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Evaluation of the diagnostic value of multi-slice spiral CT in acute mesenteric ischemic diseases: a meta-analysis of randomized controlled trials

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Abstract. – OBJECTIVE: This study aimed to investigate the diagnostic value of multi-slice spiral CT (MSCT) in acute mesenteric ischemia.

MATERIALS AND METHODS: A systematic review was performed from the databases of PubMed, Web of Science and EMBASE by two researchers updated to July 1, 2018. The search terms included in the databases were mesenteric ischemia and multi-slice spiral computed tomography. A self-made data extraction form was used for data extraction, followed by quality assessment and heterogeneity testing of literature that met the requirements. Combined specificity and sensitivity were calculated and receiver operating characteristic (ROC) analyses were conducted. Meta-analysis was performed by STATA 12.0.

RESULTS: In this meta-analysis, 231 patients with acute mesenteric ischemic disease and 651 patients in the control group in 8 independent randomized case-control studies were enrolled. Our meta-analysis showed that MSCT had significantly improved the diagnosis of acute mesenteric ischemia. Because of statistical heterogeneity in the study, we used the random effects model for analysis. The combined sensibility was 94% (95% CI: 83%-98%), and the combined specificity was 97% (95% CI: 93%-99%). The combined positive predictive value was 32.48 (95% CI: 13.53-77.98), the combined negative predictive value was 0.07 (95% CI: 0.02-0.18), and the combined diagnostic odds ratio was 6.21 (95% CI: 4.58-7.84). In terms of comprehensive diagnostic performance, the AUC was 0.99 (95% CI: 0.98-1.00) after plotting the SROC curve.

CONCLUSIONS: MSCT had a high sensitivity and specificity for the diagnosis of acute mesenteric ischemia. In addition, these studies with large samples and high quality in a multi-center hospital were needed to further confirm the reliability.

Key Words:
MSCT, Diagnosis, Mesenteric ischemic diseases, Meta-analysis.

Introduction

Mesenteric ischemia patients account for about 1% of hospitalized patients with acute abdomen[1]. With the increasing awareness of mesenteric ischemic diseases, the diagnostic rate of acute mesenteric ischemia-related diseases has increased. However, the mortality rate of mesenteric ischemia has not improved significantly due to the delayed diagnosis and inaccurate treatment, further leading to ischemic necrosis of the small intestine[2,3]. Acute mesenteric ischemic diseases include three categories, namely acute mesenteric artery embolism and thrombosis, mesenteric venous thrombosis, and non-occlusive mesenteric ischemia (NOMI)[4-6]. Due to the occult or mild symptoms of mesenteric ischemia, misdiagnosis or missed diagnosis often occurs in clinical practice[7,8]. Localized or systemic hypercoagulable state is the major risk factor for mesenteric ischemia. Therefore, accurate early diagnosis is the key to timely treatment of mesenteric ischemia. Imaging diagnosis is a very effective diagnostic approach, such as CT and selective arteriography[8,9]. Although imaging diagnosis has a high sensitivity to vascular embolization, it is an invasive procedure and requires experienced radiologists. More importantly, it is often difficult to diagnose NOMI[10,11].

The onset of mesenteric ischemic disease is insidious and rapid. It is difficult to diagnose only based on clinical manifestations. Symptoms of mesenteric ischemia are not very specific, which are often inconsistent with physical examinations[8]. Hence, mesenteric ischemia is often be misdiagnosed, and sometimes only be confirmed until laparotomy. The prognosis of mesenteric ischemia greatly relies on the early diagnosis and timely recanalization of blood vessels[10]. Although

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the development of CT angiography contributes to the improved diagnosis of mesenteric ischemia, an objective evaluation index for the vitality of intestinal tubes is still lacked[12]. Multi-slice spiral CT (MSCT) is a non-invasive method with high diagnostic accuracy, which has been well recognized in recent years[13]. In addition, MSCT makes it possible to examine patients faster, better, and more extensively. It also expands the clinical application of CT, such as isotropic imaging, musculoskeletal examination, multi-directional reconstruction in special cases, CT myelography, extensive and multi-temporal studies[14,15]. Therefore, MSCT is superior to single-slice spiral CT in almost all aspects of clinical practice, making it a valuable method for the diagnosis of acute mesenteric ischemia disease[16].

