



Safety and effectiveness of MRE in comparison with CTE in diagnosis of adult Crohn's disease

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Abstract

Background: Crohn's disease (CD) is a chronic inflammatory disease of the gastrointestinal tract that is characterized by recurrent attacks and frequent recovery. The lifelong course of this disease requires frequent assessment of the disease activity. The aim of this study was to compare the effectiveness and safety of computed tomography enterography (CTE) to magnetic resonance enterography (MRE) in adults with CD.

Methods: A systematic review of the literatures was performed to evaluate the effectiveness and safety of CTE in comparison with MRE. PubMed, Cochrane Library, Scopus, Web of Science, and Embase were searched. Effectiveness outcomes included were sensitivity, specificity, diagnosis difference, diagnostic odds ratio, and positive and negative likelihood. Quality assessment of the studies was conducted using the QADAS score. Meta-analysis was done by RevMan 5.3 for selected outcomes.

Results: Five studies had eligibility for analyzing effectiveness. The meta-analysis results showed that diagnosis difference of MRE and CTE, for diagnosing active CD (0.03 CI 95% -0.07–0.13), fistula (-0.01 CI 95% -0.09–0.07), and cramping (-0.02 CI 95% -0.1–0.06) were not statistically significant. Six studies were finally selected for safety assessment. The results showed that people who are examined with CTE frequently are at increased risk of developing cancer significantly, as they receive more than 50 msv of radiation per year.

Conclusion: There was no significant difference between MRE and CTE in diagnosis of Crohn's activity, detection of bowel obstruction, and detection of fistula and stenosis of the alimentary canal. However, the assessment of the safety profile of MRE and CTE showed that MRE is meaningfully safer than CTE for evaluating the recurrence of CD.

Keywords: Magnetic resonance enterograph, Computed tomography enterography, Crohn disease, Radiation, 50 mSv

Conflicts of Interest: None declared

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Introduction

Crohn's disease (CD) is a chronic inflammatory disease of the digestive tract that is characterized by recurrent

attacks and frequent recovery. The prevalence of this disease has increased in Western countries, Eastern Europe,

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↑What is "already known" in this topic:

Crohn disease (CD) is characterized by recurrent attacks. Two common diagnostic methods, computed tomography enterography (CTE) and magnetic resonance enterography (MRE) are used to diagnose and follow-up CD activity. CTE is equipped with special X-ray radiation and can increase the risk of cancer. However, MRE has no X-ray radiation.

→What this article adds:

No significant difference was found between MRE and CTE in the diagnosis of Crohn's activity. Patients, who are examined with CTE frequently, receive more than 50 msv of radiation per year and are at the risk of developing cancer significantly. Therefore, MRE is much safer than CTE for evaluating the recurrence of CD.

Asia, and developing countries since the Second World War (1). Although the prevalence of this disease is still unknown in Iran, recent studies have shown that the incidence of this disease is increasing in recent years (2). CD could cause death rarely, but it causes morbidity and disability frequently, especially in young patients. Since this group of patients have a high potential for growth, education, and productivity, their disease can negatively affect the economic dimensions of the society significantly (3).

Given the specific nature of CD, including its chronicity, recurrence, frequency, and difficulty of access to the small bowel, it is necessary to evaluate the disease activity frequently. Thus, the safety and effectiveness of the diagnostic methods are crucial (4, 5). Imaging techniques such as computed tomography enterography (CTE) and magnetic resonance enterography (MRE) are used to diagnose CD. The main purpose of imaging is to detect the disease early; it can also help to identify the presence and severity of the disease and to evaluate the response of the treatment and extraintestinal complications.

CTE offers superior small bowel visualization. It uses special x-ray equipment and can increase the risk of cancer slightly (6). MRE uses a magnetic field to create detailed images that provide multidimensional photos (7). Its advantages are creating detailed imaging with the high-contrast resolution to evaluate the small bowel in CD patients with no radiation exposure (5, 6). Nonetheless, some of the MRE's limitations such as taking a long time for imaging, less availability, and expensive price have caused doctors to prescribe CTE more. However, since the imaging of the bowel of CD patients is highly important for CD management, the evaluation of effectiveness and safety of CTE and MRE is highly important.

Thus, the aim of this systematic review was to evaluate the effectiveness and safety of MRE compared to CTE in adult patients with CD or adults suspected with CD.

