (95% CI: 0.01–0.13), respectively (Fig. 7). The DOR of MRC for diagnosing early CRC was 642.51 (95% CI: 145.05–2846.02; Fig. 8). Finally, the summary AUC was 1.00 (95% CI: 0.99–1.00) in patients using CTC for diagnosing CRC (Fig. 9).

3.5. Subgroup analysis

Subgroup analyses for DOR of MRC and CTC are shown in Table 3. The DOR in patients using MRC and CTC showed statistically significant differences in all the subsets. However, no significant differences between MRC and CTC for DOR in all the subsets were found. Furthermore, sample size and percentage male were important factors with significant DOR of MRC. Finally, the sample size, mean age, and percentage male affected the DOR of CTC.

3.6. Publication bias

Publication biases of MRC and CTC for CRC detection are presented in Figure 10. There were no significant publication biases for MRC (P value for Deeks funnel plot asymmetry test: .59) and CTC (P value for Deeks funnel plot asymmetry test: .13).

4. Discussion

Due to varied diagnostic parameters of MRC and CTC for diagnosing CRC, the present study summarized the diagnostic value of MRC and CTC in the detection of CRC in patients with high risk. In this comprehensive quantitative meta-analysis, 25 prospective studies including 2985 individuals were recruited, and the results showed that both MRC and CTC demonstrated an excellent diagnostic accuracy in diagnosing CRC with a summary AUC of 0.98 and 1.00, respectively. Furthermore, there was no significant difference between MRC and CTC for DOR in all the subsets based on the predefined factors (such as sample size, mean age, and percentage male).

We reviewed previous meta-analyses studies that investigated the diagnostic value of MRC and CTC for detecting CRC. Firstly, Porté et al[12] pooled 7 studies and found that CTC was feasible for CRC surveillance, which was correlated with 95% of sensitivity and 100% of specificity. Furthermore, they pointed
Figure 3. The summary positive likelihood ratio and negative likelihood ratio for magnetic resonance colonography. CIs = confidence intervals.

Figure 4. The summary DOR for magnetic resonance colonography. CIs = confidence intervals.
out that CTC could offer single-test luminal, serosal and extracolonic assessment, and cost-saving alternative over standard surveillance procedures. Secondly, Purkayastha et al. conducted a meta-analysis based on 8 studies involving 563 patients, and the results pointed out that the sensitivity of MRC for detecting all lesions was 75%, the specificity was 96%, and the AUC was 0.90. Furthermore, they indicated that the diagnostic accuracy of MRC for diagnosing CRC was superior in polyps. Thirdly, Purkayastha et al. conducted another important meta-analysis and demonstrated similar diagnostic values between MRC and CTC for diagnosing CRC. The study also indicated that the study quality, size, and intravenous/intraluminal contrast agents could affect the diagnostic values of MRC and CTC. However, previous studies did not calculate the stratified analyses, limiting their results. The latest published articles should be reevaluated into the pooled results. Therefore, we conducted this comprehensive quantitative meta-analysis to evaluate the accuracy of the diagnostic value of MRC and CTC for detecting CRC.

Several RCTs included in this systemic review have reported varied diagnostic parameters. The sensitivity of MRC from individual studies ranged from 0.48 to 1.00, while the specificity ranged from 0.60 to 1.00. Huge variability occurred due to the study by Luboldt et al in 2000 and 2001. The study conducted in the year 2000 suggested that MRC was associated with lower sensitivity and appropriate specificity, while the study conducted in 2001 found higher sensitivity and lower specificity.
Figure 7. The summary positive likelihood ratio and negative likelihood ratio for computed tomography colonography. CIs = confidence intervals.

Figure 8. The summary diagnostic odds ratio for computed tomography colonography. CIs = confidence intervals.
in diagnosing CRC. Furthermore, the sensitivity of CTC in individual study ranged from 0.27 to 1.00, and the specificity ranged from 0.88 to 1.00. These differences were mainly focused in the study conducted by Sali et al.\textsuperscript{[44]} and Weinberg et al.\textsuperscript{[46]} The reason for this was due to the inclusion of individuals with different risks. The type and size of colorectal lesions also affected the diagnostic accuracy of MRC and CTC. Finally, the expertise of the radiologist could also affect the accuracy of MRC and CTC, while this was not addressed in most of the included trials.

The subgroup analysis indicated no significant differences between MRC and CTC for DOR in all subsets. The imbalances in the characteristics of included studies and participants might bias these results. Furthermore, the current comparisons of DOR between MRC and CTC were based on indirect comparisons, while the head-to-head comparisons regarding the diagnostic value of MRC and CTC for detecting CRC were not conducted.