Previous studies[17] have pointed out that MSCT has diagnostic value for acute mesenteric ischemia. In this study, we analyzed literature on the diagnostic value of MSCT in the diagnosis of acute mesenteric ischemia. We further explored the reliability of MSCT in the diagnosis of patients with acute mesenteric ischemia.

Materials and Methods

Literature Search

A systematic review was performed from the databases of PubMed, Web of Science and EMBASE by two researchers updated to July 1, 2018, without language restriction. The search terms included in the databases were mesenteric ischemia and computed tomography. The two researchers independently screened the literature through the retrieved literature titles and abstracts, and further determined whether or not to include them based on the full text. We searched again re-searched the references provided in the searched literature. After cross-checking, the disputed literature was discussed to be solved. If there were multiple documents with the same data or overlapping data, the largest or most recently published literature was included.

Inclusion and Exclusion Criteria

The literature inclusion criteria were applied to those published literature, in which the effective diagnosis of acute mesenteric ischemic disease was confirmed by effective MSCT. Case-control studies on exploring the relationship between MSCT and diagnostic reliability of acute mesenteric ischemic diseases were selected.

Two researchers independently assessed the quality of the literature and extracted the data according to the designed form. In case of disagreement, it was resolved through discussion or according to the opinion of the third researcher. The specific inclusion criteria were as follows: (1) Chinese and English literature; (2) studies on evaluating the clinical diagnostic value of MSCT in the diagnosis of acute mesenteric ischemia; (3) prospective or retrospective studies; (4) over 20 subjects; (5) all subjects included in the study underwent MSCT examination; (6) if the data was published repeatedly, the most detailed data or recently published articles were selected; (7) data were provided that can be directly or indirectly calculated for true positive (TP), false positive (FP), true negative (TN), and false negative (FN), respectively.

Exclusion criteria were as follows: (1) literature on evaluating acute mesenteric ischemic disease alone; (2) other CT treatment techniques rather than MSCT for the diagnosis of acute mesenteric ischemia; (3) studies with repeated reporting and poor quality were excluded; (4) reviews and abstracts were excluded.

Data Extraction

A self-made data extraction form was used for data extraction, which achieved good results in the previously published systematic review. The data extraction table contained the following contents: author, year, country, prospective design, number of MSCT rows, collimation, section width, oral contrast agent, intravenous contrast agent, number of case and control, true positive value (TP), false positive value (FP), true negative value (TN) and false negative value (FN).

Statistical Analysis

The statistical heterogeneity between the combined studies was first evaluated, followed by combined analysis. Statistical analysis was performed using Stata software (version 12.0, Stata Corporation, College Station, TX, USA). $p<0.05$ indicated statistically significant.

Heterogeneity analysis was performed using the chi-square test and I^2 test was used to detect statistical heterogeneity between studies. The test level $\alpha = 0.10$. If $I^2>50\%$ or $p<0.10$, a random effects model was used for meta-analysis. If $I^2 \leq 50\%$ or $p \geq 0.10$, a fixed effect model was used for meta-analysis.

The test level of the meta-analysis was set at $\alpha=0.05$. Combined sensitivity, combined speci-

ficity, combined positive predictive value, combined negative predictive value, combined diagnostic odds ratio, and 95% confidence interval (CI) were calculated. Meanwhile, the summary receiver operating characteristic curve (SROC) of the meta-analysis results of each study was plotted, and the area under curve (AUC) was calculated.

A linear review of the diagnostic odds ratios for each study was performed to test its publication bias, and the test level was set to $\alpha = 0.10$.