Methods

A systematic review of the electronic databases, including the PubMed, Cochrane Library, Scopus, Web of Science, and Embase (Appendix 1), up to August 2016 was done to evaluate the effectiveness and safety of the MRE and CTE in CD patients. A structured questionnaire was used to extract the data. Based on the structured questionnaires, keywords, possible combinations, and search strategy were determined. Then, a structured search was performed in the listed databases. The target population was adults with suspected CD. The intervention and its comparator were MRE and CTE diagnostic tests, respectively. Our favorite outcomes were sensitivity, specificity, diagnostic odds ratio, and positive and negative correlation ratio. Also, prospective studies that assessed the diagnostic accuracy of MRE and CTE were searched to assess CD activity in adult CD patients or adults suspected with CD.

Also, a manual search was conducted in key magazines in the field of CD. A standard extraction form was prepared for data extraction. The extracted data included (1) type of study and methods, (2) patients' attributes (number, age, and gender), (3) the characteristics of the disease, (4) diagnostic interventions, and (5) outcomes. Two coau-

thors extracted the data independently (E.S.S. and R.I.); and in the case of any disagreement, the third author (M.D.) made the decision, and this was according to inclusion criteria.

No limitation was considered in this search strategy; however, only English language studies were included in the final selection. The quality of the selected studies was assessed by the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) (Appendix 2) tool by 2 independent authors. This 14-item checklist has been designed to assess the quality of the diagnostic studies. In this study, quality was not used as a criterion for exclusion but it was considered in the final result.

Information of the National Medical Device Directorate was used to assess the safety of MRE and CTE. In addition, a review was conducted in PubMed to find any relevant safety studies on MRE and CTE.

A Meta-analysis was done using RevMan 5.3 for all of the effectiveness outcomes. Also, a meta-analysis was done for effectiveness outcomes.

Results

Figure 1 shows the process of identifying the search for texts, removing duplicates, screening by title, abstract, and full-text. The literature search yielded 1784 eligible articles, of which 63 were selected to be reviewed in full-text and 186 patients in 5 studies were eventually selected for analysis. All studies were prospective. The summary of the characteristics of the studies are presented in Table 1.

All studies were prospective. The summary of the characteristics of the studies are presented in Table 1.

Five studies were qualified for inclusion, and Meta-Disc was performed to analyze sensitivity and specificity of diagnosing Crohn's disease. The RevMan software was used for meta-analysis of outcome of effectiveness such as fistula, stenosis of the alimentary canal, and detection of the disease activity.

Detection difference of Crohn's activity between CTE and MRE

The levels of CD activation in the 5 selected studies were reported quantitatively. Therefore, the risk difference method was used for analyzing these levels. Also, Mantel-Haenszel method was used for weighting. To calculate the total effect, the modified risk ratio values were used. Moreover, to measure heterogeneity in these studies, I^2 parameters and the chi-two tests were applied. The value of I^2 was 18%. Since the value of this index was less than 30%, the degree of heterogeneity was low, according to the Cochrane guide book. In addition, the value of χ^2 indicated that the homogeneity in these studies was good. Thus, the fixed effects method was used to analyze the results. The results are presented in Figure 2.

This fixed model showed that the risk difference in detecting CD activation was 0.03 in these 5 studies. In other words, it showed no significant difference between the risk differences of MRE and CTE. Also, the confidence intervals were 0.13 and -0.07, respectively, and the interval also included zero, which can confirm that there was no statistically significant difference between MRE and

