

Accuracy of Computed Tomographic Enterography for Obscure Gastrointestinal Bleeding: A Diagnostic Meta-analysis

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Rationale and Objectives: Obscure gastrointestinal bleeding (OGIB) is the bleeding from the gastrointestinal tract without definite source that persists and recurs after a negative endoscopic evaluation. The study aimed to systematically evaluate the diagnostic accuracy of computed tomography enterography on OGIB detection by meta-analysis.

Materials and Methods: Studies were searched in relevant databases. With predefined inclusion criteria, eligible studies were included, followed by quality assessment using the Quality Assessment of Diagnostic Accuracy Studies scoring system. The Meta-DiSc software was used to implement the meta-analysis, and sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio with their 95% confidence intervals (CIs) were used as the effect size. Publication bias was determined by Egger test.

Results: A set of nine studies was included in this meta-analysis, having a relatively high quality. Under the random effects model, the pooled sensitivity and specificity were 0.724 (95% CI: 0.651–0.789) and 0.752 (95% CI: 0.691–0.807), respectively. Under the fixed effects model, the pooled positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio were 2.949 (95% CI: 2.259–3.850), 0.393 (95% CI: 0.310–0.497), and 9.452 (95% CI: 5.693–15.692), respectively. The area under curve of the summary receiver operating characteristic curve was 0.7916 (95% CI: 0.723–0.860). No obvious publication bias was detected ($t = 1.62$, $P = .181$).

Conclusions: Computed tomography enterography might be used as a complementary to video capsule endoscopy instead of an alternative for the detection of OGIB.

Key Words: Obscure gastrointestinal bleeding; computed tomography enterography; diagnosis; sensitivity; specificity; meta-analysis.

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INTRODUCTION

Gastrointestinal (GI) bleeding is a common clinical emergency. Annually, the incidence of GI bleeding is estimated about 150 per 100,000 persons, and the mortality is varied from 2% to 10% (1). Obscure GI bleeding (OGIB) is designated as the bleeding from the GI tract without definite source that persists and recurs after a negative endoscopic evaluation, and it accounts for nearly 5% of

all GI hemorrhage cases (2). Based on whether the bleeding is visible or, OGIB is classified into two types as overt or occult bleeding (3).

With the standard endoscopic techniques, there is a huge challenge on diagnosis of patients with OGIB because it is hardly accessible to the jejunum and ileum (4). The video capsule endoscopy (VCE), a noninvasive diagnostic method for the entire small bowel, has been identified as the first-line evaluation tool for OGIB (5). Other advanced endoscopic methods like deep enteroscopy (eg, single-balloon enteroscopy, double-balloon enteroscopy, and spiral enteroscopy) have been developed for a better identification of the small bowel bleeding sites (6,7). Despite these improvements, the diagnostic results are undesirable, and the diagnostic yield of VCE is only 32%–83% (5). Meanwhile, VCE has its own limitations. For instance, its high sensitivity in occult bleeding might reduce the specificity. Additionally, the images of VCE tend to be obscured by blood, which could conceal the location of underlying lesion (8). Having the advantages of easy operation and extra evaluation on small bowel strictures, the computed tomography

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(CT) is often considered as a complementary of VCE (9). CT enterography (CTE) integrates the resolution of CT with the neutral oral contrast agents, which allows detailed visualization of the small intestines (8). For the diagnosis of potential small bowel bleeding, CTE, in combination with VCE, has a significantly greater sensitivity than VCE or CTE alone ($P < .05$), but the sample size with 52 patients is relatively small (10). A meta-analysis has been published to evaluate the yield of CTE in evaluating OGIB, compared to CE, double-balloon enteroscopy, and digital subtraction angiography (11), and finds that CTE has a better diagnostic result than other alternate modalities in the evaluation of OGIB, especially of overt bleeding. However, detailed sensitivity and specificity of CTE have not been evaluated.

Therefore, we performed this diagnostic meta-analysis to comprehensively evaluate the accuracy of CTE for the diagnosis of OGIB.

METHODS

Literature Search

A systematic search was conducted in databases such as PubMed, Embase, Chinese National Knowledge Infrastructure, and Wanfang for studies evaluating the diagnostic value of CTE for OGIB, using the search strings of “obscure gastrointestinal bleeding” OR “gastrointestinal hemorrhage of unknown causes” OR “obscure gastrointestinal bleeding,” combined with “Computed Tomographic Enterography” OR “Computed Tomography Enterography” OR “computed tomography enteroclysis” OR “CT enterography” OR “CT enteroclysis” OR “CTE.” The search was up to July 2016, without language restriction.

Inclusion and Exclusion Criteria

A study was included if the following criteria were met: (1) it was a clinical publication assessing the diagnostic accuracy of CTE for OGIB; (2) the reference standard was mentioned; (3) diagnostic data on cases of true positive, false positive, true negative, and false negative were available or could be calculated. The studies were excluded if they were reviews, reports, comments, or letters. Most of the studies used pathology, endoscopy, and surgery as the reference standard.

Data Extraction and Quality Assessment

Two authors abstracted data from the included studies, independently, such as the first author name, publication year, countries, study region, gender and age composition, case numbers of true positive, false positive, true negative, and false negative.

Quality of the included studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies scoring system, which evaluates 14 items based on three criteria “yes” (met with this item), “no” (did not meet or mention this item),

and “unclear” (partly met with this item or could not get sufficient information from the study) (12).

If there were disagreements during the above processes, a third author was required in the discussion to reach a final agreement.

Statistical Analysis

The diagnostic meta-analysis was conducted by the Meta-DiSc software (version 1.4). Sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR) with their 95% confidence intervals (CIs) were used as the measure of effect size. The between-study variation that might be generated by the threshold effect was determined by the correlation coefficient (CC) between logit sensitivity and specificity (13), and $P < .05$ was the cutoff for significance. Heterogeneity across the studies was determined by Cochran-Q statistic and I^2 test. A random effects model was used to calculate the pooled results if significant heterogeneity was detected ($P < .05$ or $I^2 \geq 50\%$), and a fixed effects model was used if there lacked heterogeneity ($P > .05$ or $I^2 < 50\%$) (14). Egger test was selected to examine publication bias among the included studies, using the Stata software (version 12.1, Stata Corp). A P value $< .05$ indicated a significant publication bias.

RESULTS

Eligible Studies and Their Characteristics

We retrieved a total of 168 studies following the preliminary search strategy, and 34 duplications were removed. Then, 94 irrelevant studies were excluded by reading the titles and abstracts. Letters ($n = 3$), reports or case series ($n = 5$), and reviews ($n = 7$) were eliminated, and the remaining 25 studies were examined by full-text reading. Among them, studies that did not provide relevant data ($n = 10$) or replicated data were further excluded ($n = 6$). Therefore, nine eligible studies were finally selected to combine their results by meta-analysis (15–23) (Fig 1). As shown in Table 1, these studies were published from 1998 to 2014 and finally detected 396 patients. The study objects were distributed in many countries such as China, America, Korea, and France, and most of them were male. There was a huge age range, which ranged from 18 to 85. All patients received CTE diagnosis, and 22 out of them also received CTA diagnosis. Based on the Quality Assessment of Diagnostic Accuracy Studies scoring system, a majority of the studies had a score above 9, indicating a relatively high quality.

Pooled Effect Size of the Diagnostic Indicators

Based on the Spearman CC of the logarithm of sensitivity and 1-specificity, there was no threshold effects among these studies (CC = 0.074, $P = .7159$). Therefore, we combined individual results using different models.

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