Results

Characteristics of the Studies

In this meta-analysis, 231 patients with acute mesenteric ischemic disease in 8 independent randomized case-control studies and 651 patients in the control group were enrolled[18-25]. The diagnostic effect of the acute mesenteric ischemic disease was evaluated by MSCT. Characteristics and methodology assessment of individual studies included in the meta-analysis are shown in Table I. The process of document search and selection is illustrated in Figure 1.

Quantitative Synthesis Results

Our meta-analysis showed that MSCT has significantly improved the diagnosis of acute mesenteric ischemia. The random effects model was used since the combined sensitivity results of I^2=87.58%, and the combined sensitivity was 94% (95% CI: 83%-98%). In addition, the combined specificity results showed that I^2=69.61%, suggesting statistical heterogeneity. Hence, we used the random effects model for analysis, and the combined specificity was 97% (95% CI: 93%-99%, Figure 2). The combined positive predictive value was 32.48 (95% CI: 13.53-77.98), and the combined negative predictive value was 0.07 (95% CI: 0.02-0.18), and the combined diagnostic odds ratio was 6.21 (95% CI: 4.58-7.84, Figure 3). In terms of comprehensive diagnostic performance, the AUC was 0.99 (95% CI: 0.98-1.00) after plotting the SROC curve (Figure 4).

Test of Heterogeneity

I^2-square of the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic odds ratio was 87.58%, 69.61%, 48.67%, 88.62% and, 72.35%, respectively.

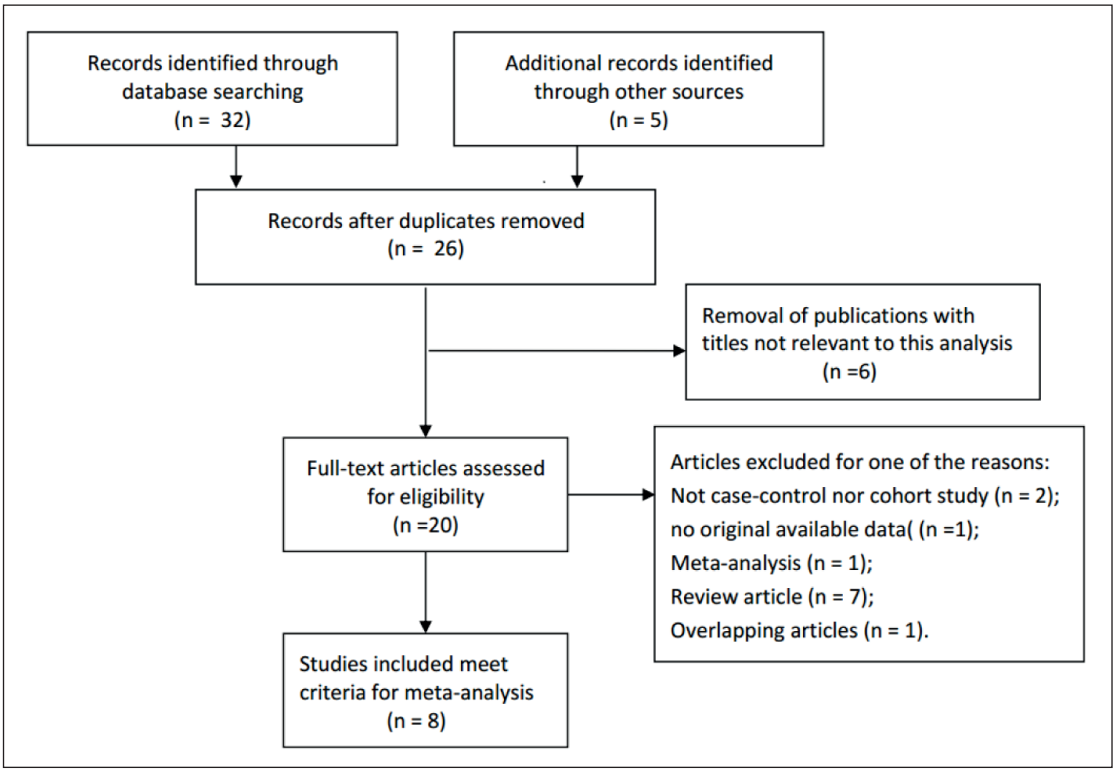

Figure 1. Flow diagram of selection process.