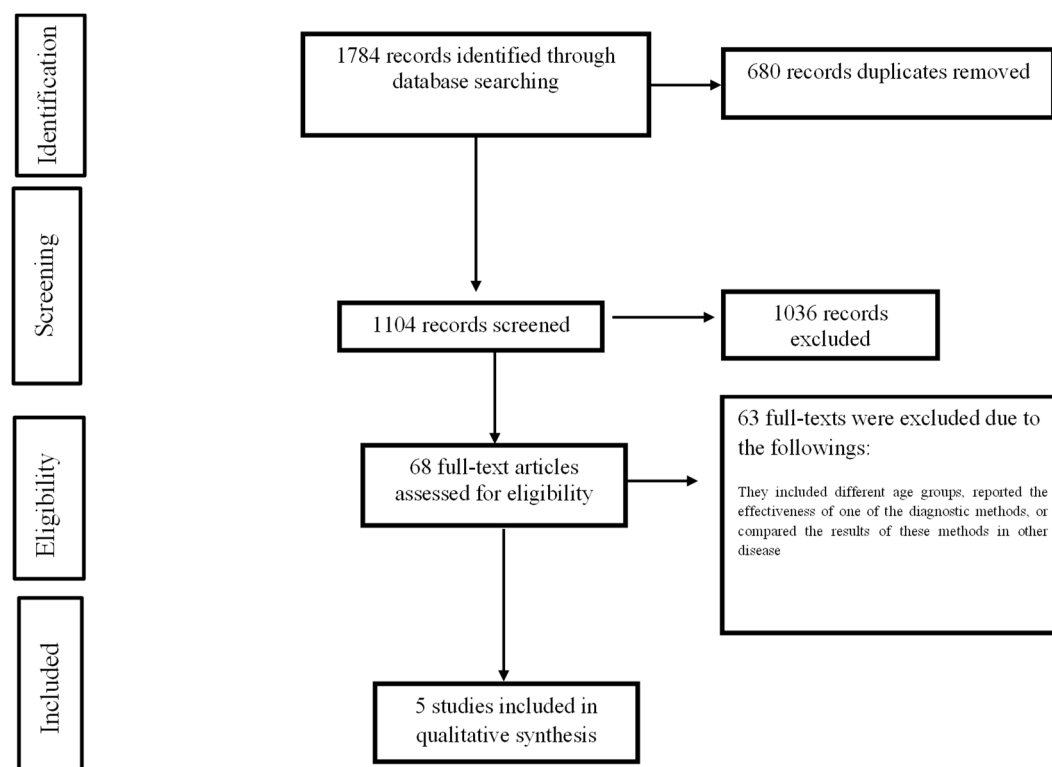


Fig. 1. PRISMA Flow Diagram

Table 1. Characteristics of the selected studies

Author's name	Year	Country	Study design	Disease status	Female	Man	Whole	Intervention	QUADAS mark
Siddiki (8)	2008	USA	Prospective	Suspected	15	18	33	MRE vs CTE	11
Lee (9)	2009	Korea	Prospective	Sick or suspected	13	17	30	MRE vs. CTE vs. SBFT	11
Fiorino (10)	2011	Italy	Prospective	Sick	11	23	44	MRE vs CTE	11
Jensen (11)	2011	Denmark	Prospective	Sick or suspected	37	13	50	MRE vs CTE	12
Masselli (12)	2015	Italy	Prospective	Suspected	-	-	29	MRE vs CTE	12

CTE in detecting CD activity with 95% confidence interval.

Comparison of detection differences of fistula between CTE and MRE

To conduct meta-analysis of MRE and CTE in detecting fistula, 3 studies were finally included for analysis. The fistula detection rate was reported quantitatively. Therefore, the risk difference of the methods was used for anal-

ysis. Also, Mantel-Haenszel method was used for weighing the modified risk ratio values to calculate the total effect. Moreover, to measure heterogeneity in these studies, I^2 parameters and the χ^2 tests were used. The value of I^2 was considered zero. Since the value of this index is less than 30%, it can be stated that the degree of heterogeneity was low according to the Cochrane guide book. The results are presented in Figure 3.

This fixed model showed that the risk difference in de-

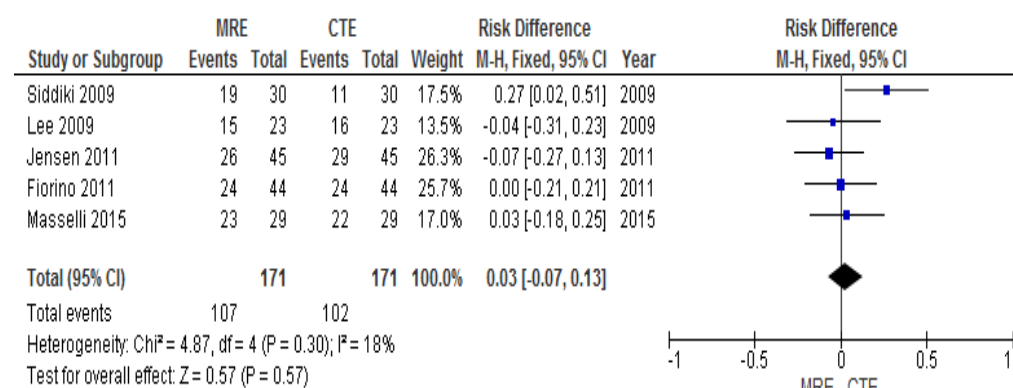


Fig. 2. Comparison of detection difference of Crohn's disease activity between CTE and MRE

