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Review Article

Meta-analysis shows similar re-bleeding rates among Western and Eastern populations after index video capsule endoscopy

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ABSTRACT

Background & aims: Video capsule endoscopy (VCE) is the first-line diagnostic procedure for investigating obscure gastrointestinal bleeding (OGIB). Different re-bleeding rates following index VCE have been reported among Western and Eastern studies.
Methods: We conducted a comprehensive literature search to identify studies examining re-bleeding rates after VCE for OGIB. Meta-analysis assessed the pooled proportion of re-bleeding events after VCE for OGIB according to study's origin (Western vs. Eastern) and according to the length of follow-up (≥24 months vs. <24 months). We also calculated the re-bleeding odds ratios (OR; 95% CI) after positive vs. negative index VCE, overt vs. occult initial presentation of bleeding and after interventional treatment for positive index cases, according to the study's origin.
Results: We included 46 (30 Western and 16 Eastern) studies with 5796 patients. Significant heterogeneity was detected among meta-analyzed studies. Overall, the pooled re-bleeding rate was similar between Western (29%; 95% CI: 23–34) and Eastern (21%; 95% CI: 15–27) populations, irrespective of the length of follow-up. The odds of re-bleeding was significantly higher after positive as compared to negative index VCE in Eastern studies (OR: 1.77; 95% CI: 1.07–2.94). Application of specific treatment after positive index VCE was associated with lower re-bleeding odds in both Western (OR: 0.37; 95% CI: 0.16–0.87) and Eastern (OR: 0.39; 95% CI: 0.21–0.72) populations.
Conclusions: Patients undergoing VCE for OGIB have similar re-bleeding rates in the East and the West, regardless of the length of follow-up. However, increased re-bleeding odds after positive index VCE is observed in Eastern studies.

1. Introduction

Obscure gastrointestinal bleeding (OGIB) is the key indication for video capsule endoscopy (VCE), accounting for 60–70% of these examinations [1–3]. When a lesion is detected, a specific (endoscopic, surgical, medical) treatment may be performed, whilst in the event of a negative VCE result, a "watch and wait strategy" with scheduled clinical re-evaluation is advised in the current guidelines [3–5]. Some studies indicate a discrepancy in the re-bleeding rates following index VCE examination in studies originating from Western and Eastern countries [6,7]. In most Western studies, a distinctly lower re-bleeding rate is reported for patients with OGIB and negative VCE result, as compared to those with positive index VCE examination [8–19]. On the contrary, it has been reported that the risk of re-bleeding remains high in Eastern populations with negative VCE examination [20–27]. Therefore, geographical distinctions in OGIB could have substantial implications in management decisions. To the best of our knowledge, no systematic documentation of geographical background as a factor influencing the outcome of OGIB is available. We conducted a systematic review and a meta-

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analysis of eligible studies, aiming to examine the potential impact of regional variations on VCE's clinical outcomes.

2. Material and methods

2.1. Eligibility criteria

Inclusion criteria, delineated before the commencement of the literature search were as follows: (a) prospective or retrospective studies evaluating patients undergoing VCE for OGIB, allowing calculation of re-bleeding rate after index VCE and (b) studies published as full text. Studies comparing VCE and other endoscopic or diagnostic imaging modalities were also considered eligible for inclusion, but only data from the VCE arm were included in the analysis. Non-human and pediatric studies, meta-analyses or systematic reviews, editorials, case reports or case series, narrative reviews and conference abstracts, studies that did not detail patient follow-up period and/or number of re-bleeding episodes, studies not published in English and duplicate publications were excluded.

