1130-0108/2015/107/12/753-758
Revista Española de Enfermedades Digestivas

Rev Esp Enferm Dig (Madrid)
Vol. 107, N.º 12, pp. 753-758, 2015

ORIGINAL PAPERS

What is the long-term outcome of a negative capsule endoscopy in patients with obscure gastrointestinal bleeding?

Iolanda Ribeiro, Rolando Pinho, Adélia Rodrigues, Joana Silva, Ana Ponte, Jaime Rodrigues and João Carvalho

Department of Gastroenterology. Centro Hospitalar Vila Nova Gaia. Vila Nova Gaia, Portugal

ABSTRACT

Background and aims: There are contradictory findings regarding long-term outcome in patients with obscure gastrointestinal bleeding and negative capsule endoscopy. Factors associated with rebleeding after a negative videocapsule are not entirely known.

Objective: The aim of this study was to compare the rebleeding rate between negative and positive capsule endoscopy patients and to identify predictive factors for rebleeding in patients with negative findings.

Material and methods: Consecutive patients with obscure gastrointestinal bleeding referred to a single center over a period of 5 years were identified. After exclusion of patients with a follow time < 6 months, 173 patients were included. Clinical information was retrospectively collected from medical records. Rebleeding was defined as evidence of melena/hematochezia, a drop in hemoglobin of ≥ 2 g/dL, or the need for transfusion 30 days after the index episode.

Results: The mean age was 61.7 years and 60% were female. The median follow up time was 27 months. Most patients were referred for occult gastrointestinal bleeding (67.1%) while 32.9% were referred for overt bleeding. More than 50% of the patients had negative capsule endoscopy. The rebleeding rate in negative capsule endoscopy is 16%, with a mean follow-up time of 25.8 months and is significantly lower than positive capsule endoscopy (16% *vs.* 30.2%, p = 0.02). Rebleeding after negative capsule endoscopy is higher in patients who need more transfusions of packet red blood cells before capsule endoscopy (3.0 *vs.* 0.9, p = 0.024) and have overt bleeding (46% *vs.* 13.9%, p = 0.03). In 53% of these patients, rebleeding occurs > 12 months after a negative capsule endoscopy.

Conclusions: Patients with obscure gastrointestinal bleeding and a negative capsule endoscopy had a significantly lower rebleeding rate and can be safely followed. However, a higher transfusion of red blood cells previous to capsule endoscopy and an overt bleeding are associated with a higher rebleeding. So, it is reasonable to consider that these patients may benefit of at least one year of follow-up.

Key words: Negative capsule endoscopy. Obscure gastrointestinal bleeding. Rebleeding.

Received: 22-06-2015
Accepted: 09-09-2015

Correspondence: Iolanda Ribeiro. Department of Gastroenterology. Centro Hospitalar Vila Nova Gaia. Rua Conceição Fernandes, nº 4434-502. Vila Nova Gaia, Portugal
e-mail: iolandacribeiro@gmail.com

INTRODUCTION

Obscure gastrointestinal bleeding (OGIB), which represents about 5% of all gastrointestinal bleeding (GIB), is defined as recurrent or persistent bleeding or iron deficiency anemia after negative findings on an initial evaluation (1). OGIB is an uncommon presentation of GI bleeding that can be difficult to diagnose and continues to be a challenging problem encountered by gastroenterologists. It has been reported that almost 75% of all causes of OGIB have origin in the small bowel (2), and, in these cases, patients tend to undergo more diagnostic procedures, have longer hospital stays, require more blood transfusions, and have higher healthcare costs when compared with patients with colonic or upper GI bleeding (3).

Capsule endoscopy (CE) is the diagnostic test of choice in the investigation of OGIB. It enables visualization of the entire small bowel and it is safe and non-invasive. CE has been shown to be superior to push enteroscopy (4), small bowel follow-through (5) and computed tomography (6) scan in detecting bleeding lesions in the small bowel. However, limitations include inability to provide therapy, false negative results and the potential for erratic passage resulting in missed lesions (7,8).

Some studies have evaluated the clinical implications of negative CE results over the long-term. However, there are contradictory findings regarding long-term outcome in patients with OGIB and negative CE results. Park et al. (9) suggests that a negative CE examination does not accurately predict a good long-term outcome. However, in another study published by Riccioni et al., patients with OGIB and a negative CE had a significantly lower rebleeding rate and further invasive investigations could be deferred (10). A negative CE, though it does not confirm a specific diagnosis, may still be useful, because it allows the physician to quit a certain line of investigation, thereby impacting

Ribeiro I, Pinho R, Rodrigues A, Silva J, Ponte A, Rodrigues J, Carvalho J. What is the long-term outcome of a negative capsule endoscopy in patients with obscure gastrointestinal bleeding? Rev Esp Enferm Dig 2015;107:753-758.

patient care (10). Male sex, younger age, anticoagulation use and the presentation of bleeding as melena are thought to be independent risk factors of re-bleeding after a negative CE. However the results are contradictory.

On the basis of these results, the long-term clinical outcome in patients with OGIB and negative CE and the risk factors associated with rebleeding remain poorly investigated.

The primary aim of this study was to evaluate the rebleeding rate in OGIB in patients with positive and negative CE findings; we also aimed to identify predictive factors for rebleeding in patients with a negative CE.

MATERIAL AND METHODS

Patients and data collection

Between January 2006 and January 2013, a total of 232 consecutive patients evaluated with CE for OGIB from Centro Hospitalar de Vila Nova de Gaia (Portugal) were selected. All patients had undergone at least one upper endoscopy (EGD) and colonoscopy prior to CE, which had not detected the source of bleeding. Patients with a follow-up time < 6 months and with poor small bowel visualization were excluded.