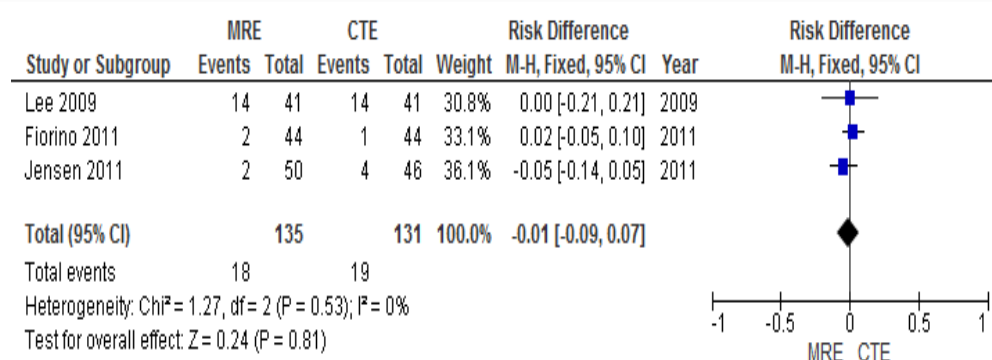


Fig. 3. Comparison of detection difference of fistula between CTE and MRE

detecting fistula in these 3 studies was -0.01. In other words, it showed no significant difference in risk difference between the 2 methods. Also, as the amount of confidence intervals was -0.09 and 0.07, the interval included zero value, showing no statistically significant difference between the 2 methods in detecting fistula with 95% confidence interval.

Comparison of detection difference of bowel obstruction between CTE and MRE

Two studies were found to conduct meta-analysis of MRE and CTE in detecting intestinal obstruction. The detection of intestinal obstruction rate was reported quantitatively. Therefore, the risk difference method was used. Also, the Mantel-Haenszel method was used for weighing to calculate the total effect, and the modified risk ratio values were used. To measure heterogeneity in these studies, I² parameters and the chi-2 tests were used. The value of I² was zero, since the value of this index was less than 30%, the degree of heterogeneity was low,

according to the Cochrane guide book and the value of chi-2 indicated homogeneity in these studies. Therefore, the fixed effect method was used to report the results (Figure 4).

This fixed model showed that the risk difference in detecting intestinal obstruction in 2 studies was -0.02. In other words, it showed no significant difference between the risk difference in the 2 methods. Also, the amount of confidence intervals was -0.1 and 0.06, and the interval included zero value. These could reveal that there was no statistically significant difference between the 2 methods in detecting intestinal obstruction with 95% confidence interval. Characteristics of the included studies for meta-analysis of diagnostic accuracy are presented in Table 2.

Meta-analysis of sensitivity of MRE and CTE

To analyze the sensitivity of MRE and CTE, 5 studies were finally included for analysis. The values of true positive, false positive, true negative, and false negative were reported in these studies.

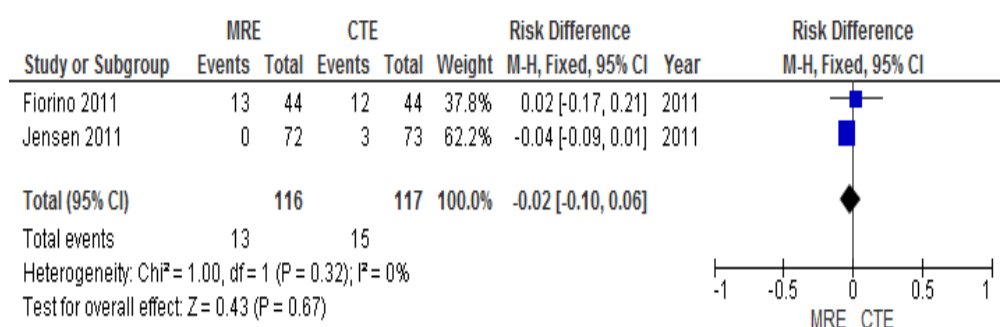


Fig. 4. Comparison of detection difference of bowel obstruction between CTE and MRE