In addition, sample size and percentage male could affect the diagnostic value of MRC, while sample size, mean age, and percentage male could affect the DOR in CTC. The reason for this was due to the contribution of sample size for the weighted pooled results, mean age of the included patients was associated with the progression of CRC, and the percentage male was

| Variable          | Subgroups | Diagnostic tool | Number of studies | DOR and 95% CI | P value for heterogeneity | P value between MRC and CTC | P value between subgroups for MRC | P value between subgroups for CTC |
|-------------------|-----------|-----------------|-------------------|----------------|---------------------------|-----------------------------|-----------------------------------|-----------------------------------|
| Sample size       | ≥100      | MRC             | 3                 | 101.69 (2.18–4736.27) | <.001 | .319 | .003 | .043 |
|                   |           | CTC             | 8                 | 1116.81 (73.19–1.7e+04) | <.001 | .402 |
|                   | <100      | MRC             | 5                 | 156.55 (38.48–636.91) | <.001 | .012 |
|                   |           | CTC             | 9                 | 386.53 (79.52–1878.92) | <.001 | .003 |
| Mean age (years)  | ≥65.0     | MRC             | 1                 | 35.00 (1.34–911.28) | <.001 | .066 | .920 | <.001 |
|                   |           | CTC             | 4                 | 1037.08 (219.60–4897.95) | <.001 | .891 |
|                   | <65.0     | MRC             | 6                 | 157.44 (13.43–1845.62) | <.001 | .417 |
|                   |           | CTC             | 11                | 581.95 (80.84–4189.45) | <.001 | .787 |
| Percentage male (%)| ≥50.0    | MRC             | 5                 | 65.85 (5.72–735.77) | <.001 | .321 | <.001 | <.001 |
|                   |           | CTC             | 9                 | 325.46 (43.29–2446.88) | <.001 | .312 |
|                   | <50.0     | MRC             | 2                 | 506.91 (118.39–2170.37) | <.001 | .411 |
|                   |           | CTC             | 6                 | 1659.83 (46.42–5894.39) | .787 | .787 |

CIs = confidence intervals, CTC = computed tomography colonography, DOR = diagnostic odds ratio, MRC = magnetic resonance colonography.
correlated with differences in the lifestyle. Although mean age of the patients was not a significant factor for the DOR of MRC, the reason for this could be due to the evaluation of smaller number of studies on the diagnostic value of MRC for diagnosing CRC, and only 1 study included patients with mean age of >65.0 years. Several advantages of this meta-analysis should be highlighted. First, only prospective studies were included for evaluation, which could avoid uncontrolled biases in the retrospective studies. Second, the current meta-analysis was based on large sample size, and the results were stable, providing the accurate assessment of the diagnostic ability of MRC and CTC. Third, comprehensive diagnostic parameters were calculated, which ensures guidance to further directions. Finally, subgroup analyses for DOR based on sample size, mean age, and percentage male were calculated, and the indirect comparisons for DOR between MRC and CTC were provided.

However, our study has few limitations which were as follows: substantial heterogeneity across the included studies was observed, indicating differences in the characteristics of the study and participants. However, stratified analyses based on most of the characteristics of patients were not conducted due to alterations in the inclusion criteria of patients in each individual study and these items were qualitative; the current meta-analysis was based on published studies, and the publication bias remained an inevitable problem; the analysis of this study was based on pooled data, and the individual data of patients’ characteristics were not available, restricting us to conduct a more detailed analyses.

In conclusion, the results of this quantitative meta-analysis indicated that both MRC and CTC have relatively higher diagnostic values for detecting CRC. The DOR was relatively high in sample size of <100, mean age of <65.0 years, and percentage male <50.0% in patients who received MRC, while the DOR in CTC was higher if sample size ≥100, mean age ≥65.0 years, and percentage male <50.0%. Also no significant differences were found between MRC and CTC for DOR in all the subsets. Large-scale prospective head-to-head studies should be conducted to directly compare the diagnostic values of MRC and CTC for detecting CRC in future.

**Author contributions**

Conceptualization: Yanjun Gao, Jing Wang.

Data curation: Yanjun Gao, Jing Wang, Ge Liu.

Formal analysis: Hairong Lv, Yongjie Xue, Ge Liu.

Resources: Rongrong Jia.

Writing – original draft: Rongrong Jia, Weixian Bai, Yi Wu, Lang Zhang, Junle Yang.

Writing – review & editing: Lang Zhang.

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