Table I. Characteristics and methodology assessment of individual studies included in the meta-analysis.

Author	Year	Country	Prospective Design	No. of Multidetector CT Rows	Collimation (mm)	Section Width (mm)	Oral Contrast Agent	Intravenous Contrast Agent	Case	Control	TP	FP	FN	TN
Taourel et al[24]	1996	France	No	4	-	-	None		39	24	25	2	14	22
Kirkpatrick et al[18]	2003	Canada	Yes	4	A: 1.25, PV: 5	A: 1.25, PV: 5	500–750 mL of water, as tolerated	140 mL of Omnipaque 300 at 4 mL/s	26	36	26	4	0	32
Wiesner et al[19]	2004	Switzerland	Yes	4	PV: 2.5	PV: 3	Positive contrast, as tolerated	100–120 mL of nonionic contrast agent at 2 mL/s	16	267	13	9	3	258
Zandrino et al[20]	2006	Italy	No	4	A: 2.5, PV: 2.5	A: 2.5, PV: 2.5	None (water in 4 cases)	130 mL of Iomeron 350 at 4 mL/s	26	34	24	0	2	34
Aschoff et al[21]	2009	Germany	No	16 or 40	16 rows: 0.75, 40 rows: 0.625	A: 1.0, PV: 2.0	None	1.2 mL/kg of Iomeron 400 at 4 mL/s	28	47	27	1	1	46
Ofer et al[22]	2009	Israel	No	16	A: 1.5, PV: 1.5 PV: 5	A: 2,	None	65–130 mL of Iomeron 300 at 3.5–4.0 mL/s	18	74	16	2	2	72
Akyildiz et al[23]	2009	Turkey	Yes	4	A: 1.25, PV: 5	A: 1.25, PV: 5	500–750 mL of water, as tolerated	140 mL of Omnipaque 300 at 4 mL/s	28	19	26	2	2	17
Yikilmaz et al[24]	2011	Turkey	No	16	–	–	–	–	50	150	50	0	0	150

A = scanning in arterial contrast phase, PV = scanning in portal venous contrast phase; TP = True Positive, FP = False Positive, FN = False Negative, TN = True Negative.

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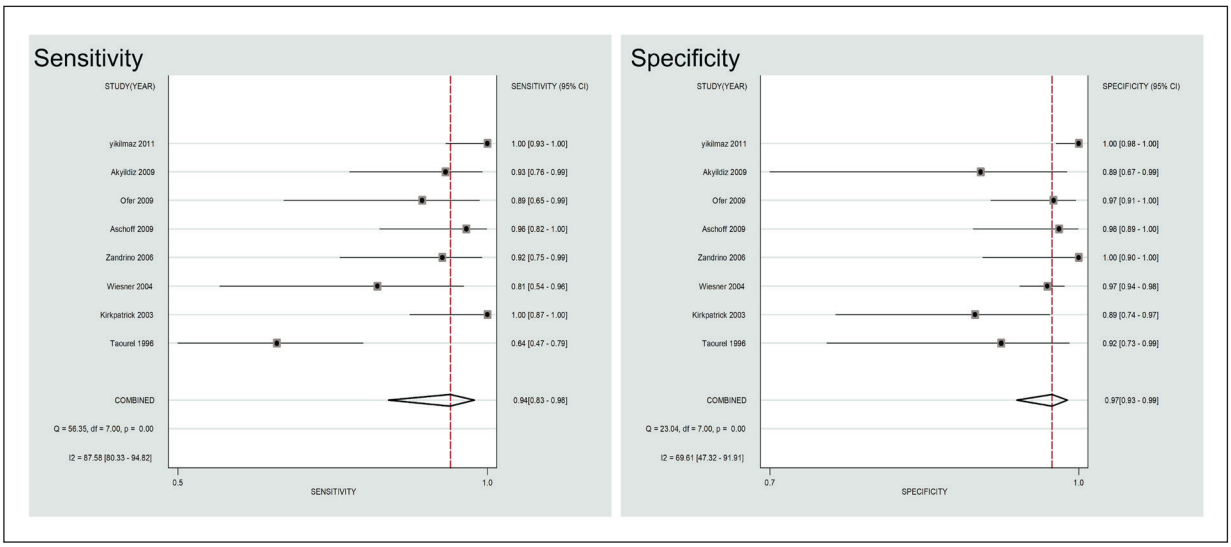