Table 2. Characteristics of the included studies for diagnostic accuracy meta-analysis

Tech	Studies	True positive	False positive	False negative	True negative	Total
MRE	Lee (2009)	15	0	3	5	23
	Siddiki (2009)	19	3	2	6	30
	Fiorino (2011)	24	0	4	16	44
	Jensen (2011)	29	3	6	7	45
	Masselli (2016)	23	0	0	6	29
CTE	Lee (2009)	16	1	2	4	23
	Siddiki (2009)	11	2	1	16	30
	Fiorino (2011)	24	0	4	16	44
	Jensen (2011)	26	2	9	8	45
	Masselli (2016)	22	1	1	5	29

As the heterogeneity for MRE sensitivity was 44.9% and for CTE was 34.8% (both more than 30%), a random-effects meta-analysis was done using DerSimonian and Laird method on the pooled sensitivity for MRE and CTE. It was observed that the value of pooled sensitivity analysis of MRE and CTE was 0.88 and 0.85, respectively. The 0.88 sensitivity for MRE demonstrated that the power of the test was high for diagnosis of true CD patients and was higher than CTE.

Meta-analysis of specificity in MRE and CTE

For the purpose of the attribute specificity analysis, 5 studies were finally entered the analysis. The values of true positive, false positive, true negative, and false negative were reported in these studies.

The pooled specificity for MRE and CTE was calculated by the DerSimonian and Laird method, as the heterogeneity for MRE and CTE was 66.5% and 18.9%, respectively (both more than 30%). The value of pooled specificity for MRE and CTE was 0.87 and 0.89, respectively. The 0.87 specificity for MRE indicated that although the power of MRE was high for diagnosis of true patients, the specificity of CTE was slightly higher.

Positive likelihood ratio

To examine the value of performing a diagnostic test, positive likelihood ratio (LR) was used in MRE and CTE tests, with the greater values showing better results.

The results of positive LR for MRE and CTE was 4.44 and 6.04, respectively. The results showed that although both of the tests were reliable, positive LR for CTE was higher than MRE.

The negative LR for MRE and CTE was 0.16 and 0.18, respectively. These figures also confirmed that although both methods were reliable, the value for the MRE was less than CTE.

Diagnostic odds ratio

The odds ratios greater than 1 indicate that the test is efficient in practice. Likewise, odds ratios less than 1 indicate that the test does not work efficiently. The higher value shows a better efficacy.

The meta-analyses showed that the diagnostic odds ratio of CTE was 40.58, which was higher than the diagnostic odds ratio of MRE 34.99.