2.2. Information sources and search strategy

This meta-analysis adhered to the PRISMA (Preferred reporting items for systematic reviews and meta-analysis) recommendations, available at Supplemental File Appendix A [28]. A thorough computer-aided search of the medical literature was conducted across the MEDLINE (PubMed – including in-process citations), Cochrane Central Register of Clinical Trials and Google Scholar from database inception to July 2017, aiming to identify all studies investigating clinical outcomes of patients undergoing VCE after an episode of OGIB. The search was initially performed on March 18th and repeated on July 1st, 2017. We employed a broad strategy to identify as many articles and abstracts possible, using the term: *capsule endoscopy* combined with the Boolean set operator AND "follow-up", "obscure gastrointestinal bleeding", "negative", "positive", "re-bleeding", "outcome" and "long-term", in various combinations. All used terms had been searched both as medical subject headings (MeSH) and free text terms. The full electronic search strategy is available in Supplemental File Appendix B. To maximize the yield, we performed a stepwise approach as we carried out our research into different stages and combined them at the end. The search was conducted independently by two investigators (GT, PG). All titles and abstracts resulting from the search were screened for inclusion. Additionally, bibliographies of all pertinent studies and meta-analyses acquired from the electronic search were manually searched for potentially suitable references that had not been identified initially, completing a recursive search. In case of studies with missing or unavailable data, an attempt to contact the corresponding author to provide additional information on trials was made.

2.3. Study selection

Two reviewers (GT, PG), independently screened all articles retrieved from the search to identify those meeting our predetermined eligibility criteria, using pre-designed eligibility forms. Results were cross-checked by both reviewers, to ensure no publication(s) had been missed. In the event of uncertainty, any disagreement was resolved by consensus and discussion with the senior author (KT), expert in capsule endoscopy. The "Find Duplicates" tool in EndNote® 7.0 and manual examination subsequently, were used to identify all duplicate results [29]. Titles and abstracts of all results were initially reviewed and the full-text content of eligible studies was obtained and independently assessed for eligibility. In case two or more publications from the same institution appeared to review the same patients, the most recent update with the largest cohort or the most informative was selected to avoid redundancy.

2.4. Data collection process

All data were extracted from eligible peer-reviewed articles independently by two investigators (GT, PG) using a standardized extraction form, onto a Microsoft Excel spreadsheet. Initially a database was produced, pilot-tested, and refined to maintain consistency with outcomes reported. Discrepancies regarding data extraction were resolved by consensus or were adjudicated by the senior author (KT), who verified for accuracy the results and finally approved the data.

2.5. Data items

For each included study, we collected information regarding: country of study origin, number of patients enrolled, study design, number of centers, length of follow-up period (any duration according to each study), and predominant lesion detected at index VCE. The following clinical data were extracted from each study: total number of patients with positive and negative VCE completing the follow-up period (patients lost to follow-up were excluded from the analysis), number of patients with positive or negative index VCE, as well as, the number of patients with overt or occult OGIB at presentation who experienced re-bleeding during follow-up. For the purpose of our study, re-bleeding was considered the main outcome and defined as evidence of recent or active bleeding at least 30 days after the index VCE. Positive finding is defined as the likelihood of a test or procedure to provide the information needed to establish a diagnosis. In the field of VCE the definition of positive finding incorporates any examination able to explain patient's clinical status, complaints or symptoms, as well as any examination whose findings lead to modification of patient's management. Additionally, the number of patients with positive index VCE that received "specific intervention" for OGIB was extracted. Specific intervention was defined as any treatment specifically directed at the presumed cause of bleeding, including endoscopic and/or surgical and/or radiological modalities (endoscopic or surgical hemostasis, angiographic embolization). Discontinuation of anticoagulants, nonsteroidal anti-inflammatory drugs (NSAIDs) withdrawal due to NSAIDs-induced enteropathy and disease-specific medical treatment such as corticosteroids for Crohn's disease were also classified as specific treatments and presented as "specific drug therapy" [13,20,22,30]. The type of intervention and the number of patients that experienced re-bleeding after any type of specific intervention was recorded. In addition, we extracted the number of patients with positive index VCE that received "non-specific treatment" classified as watchful waiting, blood transfusion, or iron supplementation and the number of those experiencing re-bleeding. We also compared the re-bleeding rate between studies with a follow-up less or more than 24 months post-VCE [31].

2.6. Risk of bias in individual studies

A comprehensive quality assessment for all selected studies was performed using a scale adapted from the Newcastle–Ottawa Scale (NOS) for Assessing the Quality of Nonrandomized Studies [32]. Studies with a cumulative score ≥ 7 were classified as high quality. The NOS scale was also used to assess the risk of bias for the three randomized control trials since only the data from the VCE arm were included in the analysis [33–35]. The score for each study

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