Figure 2. Forest plots of sensitivity and specificity by multi-slice spiral CT as a diagnostic technique for acute mesenteric ischemic disease in the 8 studies included for meta-analysis. Each solid circle represents an eligible study. The size of solid circle reflects the sample size of each eligible study. Error bars represent 95% CI.

It is indicated that there is a great heterogeneity between the included studies. To verify whether heterogeneity can be explained by threshold effects, the Spearman method was performed using different cut-offs, objective methods, and population to avoid the heterogeneity.

Publication Bias

Potential publication biases included in the study were evaluated by drawing symmetrical funnel shape. *p*-value for the slope coefficient was 0.91, indicating significant asymmetry and no possibility of publication bias (Figure 5).

Discussion

With the aging of the population, the incidence of acute mesenteric ischemic disease has increased significantly, which has become one of the major diseases that threatening human health[26]. The activity of the diseased intestine and the survival rate of patients with mesenteric ischemia are mainly determined by the time difference between the onset of symptoms and the definitive diagnosis. As a result, early diagnosis and treatment are the keys to reducing the mortality rate of mesenteric ischemic diseases[10,11].

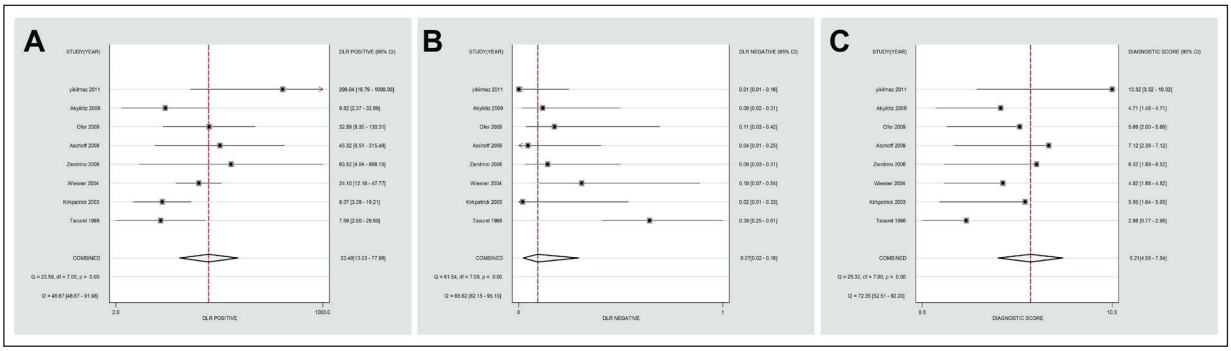

Figure 3. Forest plots of positive predictive value, negative predictive value and diagnostic odds ratio by multi-slice spiral CT as a diagnostic technique for acute mesenteric ischemic disease in the 8 studies included for meta-analysis. Each solid circle represents an eligible study. The size of solid circle reflects the sample size of each eligible study. Error bars represent 95% CI.