Receiver operating characteristic (ROC) curve

The receiver operating characteristic (ROC) curve was

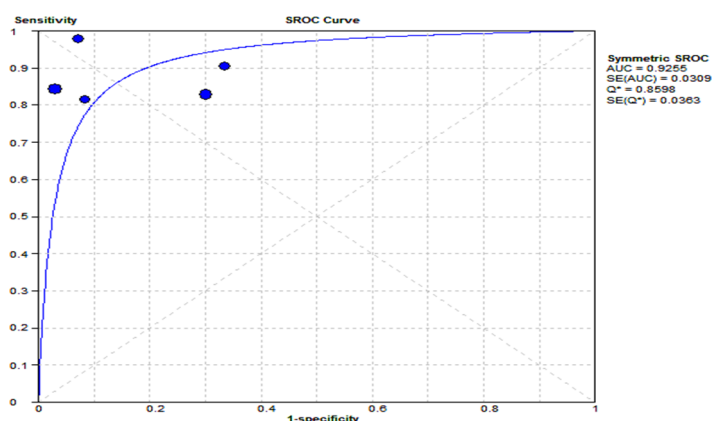


Fig. 5. ROC curve of MRE

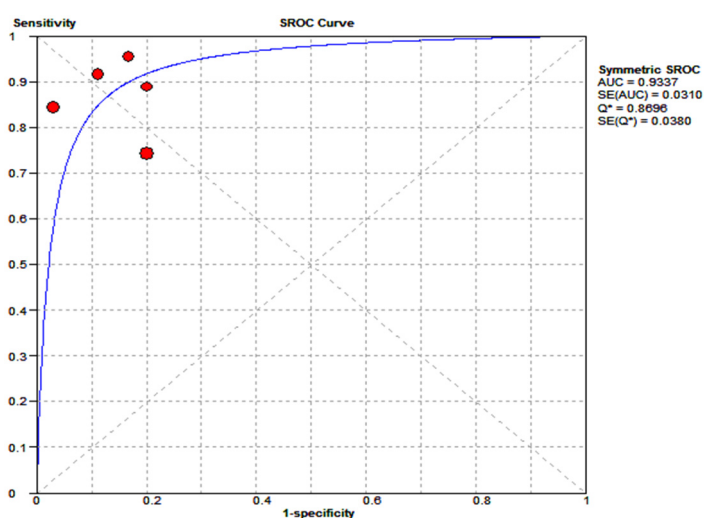


Fig. 6. ROC curve of CTE

used to evaluate the performance of the diagnostic tests. Figures 5 and 6 demonstrate the ROC curve for MRE and CTE.

The ROC curve showed that the area under the curve was 0.925. Also, the value of the index Q was about 0.86. Both values indicated the high diagnostic power of MRE. Also, the surface under the curve and the Q index for CTE was 0.934 and 0.87, respectively. Comparing the results of rock curves confirmed that CTE has a higher diagnostic power.

Results of MRE and CT safety

To evaluate the safety of MRE and CTE, a rapid review was conducted. The keywords of computed tomography, diagnostic radiation, ionizing radiation, radiation exposure, Crohn disease, and inflammatory bowel disease were searched in PubMed database. A total of 935 articles were identified primarily. However, after assessing the eligibility of the articles, finally 6 retrospective studies were included and analyzed qualitatively.

The findings confirmed that exposure to ionizing radiation less than 50 millisieverts (mSv) can increase the growth of solid tumors. A millisievert (mSv) is defined as "the average accumulated background radiation dose to an individual for 1 year". However, there is no strong evidence to support this statement. Nonetheless, there is

some evidence and almost a consensus that exposures to cumulative effective dose more than mSv 50 <(CED) is dangerous for human bodies. This amount of radiation is equivalent to 5 abdominal and pelvic CT scans (13, 14). A comprehensive presentation and discussion of MR-related hazardous effects are beyond the scope of this review. We are exposed to natural ionizing radiation in the environment, and each time we are exposed to CT scans, it is as if we have been exposed to natural ionizing radiation for several years. Induced radiation doses of gastrointestinal imaging, compared to environmental radiation, which were extracted from radiological information (13, 14), are presented in Table 3.

These retrospective studies have shown that some factors such as duration of disease, severity of the disease, surgery, hospitalization, smoking, using steroids and immunosuppressive drugs, and prior surgery can cause more exposure, with cumulative effective dose more than 50 mSv, in these patients. The characteristics of studies that evaluated safety are summarized in Table 4.

MRE is a specific type of magnetic resonance imaging which produces qualified images of the digestive tract. To date, many studies have been done on magnetic fields, but there is no evidence of harmful bioeffects produced by MRE in the long-term. Even at the field strength of 10T, no unpleasant effects have been observed in monkeys. Most studies have not shown any effect on cell growth

Table 3. Radiation dose of gastrointestinal imaging studies compared to natural radiation

Duration of time identical to effective dose of background radiation	An average effective dose	Imaging techniques
10.3 years	31	Several phases CT of the abdomen and pelvis
3.3 years	10	Abdomen/pelvis CT scan
3.3 years	10	CT scan colonography
2.7 years	8	Abdomen CT scan
1.7 years	5	Small intestine CT scan

Table 4. Characteristics of the selected studies for safety

Name of study	Number of patients	Country	Design of study	Age of population	>mSv 50 Result of (CED)	Factors related to exposure to high dose of radiation
Newnham et al 2007 (15)	62	Australia	Retrospective study	Adult 16 – 24 years old	14.5 %	Age, duration of disease, cardiac surgery, using immunosuppressive drugs
Butcher et al, 2012 (16)	280	England	Retrospective study of Inflammatory bowel disease clinic	Adult	6.3 %	duration of disease, smoking, history of surgery, heart disease
Jung et al, 2013 (17)	777	South Korea	retrospective study of 13 hospitals of south Korea	Adult Average age: 29.2	34.7 %	Patient's age at diagnosis, sex, history of surgery, using steroid
Chatu et al, 2015 (18)	217	England	Retrospective study of patient who referred regularly to only sophisticated center	Adult Average age: 30.8	13.36 %	history of surgery, age, signs out of bowel
Estay et al, 2015 (19)	82	Chile	Retrospective study of Selected patients from the registry of inflammatory bowel disease	Adult 16-68 years old	19.5 %	Age, duration of disease, history of surgery, Biological agents in Crohn's disease, site of involvement
Ciáurriz-Munuce, et el, 2012 (20)	235	Spain	Retrospective study	Adult 16-82 years old	20.89 %	Age more than 40 years, need to surgery, age less than 16 at diagnosis, duration of disease

