Clinics and Research in Hepatology and Gastroenterology (2018) xxx, xxx–xxx

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EM|consulte
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LETTER TO THE EDITOR

Clinical impact of small bowel capsule endoscopy in the era of antithrombotic therapy

KEYWORDS
Small bowel capsule endoscopy;
Antithrombotic therapy;
Obscure gastrointestinal bleeding;
Bleeding risk scores

To the Editor,

Small bowel capsule endoscopy (SBCE) represents a useful noninvasive tool to identify small bowel lesions with potential bleeding, showing a high diagnostic accuracy [1]. Current guidelines recommend SBCE as the first line in patients with obscure gastrointestinal bleeding (OGIB), following a negative conventional study by upper and lower endoscopy [2,3]. Certain medications such as anticoagulants, antiplatelets and nonsteroidal anti-inflammatory drugs (NSAIDs) have been associated with an increased risk of gastrointestinal bleeding because of their contribution to direct mucosal aggression. Unlike NSAIDs, few works are available regarding antithrombotic drugs' impact on SBCE findings and their clinical significance [1,4,5]. Several clinical risk prediction tools have been developed to help quantify the bleeding risk for individual patients [6]. However, the ability of these scores to estimate the presence of small bowel lesions and their potential bleeding is poorly studied. Due to the worldwide spread of antithrombotic drugs use in the setting of cardiovascular and cerebrovascular conditions, the diagnosis and valorization of endoscopic findings represent a challenge to the endoscopist.

Thus, we aimed to evaluate the impact of antithrombotic drugs on the diagnostic yield of SBCE, the accuracy of main bleeding risk scores in predicting P2 lesions and the clinical impact on patient management.

A retrospective study was carried out at a single tertiary centre, including a total of 138 consecutive patients who underwent SBCE due to occult or overt OGIB, during 4 years (2012-2015). Patients under NSAIDs other than acetylsalicylic acid in the 3 months prior to SBCE study were excluded. SBCE study was performed using PillCam® SB2 or SB3 (Given® Imaging Ltd., Yokneam, Israel), after 12 hours of fasting and without previous bowel preparation. P2 lesions according to Saurin et al. [7] were classified as vascular (angioectasias and varices), inflammatory (multiple erosions [≥ 3] and ulcers) and neoplastic lesions. The bleeding risk scores assessed included the modified Outpatient Bleeding Risk Index (mOBRI), HEMORR2HAGES, Shireman, HAS-BLED, ATRIA risk score and ACCP 9th [6]. Clinical impact of SBCE findings on patient management was evaluated in terms of need for further endoscopic or surgical therapeutic approach and modification/withdrawal of antithrombotic therapy.

Of a total of 138 patients with OGIB, 52.2% ($n = 70$) were under antithrombotic therapy, including 57.1% ($n = 40$) with single or dual antiplatelet therapy and 42.9% ($n = 30$) with anticoagulation. Regarding antiplatelet drugs, 70.0% ($n = 28$) were taking low-dose acetylsalicylic acid (LDAA), 7.5% ($n = 3$) only thienopyridines and LDAA with thienopyridines in 22.5% ($n = 9$). For anticoagulant drugs, warfarin was found in 60.0% ($n = 18$), new oral anticoagulants in 33.3% ($n = 10$) and two patients were under low molecular weight heparin. Patients with or without antithrombotic consumption were homogeneous in terms of gender (female gender: 51.4% vs 48.5%; $P = 0.733$), age (66.5 ± 13.3 vs 64.4 ± 18.2; $P = 0.406$) and OGIB presentation (occult OGIB: 77.1% vs 89.7%; $P = 0.08$). However, patients taking antithrombotic drugs had a higher proportion of cerebrovascular disease (11.4% vs 1.5%; $P = 0.018$), heart failure (57.1% vs 17.6%; $P < 0.001$) and labile INR (10.0% vs 0.0%; $P = 0.007$) compared to patients without antithrombotic drugs. The multivariate analysis showed that chronic kidney disease (adjusted odds ratio: 17.2; $P = 0.011$) and antithrombotic therapy (adjusted odds ratio: 4.5; $P = 0.047$) were independent factors associated with P2 lesions in SBCE. The diagnostic yield of SBCE for P2 lesions was 58.0%. When compared to patients without antithrombotic therapy, patients under antithrombotic drugs revealed a higher frequency of P2 lesions (68.6% vs 47.0%; $P = 0.010$), namely vascular lesions (51.4% vs 29.4%; $P = 0.008$). Considering the antithrombotic drugs type, anticoagulation was associated with a higher frequency of P2 lesions (73.3% vs 47.0%; $P = 0.027$) and vascular lesions

https://doi.org/10.1016/j.clinre.2017.12.007

Please cite this article in press as: Gravito-Soares E, et al. Clinical impact of small bowel capsule endoscopy in the era of antithrombotic therapy. Clin Res Hepatol Gastroenterol (2018), https://doi.org/10.1016/j.clinre.2017.12.007