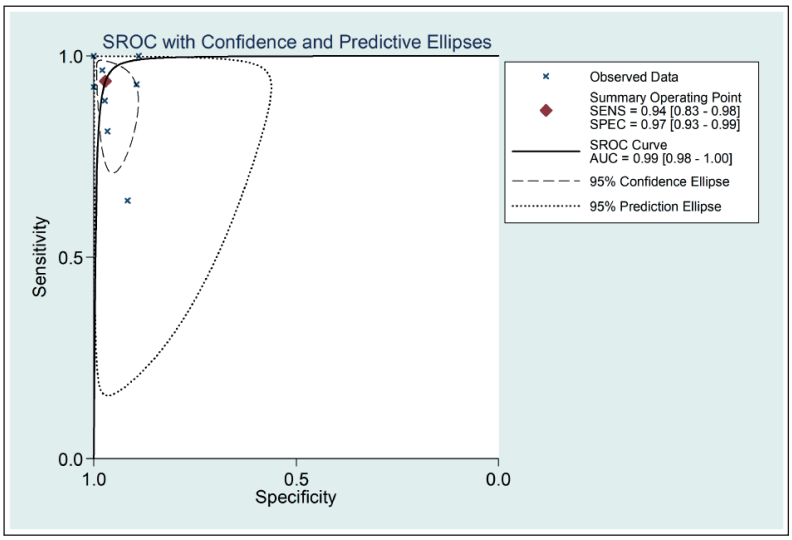

Figure 4. Summary receiver operating characteristic curves (ROCs) from the hierarchical summary receiver operating characteristic model generated from the 8 studies that found that multi-slice spiral CT as a diagnostic technique for acute mesenteric ischemic disease. Each solid circle represents an eligible study. The size of solid circle represents the sample size of each eligible study. The overall diagnostic efficiency is summarized by the regression curve.

Specific indicators for clinical manifestations and laboratory tests of acute mesenteric ischemic diseases are still lacked. Therefore, imaging studies are still the major diagnostic method[27]. In recent years, with the development of CT technology, especially the wide application of MSCT, abdominal CT has achieved rapid scanning of the thin layer of arterial phase and portal venous phase. It is also capable of reconstructing three-dimensional abdominal blood vessels on the workstation, which provides an effective examination for mesenteric ischemia[17,18]. Currently, researches on early diagnosis, recurrence and treatment of acute mesenteric ischemic diseases have been widely conducted[9]. MSCT has been proved of its significant diagnostic value, which could remarkably improve the diagnostic efficacy for patients with acute mesenteric ischemia[17,25]. MSCT examination has a high value for evaluating the range and degree of acute myocardial infarction and intestinal ischemia, which greatly improves the diagnostic accuracy of mesenteric ischemic diseases[14,15]. Previous studies have suggested that CT should be the preferred examination for mesenteric ischemia. In particular, MSCT can exclude abdominal pain and intestinal perforation resulted from other causes[17]. MSCT manifestations of mesenteric vascular embolization include direct signs and indirect signs. Direct signs indicate mesenteric intravascular thrombosis or embolism manifested in MSCT, which is the most reliable sign for the diagnosis of mesenteric ischemia[13].

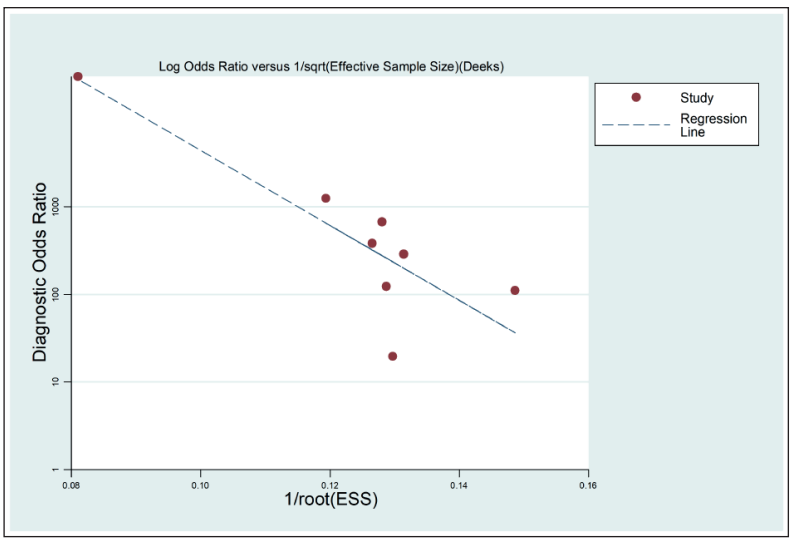

Figure 5. Linear regression test of funnel plot asymmetry. The statistically non-significant *p*-value of the slop coefficient indicates symmetry of the data and a low likelihood of publication bias.