and morphology at the field strengths up to 2T. Data reported from the National Institute for Occupational Health, World Health Organization, and the US State Department have not provided any evidence of leukemia or other malignancies due to the MRE imaging. However, the New England Journal of Medicine reported increase of leukemia in people who were exposed to electromagnetic fields in Washington from 1950 to 1979. In these cases, electromagnetic fields were caused by alternating streams leading to variable domains; also, the same effect was found in New York in 1987. However, no evidence of harmful effects was found in people who work with linear accelerators or in steady magnetic fields. However, minor and reversible effects due to magnetic fields have been observed in some studies. Metal implants produce a serious effect like torque, heat, and artifact in MRI images, so any history of surgery should be determined before MRI (21).

Discussion

The aim of this study was to determine the effectiveness and safety of MRE in comparison with CTE in adult patients with CD or suspected to have CD.

The results of the meta-analysis showed no significant difference between MRE and CTE in detecting active CD, fistula, and intestinal obstruction.

The pooled sensitivity and specificity of MRE and CTE showed that although the sensitivity of MRE was slightly higher than CTE, its specificity was lower.

The positive likelihood ratio in the diagnostic test between MRE and CTE showed that the probability of positive test for the patient was more with CTE compared to MRE. On the other hand, the negative likelihood ratio in the diagnostic test between MRE and CTE showed that the probability of negative test was less by MRE in this group.

Comparison of the diagnostic odds ratio between MRE and CTE revealed that the effectiveness of CTE was greater than MRE. Likewise, the ROC curves showed that the power of detection of CTE was higher than MRE. Nonetheless, the results confirmed that both devices have good practical efficiency in practice.

Because this review considered those studies conducted up to August 2016, another search was conducted in PubMed up to September 5, 2018. In this search, 2 related studies were found: Mitchell (22) and Wenhong Liu (23) studies. In Mitchell study, the effect of CTE and MRE were assessed in children and young people who suffered from CD in small intestine. Wenhong Liu (23) study was a systematic review of the effectiveness of magnetic resonance imaging (MRI) and computed tomography (CT) in assessing small bowel CD in different age groups. Both studies showed that CTE and MRE are good tools for diagnosing and evaluating CDs. This study showed that MRE can be a good alternative to CTE in patients with CD. Another systematic review conducted by Y. Qiu et al in 2014 (24) assessed 6 studies with 290 patients in different age groups. This study also showed that MRE had as much diagnostic power as CTE and could be a good alternative to assess CD (24). All of these studies were excluded

from the present study because of their populations' age groups.

The assessment of the safety of MRE and CTE showed that MRE is a safer method to evaluate the recurrence of CD mainly because it does not use X-ray for imaging.

The nature of CD is characterized by recurrence; thus, to detect the relapse of the disease frequently, all patients are required to undergo several imaging tests. The majority of the patients are young adults, and the repeated X-ray-based imaging increases their exposure to harmful cumulative levels of ionizing radiation, increasing the risk of cancer. Many studies have shown that these patients will be exposed to high radiation doses more than 50 mSv, which can increase the chances of developing cancer seriously (15-20).

One of the strengths of this study was its focus on safety. The results showed that frequent X-ray imaging would cause an accumulation of harmful level of radiation, which in turn would increase the risk of cancer during the patients' lifetime. As MRE is a magnetic resonance imaging, it can produce qualified images of the digestive tract with no evidence of harmful bioeffects (21).

Conclusion

No significant difference was found between MRE and CTE in the diagnosis of CD activity, detection of bowel obstruction, and detection of fistula and stenosis of the alimentary canal. However, the assessment of the safety profile of MRE and CTE showed that MRE is meaningfully safer than CTE for evaluating the recurrence of CD. This is a highly significant result, particularly when considering the frequent use of imaging by CD patients and the importance of avoiding potential risk of cancer development in using CTE.

