Diagnostic yield of small-bowel capsule endoscopy in patients with iron-deficiency anemia: a systematic review (CME)

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Background: Iron-deficiency anemia (IDA) is the most common cause of anemia worldwide. Current guidelines recommend the use of small-bowel capsule endoscopy (SBCE) in IDA. Evidence of the validity of SBCE in patients with IDA alone is still limited.

Objective: To assess the diagnostic yield (DY) of SBCE in IDA by pooling data from relevant studies.

Design: Systematic review and meta-analysis. Fixed-effects or random-effects models were used as appropriate.

Setting: Studies that estimated the DY of SCBE in IDA were identified. Two investigators independently conducted the search and data extraction.

Patients: A total of 24 studies enrolling 1960 patients with IDA who underwent SBCE were included.

Main Outcome Measurements: Per-patient DY, with 95% confidence intervals. Subgroup analysis was also performed.

Results: The pooled DY of SBCE in IDA, evaluated by a random-effects model, was 47% (95% CI, 42%-52%), but there was statistically significant heterogeneity among the included studies (inconsistency index [I^2] = 78.8%, $P <$ .0001). The pooled DY of SBCE in studies focused solely on patients with IDA (subset 1, 4 studies) was 66.6% (95% CI, 61.0%-72.3%; I^2 = 44.3%); conversely, that of studies not focusing only on IDA patients (subset 2, 20 studies) was 44% (95% CI, 39%-48%; I^2 = 64.9%). In particular, more vascular (31% vs 22.6%, P = .007), inflammatory (17.8% vs 11.3%, P = .009), and mass/tumor (7.95% vs 2.25%, $P <$ .0001) lesions were detected with SBCE in patients participating in the studies in subset 1.

Limitations: Heterogeneity of studies, retrospective design, and selection bias.

Conclusions: This analysis demonstrates the validity of SBCE in the investigation of patients with IDA and negative findings on a previous diagnostic workup, although certain factors such as heterogeneity and quality of the included studies should be taken into account. (Gastrointest Endosc 2012;76:983-92.)

Abbreviations: CI, confidence interval; DY, diagnostic yield; FOBT, fecal occult blood test; Hb, hemoglobin; I^2, inconsistency index; IDA, iron-deficiency anemia; OGIB, obscure GI bleeding; QUADAS, Quality Assessment of Diagnostic Accuracy Studies; SBCE, small-bowel capsule endoscopy.

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Obscure GI bleeding (OGIB) is defined by visible GI bleeding (eg, melena or hematochezia), iron-deficiency anemia (IDA), or positive results on fecal occult blood tests (FOBTs) in the setting of normal bidirectional endoscopy, ie, upper GI endoscopy and colonoscopy.[1] Furthermore, OGIB is subdivided into occult (ie, IDA and/or positive FOBT results) and overt OGIB. The diagnostic workup of patients with OGIB is often challenging and time-consuming. Nevertheless, the introduction of capsule endoscopy has revolutionized the evaluation of these patients.[2,3] In fact, several studies and meta-analyses showed that small-bowel capsule endoscopy (SBCE) is superior to push enteroscopy and most radiological imaging techniques for diagnosing clinically significant small-bowel pathology in patients with OGIB.[4,5] Therefore, guidelines have been updated to include SBCE as a third step, after negative findings on upper GI endoscopy and colonoscopy, in the diagnostic workup of patients with OGIB.[1,6]

In the setting of occult OGIB, the majority of SBCE studies do not consider patients referred for investigation of positive FOBT results or IDA as separate groups. Moreover, prospective SBCE studies focusing solely on IDA patients are few and likely underpowered. Although results of retrospective studies suggest that the diagnostic yield (DY) of SBCE in the 2 patient subgroups (positive FOBT results and IDA) is similar, evidence of the validity of SBCE in patients with IDA is still limited.

IDA is the most common cause of anemia worldwide, causing significant disease-related morbidity, and has a negative impact on well-being and health outcomes.[7] Furthermore, it represents one of the major indications for referral to gastroenterologists (13% of referrals).[6,7] Even after negative findings on a bidirectional endoscopy, approximately 30% of IDA patients lacking a diagnosis[6]; the majority of those will be eventually referred for SBCE.

With this review, we aimed to evaluate the DY of SBCE in the group of patients who have undergone the procedure because of unexplained IDA. This article was prepared according to previously published guidelines for meta-analyses of observational studies.[8]

Take-home Message

- Pooled data from 1922 patients with iron-deficiency anemia showed small-bowel capsule endoscopy to have a per-patient diagnostic yield (DY) of 48%. Studies with strict inclusion criteria showed a higher DY.
- Clarification of risk factors for sinister small-bowel pathology is needed.

MATERIALS AND METHODS

Data identification and study selection

A thorough and extensive recursive search of PubMed/MEDLINE, EMBASE, Scirus, Biosis, and Scopus databases for human studies, published between January 2001 (the year of the introduction of capsule endoscopy in clinical practice) and November 2011, was performed. To capture as many articles as possible, a broad search strategy was used (using both MeSH and non-MeSH terms, with an "automatic explosion" and "all fields" search where applicable). The following terms were searched first alone and eventually connected either with AND: "capsule endoscopy," "anemia," "bleeding, "hemorrhage," "gastrointestinal bleeding." Furthermore, the reference list of all the selected articles was manually checked for potentially suitable references that were not identified by the initial search. Studies were selected based on title and abstract (where available), by 2 of the authors (A.K. and E.R.). After retrieving the full text of selected papers, both reviewers independently checked whether inclusion criteria were met; in the event of uncertainty, any discrepancies were resolved by discussion and consensus of all of the authors.

For a study to be included in this review, the following predefined inclusion criteria had to be met: written in English language and published as full paper; provided sufficient data for the authors to confirm iron-deficiency either in part or for the entire study cohort; provided either DY or enough data to allow us to calculate the DY of SBCE in IDA patients. Where applicable, we defined DY as the proportion of patients with clinically significant angioectasias (P2 lesions)[9] or other clinically significant SBCE findings (ie, mucosal ulcers, intraluminal bleeding, celiac changes, mass-type lesions). Patients with "suspicious" or "uncertain" SBCE findings (eg, P0 or P1 lesions)[9] were not taken into account in calculation of the DY.

Finally, we excluded those studies in which SBCE was performed in patients with IDA and preexisting clinical conditions that could potentially explain IDA (ie, patients with Crohn's disease, celiac disease, hereditary hemorrhagic telangiectasias, chronic renal failure, and/or cirrhosis).

For the purpose of statistical analysis, any study presenting fewer than 10 cases of IDA was excluded.[10] Duplicate publications were deleted. When 2 or more articles reported results from the same patient cohort, either the more recent or more complete publication was selected.

Data extraction

The 2 authors (A.K. and E.R.) extracted data from each selected study by using a predefined form in Microsoft Excel (Microsoft Corp, Redmond, Wash). From each paper, the 2 reviewers independently abstracted the following: (1) first author name and the year of publication; (2) whether it was a single-center or multicenter study; (3) country where the study was performed; (4) design (prospective or retrospective); (5) whether consecutive patients were included; (6) total number of patients recruited; (7) number of patients with IDA; (8) the DY of SBCE in patients with IDA or the number of IDA patients with clinically significant SBCE findings (as defined by the