Indirect signs include the following six items: (1) the degree of intestinal wall thickening depends on the degree of intestinal dilatation. In the case of intestinal peristalsis or contraction, larger than 5 mm of the thickness of the colon wall is considered as abnormal. However, when the colon is dilated, the thickness of the intestinal wall of larger than 3 mm is served as abnormal. Due to intestinal wall hemorrhage or infection, intestinal wall thickening caused by mesenteric vein embolization is more obvious than that caused by arterial embolization, and often accompanied by intestinal lumen dilatation and effusion. In the case of acute onset of superior mesenteric artery embolism without infection, there may be no abnormalities in the intestinal wall. If the intercostal nerve and muscle structure are destroyed, the intestinal wall may be as thin as paper. (2) Dilated effusion of the intestine. (3) Stranding sign is caused by mesenteric vascular congestion and edema, characterized by thickening of mesenteric vessels with rough edges. (4) Mesenteric effusion is manifested as increased diffuse density of the mesentery. (5) Pneumatosis of intestinal wall and portal vein. (6) Changes in intestinal wall density[21,22, 24-26].

In recent years, early diagnosis and treatment of acute mesenteric ischemic diseases have been emphasized[13]. This study aims to search for the most sensitive and specific diagnostic protocols for patients with acute mesenteric ischemic disease by including literature on the relationship between MSCT and the diagnostic value of acute mesenteric ischemia[18-25]. In this systematic review, a total of 882 patients with mesenteric ischemia were included. The results showed that the combined sensitivity was 94% and the combined specificity was 97% when MSCT to diagnose acute mesenteric ischemic disease. Results of the comprehensive diagnostic efficacy study showed that the combined positive predictive value was 32.48, the combined negative predictive value was 0.07, the combined diagnostic odds ratio was 6.21, and the AUC was 0.93. It is indicated that MSCT exerts higher sensitivity and specificity in diagnosing mesenteric ischemia than other known imaging methods.

Strict inclusion criteria minimize the influences of bias and confounding variables. However, there are still some limitations to our study. First of all, different sources of patients may affect the comparability of the study. Secondly, our results may be influenced by precision errors and technician experience. Therefore, the accuracy assessment must be performed by each technician to ensure the judgment error is small. Thirdly, our results were based on unadjusted estimates. Effects of multiple confounding factors should be considered, such as age, lifestyle, environmental factors, etc. Fourthly, most of the studies in the mixed population were investigated and it is recommended that the analysis results should be cautiously interpreted. In addition, the source of heterogeneity in this study may be related to the number of CT layers. Studies have shown that the sensitivity and specificity of the 16-layer and 64-layer subgroups are higher than those of the 2-layer and 4-layer subgroups. With the development of dual-source CT, 256-slice CT, and 320-slice CT, more large-scale studies are needed in the future to confirm the impact of CT layer on diagnostic performance. Therefore, further examinations are required to confirm the validity of the previously reported associations in more participants.

In summary, the present study showed that MSCT is directly related to the accurate diagnosis of acute mesenteric ischemic disease by meta-analysis of the eight included literature. However, since the meta-analysis is limited by the number and level of existing clinical trials, the strength of the research argument may not be satisfactory as we expected. Therefore, large-scale case-control or prospective study in different ethnic groups is needed in further explorations. Meanwhile, genetic and environmental factors should be taken into account as well, so as to further elucidate the pathogenesis of acute mesenteric ischemic disease.

Conclusions

MSCT has a high sensitivity and specificity for the diagnosis of acute mesenteric ischemia. In addition, studies with large sample and high quality in a multi-center hospital are needed to further confirm the reliability.

Acknowledgments

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Conflict of Interests

The authors declared no conflict of interest.

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