Conflict of Interests

The authors declare that they have no competing interests.

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Appendix

Appendix 1. Strategy of search

<p>PubMed</p> <ol style="list-style-type: none"> 1. Crohn's* disease 2. Regional Enteritis 3. Inflammatory Bowel Disease 4. Enteritis AND Granulomatous 5. Granulomatous Enteritis 6. Enteritis AND Regional 7. Ileocolitis 8. Colitis AND Granulomatous 9. Granulomatous Colitis 10. Ileitis AND Terminal 11. Terminal Ileitis 12. Ileitis AND Regional 13. Regional Ileitis 14. #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 15. Magnetic resonance enterography OR MR enterography OR MRE 16. Computed Tomography Enterography OR CT Enterography OR CTE 17. #15 or #16 18. #14 AND #17 <p>Cochrane library</p> <ol style="list-style-type: none"> 1. Crohn's* disease 2. Regional Enteritis 3. Inflammatory Bowel Disease 4. Enteritis and Granulomatous 5. Granulomatous Enteritis 6. Enteritis and Regional 7. Ileocolitis 8. Colitis and Granulomatous 9. Granulomatous Colitis 10. Ileitis and Terminal 11. Terminal Ileitis 12. Ileitis and Regional 13. Regional Ileitis 14. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 15. Magnetic resonance enterography 16. MR enterography 17. MRE 18. #15 or #16 or #17 19. Computed Tomography Enterography 20. CT Enterography 22 21. CTE 22. #19 OR #20 OR #21 23. #18 OR #22 24. #14 AND #23 	<p>Scopus</p> <ol style="list-style-type: none"> 1. Crohn's* disease 2. Regional Enteritis 3. Inflammatory Bowel Disease 4. Enteritis AND Granulomatous 5. Granulomatous Enteritis 6. Enteritis AND Regional 7. Ileocolitis 8. Colitis AND Granulomatous 9. Granulomatous Colitis 10. Ileitis AND Terminal 11. Terminal Ileitis 12. Ileitis AND Regional 13. Regional Ileitis 14. #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 15. Magnetic resonance enterography OR MR enterography OR MRE 16. Computed Tomography Enterography OR CT Enterography OR CTE 17. #15 or #16 18. #14 AND #17 <p>Web of science</p> <ol style="list-style-type: none"> 1. TI= (Crohn's* disease OR Regional Enteritis OR Inflammatory Bowel Disease OR Granulomatous Enteritis OR Ileocolitis OR Colitis OR Granulomatous Colitis OR Terminal Ileitis OR Regional Ileitis) 2. TI= (Magnetic resonance enterography OR MR enterography OR MRE) 3. TI= (Computed Tomography Enterography OR CT Enterography OR CTE) 4. #2 OR #3 5. #1 AND #4 <p>Embase</p> <ol style="list-style-type: none"> 1. Crohn's* disease/exp 2. Regional Enteritis 3. Inflammatory Bowel Disease 4. Enteritis AND Granulomatous 5. Granulomatous Enteritis 6. Enteritis AND Regional 7. Ileocolitis 8. Colitis AND Granulomatous 9. Granulomatous Colitis 10. Ileitis AND Terminal 11. Terminal Ileitis 12. Ileitis AND Regional 13. Regional Ileitis 14. #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 15. Magnetic resonance enterography OR MR enterography OR MRE 16. Computed Tomography Enterography OR CT Enterography OR CTE 17. #15 or #16 18. #14 AND #17
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Appendix 2. QUADAS check list

Item		Yes	No	Unclear
1.	Was the spectrum of patient's representative of the patients who will receive the test in practice?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2.	Were selection criteria clearly described?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.	Is the reference standard likely to correctly classify the target condition?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4.	Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5.	Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6.	Did patients receive the same reference standard regardless of the index test result?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7.	Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8.	Was the execution of the index test described in sufficient detail to permit replication of the test?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9.	Was the execution of the reference standard described in sufficient detail to permit its replication?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10.	Were the index test results interpreted without knowledge of the results of the reference standard?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11.	Were the reference standard results interpreted without knowledge of the results of the index test?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12.	Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13.	Were uninterpretable/ intermediate test results reported?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14.	Were withdrawals from the study explained?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>