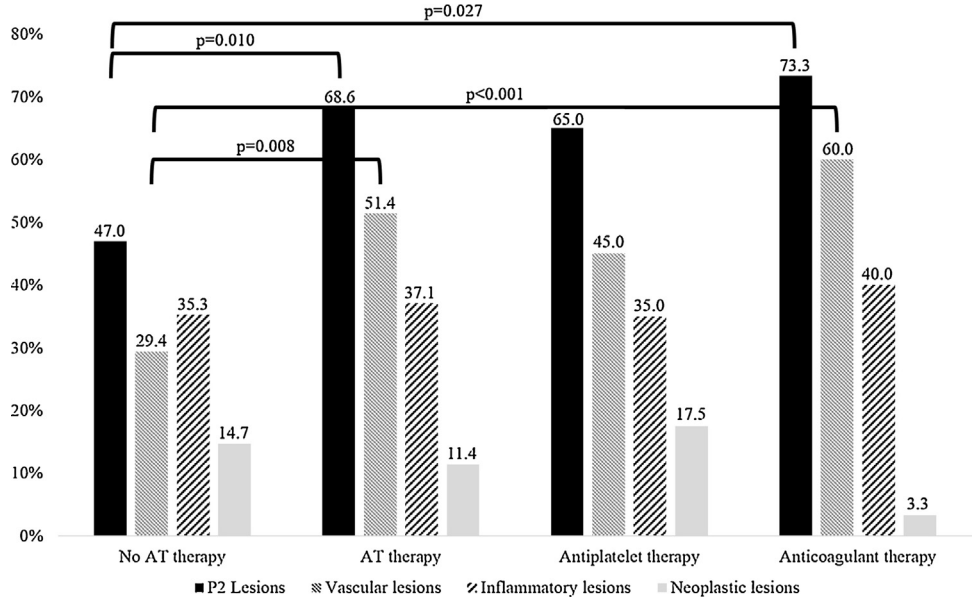

Figure 1 P2 lesions in small bowel capsule endoscopy according to antithrombotic (AT) therapy.

(60.0%vs29.4%; $P < 0.001$) (Fig. 1). Regarding bleeding risk scores, none of the evaluated scores were able to predict vascular, inflammatory or neoplastic lesions in SBCE. ATRIA Risk score (AUROC: 0.739; $P = 0.002$), HEMORR2HAGES (AUROC: 0.730; $P = 0.003$) and mOBRI (AUROC: 0.708; $P = 0.008$) showed only a fair predictive power for angioectasias. (Fig. 2) Relatively to patients with P2 lesions, SBCE findings conditioned changes in the subsequent management of 68.8% ($n = 55$) of cases. In patients under antithrombotic therapy, 33.3% ($n = 16$) switch/withdrawal antithrombotic drugs, 35.4% ($n = 17$) were submitted to double-balloon enteroscopy or surgery and one patient started thalidomide. In patients without antithrombotic therapy, 65.6% ($n = 21$) were submitted to double-balloon enteroscopy or surgery.

SBCE has been increasingly used in clinical practice because of its high diagnostic yield for small bowel lesions with high bleeding potential [1,4,8]. Antithrombotic therapy was frequent in patients with OGIB, being an independent risk factor for P2 lesions in SBCE. Despite this new era of prophylaxis of cardio- and cerebrovascular thrombotic events resulting from the widespread use of antithrombotic drugs, there is a lack of evidence of their impact on the small bowel mucosa [4]. Our results were consistent with the fact that anticoagulant therapy was associated with P2 lesions and vascular lesions in SBCE. Other studies have shown that anticoagulation was an independent risk factor for increased diagnostic yield in SBCE, namely P2 lesions [4,5,8,9]. In relation to antiplatelet therapy, the literature is controversial regarding different types of antiplatelet drugs. Other antiplatelet drugs besides LDAA seem to have higher injury potential in the small bowel mucosa [9,10]. For the first time our study assessed the predictive ability of the most common bleeding risk scores for potentially bleeding lesions. However, these scores revealed to be insufficient to predict P2 lesions in SBCE. Additionally, our study showed that more than 2/3 of patients underwent management changes due to P2 lesions detected in SBCE. In the context of antithrombotic therapy, besides device-assisted enteroscopy and surgery, the management of OGIB also involves switching to a different antithrombotic class with less bleeding potential or even antithrombotic withdrawal, according to patient's thrombotic risk.

Our data suggest that a prompt evaluation of the small bowel mucosa should be considered in patients with OGIB under anticoagulation. The adjustment of antithrombotic therapy within a multidisciplinary team-based work should be the mainstay of management, being the endoscopic or surgical therapy performed when necessary. Further studies are needed to clarify the deleterious impact of other antiplatelet drugs than LDAA and assess new predictive models of small bowel bleeding.

Contributors' statement

Elisa Gravito-Soares and Marta Gravito-Soares contributed equally, writing the manuscript and reviewing the literature. Elisa Gravito-Soares is the article guarantor. Nuno Almeida, Sandra Lopes and Pedro Figueiredo critically reviewed the manuscript and approved the final manuscript as submitted.

Please cite this article in press as: Gravito-Soares E, et al. Clinical impact of small bowel capsule endoscopy in the era of antithrombotic therapy. Clin Res Hepatol Gastroenterol (2018), https://doi.org/10.1016/j.clinre.2017.12.007