Small-bowel capsule endoscopy in patients with unexplained chronic abdominal pain: a systematic review

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Background: Patients frequently consult primary care physicians and gastroenterologists when experiencing chronic abdominal pain. Although its diagnostic efficacy in these settings is uncertain, small-bowel capsule endoscopy (SBCE) has been used to evaluate the unexplained reasons for abdominal pain.

Objective: To evaluate the diagnostic yield of SBCE in patients with unexplained chronic abdominal pain.

Design: We performed a retrospective review of publications reporting the diagnostic yield of SBCE in patients with unexplained chronic abdominal pain and calculated the overall diagnostic yield.

Setting: Two investigators independently searched studies from databases and analyzed the results.

Patients: A total of 1520 patients from 21 studies were included.

Interventions: Small-bowel capsule endoscopy.

Main Outcome Measurements: Per-patient diagnostic yield, with 95% confidence intervals (CI), was evaluated by a random-effect model. Clear categorical analysis also was performed.

Results: The pooled diagnostic yield of SBCE in patients with unexplained chronic abdominal pain was 20.9% (95% CI, 15.9%-25.9%), with high heterogeneity (I^2 = 80.0%; P < .001). Inflammatory lesions were the most common (78.3%) positive findings, followed by tumors (9.0%).

Limitations: Heterogeneity among studies, retrospective design, variable chronicity of abdominal pain, and different previous examinations before SBCE.

Conclusion: SBCE provides a noninvasive diagnostic tool for patients with unexplained chronic abdominal pain, but the diagnostic yield is limited (20.9%). Among patients with positive findings, inflammatory lesions are the most common. (Gastrointest Endosc 2015;81:186-93.)

A previous survey in the United States showed that 28.6% of outpatients complained of lower abdominal pain or stomach pain.[1] Most cases were accompanied with pathologic lesions occurring in the GI tract. Despite numerous endoscopic advancements, the small intestine was considered the last frontier of endoscopy until the arrival of small-bowel endoscopy, including small-bowel capsule endoscopy (SBCE), device-assisted enteroscopy with single or double balloons, and spiral enteroscopy.[2]

As an invasive diagnostic tool, device-assisted enteroscopy examination will inevitably induce certain mucosal injury or even intestinal perforation. Because the small

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; QUADAS, Quality Assessment of Diagnostic Accuracy Studies; SBCE, small-bowel capsule endoscopy.

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intestine is relatively long, tortuous, and highly mobile, this endoscopic modality is time consuming and labor intensive.[3] Many patients could not bear the long-lasting discomfort without the use of sedatives,[2] which, however, would bring anesthesia-related adverse events. Given these disadvantages of device-assisted enteroscopy, SBCE has been widely used since its introduction into clinical practice in 2001.[4] SBCE makes it possible to inspect the entire small bowel without causing any obvious discomfort or need for sedation.[5]

The value of SBCE in obscure GI bleeding, recurrent iron deficiency anemia, and Crohn's disease has already been confirmed by the National Institute of Clinical Excellence in the United Kingdom.[6] However, the utility of SBCE in chronic abdominal pain is still controversial.[7] The diagnostic yield rate of SBCE was documented as 4% and 44%, respectively, in 2 studies.[8,9] This systematic review aims to evaluate the overall diagnostic yield of SBCE in patients with unexplained chronic abdominal pain.

MATERIALS AND METHODS

Data identification and study selection

We systematically searched the databases PubMed, Medline, Web of science, EMBASE, Scopus, Ovid, and the Cochrane Library from January 2001 to June 2013. The following terms were involved in the searching of the above-named databases: ("abdominal pain" OR "bellyache") AND "capsule endoscopy." Furthermore, the list of all selected articles was manually checked for additional references that were potentially suitable. Primary screening was based on titles and abstracts and then secondary screening on available full texts. All data were collected by 2 individual investigators. Opinions were fully discussed, and an agreement was reached in the end.

The primary endpoint was the diagnostic yield of SBCE in patients with abdominal pain. Studies were required to fulfill the following inclusion criteria: written in English; providing sufficient data for the authors to confirm an accurate number of patients and providing either diagnostic yield or sufficient data to allow the calculation of diagnostic yield for SBCE. Those studies only available with abstracts were excluded. For the purpose of statistical analysis, 1 study presenting fewer than 10 cases was excluded.[10] The population included in 2 studies[11,12] overlapped (conducted by the same group in Greece, based on participants from the same hospitals, and had overlapped study periods [January 2008 to December 2009]), so only the more complete one[11] was included.

Data extraction

Two individual authors (M.X., X.C.) extracted data from each selected study with the following items: (1) first author's name and the year of publication, (2) single-center or multicenter study, (3) the country where the study was conducted, (4) prospective or retrospective study design, (5) whether consecutive patients were included, (6) the manufacturer of the capsule, (7) the total number of patients recruited, (8) the number of patients with unexplained abdominal pain, (9) male/female ratio and patient age, if available (because several studies did not record the data of pediatric or adult patients separately, different age brackets were analyzed together), and (10) the number of patients with clinically significant SBCE findings (erosions or ulcers, Crohn's disease, tumors, etc). Patients with suspicious or uncertain SBCE findings (eg, arteriovenous malformations, lymphangiectasia, erythema, red spots, polyps, lymphoid follicular hyperplasia)[13,14] were not taken into account in the calculation of diagnostic yield. Lesions including gastritis and peptic ulcer that could be reached by routine endoscopy, nonspecific lesions like lymphoid nodular hyperplasia, and those presented as *others* without specific descriptions also were excluded in the analysis.[15] Number (11) included categories of positive findings by SBCE if available.

Risk of bias in individual studies

The Quality Assessment of Diagnostic Accuracy Studies (QUADAS) was used to assess the quality of studies and detect potential bias. Because the current work is a systematic review of diagnostic yield, and most studies lack a criterion standard (definite pathologic findings or long-term follow-up), items 3 to 11 of the QUADAS were not applicable.

Statistical analysis

Data on the diagnostic yield of SBCE were extracted, pooled, and analyzed. A 95% confidence interval (CI) was equal to 2 t-fold of standard errors wide, in which t = tinv (0.05, N-1) (tinv is a t distribution function; N: the total number of patients in each study).[16] The Q statistic of I^2 was used to estimate the proportion of unexplained variation across studies. $I^2 > 50\%$ was considered significant for heterogeneity, which would indicate that the random-effect model, DerSimonian-Laird method, instead of the Mantel-Haenszel method, should be performed to derive pooled results with corresponding 95% CI.[10]

Meta-regression analysis was used to investigate the possible sources of heterogeneity on the basis of the following covariates: design of studies (prospective vs retrospective), capsule manufacturer (Pillcam; Given Imaging [Yoqneam, Israel] vs not Given Imaging or no record), number of centers (multiple vs single), and sample size (>60 vs ≤ 60). Publication bias was assessed by using funnel plots (based on diagnostic yield vs the standard error). Statistical analysis was carried out by using the Metan, Metareg, and Metabias packages of STATA version 12.0 (StataCorp, College Station, Tex).