Patients' clinical information were retrospectively collected from medical records, including demographic characteristics, type of OGIB (occult *vs.* overt), CE findings (negative *vs.* positive), hemoglobin levels, number of transfusions prior CE, medical therapy (anticoagulants, antiplatelet and steroidal anti-inflammatory drugs [NSAID´s]), type of treatment for bleeding, interval of follow-up after CE for each patient, and the occurrence and timing of rebleeding episodes.

Specific treatments were defined as treatments directly aimed at presumed bleeding causes including endoscopic or surgical treatment and medical therapies such as discontinuation of pro-hemorrhagic drugs or imunossupressive/biologic treatment for Crohn's disease. When purely symptomatic treatments such as blood transfusion, iron replacement, and close observation with regular follow-up was performed, they were classified as nonspecific treatments (9).

Capsule endoscopy

The Given® Video Capsule system and MiroCam® Video Capsule system were used in the study. CE studies were carried out according to our unit's protocol, which includes an overnight fast, suspension of iron supplements 8 days before the procedure and a liquid diet in the last dinner. Written informed consent was obtained from all patients. After capsule ingestion, patients were allowed to eat a light snack 4 hours later.

Patients were evaluated with real-time view 30 minutes after capsule ingestion. A prokinetic agent (metoclopramide 10 mg) was administered when the capsule was found in the stomach.

Diagnostic definition at CE

OGIB was subdivided into overt OGIB (melena or hematoquezias during the procedure or in the past) and occult OGIB (iron deficiency anemia with or without positive fecal occult blood). Overt OGIB was subdivided into ongoing-overt OGIB (melena or hematochezia during the procedure) and previous-overt OGIB (melena or hematochezia in the past but not during the procedure).

Lesions detected on CE were classified according to three categories, according to the definition reported by Saurin et al. (11): P0 lesions (with no potential for bleeding: Submucosal veins, diverticula without presence of blood or nodules without mucosal breaks), P1 lesions (with uncertain hemorrhagic potential: Red spots, small or isolated angiomata and erosions without bleeding), and P2 lesions (with high potential for bleeding: typical angiodysplasia, multiple erosions, ulcers, visible blood, tumors and varices). Only P2 lesions were considered positive findings, because the therapeutic impact is higher than P0 and P1 lesions. CE with no findings or with lesions classified as P0 and P1, were considered negative.

Rebleeding was defined as evidence of melena or hematochezia with nondiagnostic upper and lower GI endoscopy when performed, a drop in hemoglobin of 2 g/dL or more from baseline, or the need for transfusion 30 days after the index episode (9).

Statistical analysis

Data was analyzed using Statistical Software Package version 19.0. Descriptive statistics were used to describe the patient's demographic features, clinical characteristics and type of endoscopic findings

Categorical variables were presented as percentages and numeric variables as means. Results are expressed as percentages or means ± standard deviation (SD) for continuous variables. Chi-square test and t-student test were used to compare non-continuous and continuous data, respectively. The rebleeding rate was calculated and factors associated with re-bleeding after a negative CE were assessed by univariate analyses. $p < 0.05$ was considered to be statistically significant.

RESULTS

Patients

From a total of 232 patients, 173 were included in the study. The mean age was 61.7 years (standard deviation [SD] ±17) and 60% percent (n = 104) were female. The median time of follow up was 27 months (±20 months). Concerning medications, 17.9% (n = 31) were treated with anti-platelet drugs, 11.6% with NSAID and 14.5% with anticoagulation therapy (n = 20) (Table I). Before CE, the mean hemoglobin levels was 11.2 g/dl (±9.4 g/dl) and the mean number of units of packet red blood cells (PRBC) transfused was 2.8 (±6.4).

CE findings

Most patients were referred for occult OGIB (67.1%, n = 116), while 32.9% were referred for overt OGIB (32.9%, n = 57). There was one capsule retention in a patient with Crohn's disease. The capsule reached the cecum in 89% of all examinations.

More than half of the patients had negative CE (54.3%, n = 94): P0-15%, P1-49%, and without lesions-36.2% of negative CE. The most frequent positive findings (P2) were ulcers/erosions (34%, n = 27) and angyodisplasia (32%, n = 25). The remaining positive CE findings were: blood (22%, n = 17), tumors (7%, n = 6) and polyps (2%, n = 1).

In univariate analysis, patients with positive CE were older (mean 58.8 *vs.* 65 years, p = 0.04), had a higher number of units of packet red blood cells (PRBC) transfused before CE (mean 1.3 *vs.* 6, p = 0.001), antiplatelet use (25.3% *vs.* 11.7%, p = 0.02) and NSAID ingestion (10.6% *vs.* 19%, p = 0.02) (Table II) than patients with negative CE. Most patients with negative findings had occult OGIB (80% *vs.* 19%, p = 0.001). There was no difference in the time of follow up and the use of anticoagulation. In multivariate analysis, positive CE were older (p = 0.021), have a higher number of transfusion of PRBC (p = 0.020) and ongoing- overt OGIB (27% *vs.* 2%, p = 0.02) (Table II). Patients with negative CE had a smaller rebleeding rate (16% *vs.* 30.4%, p = 0.02) (Table III).

Table I. Patients characteristics

Number of patients (n = 173)	*N (%) or SD*
Age (mean)	61.7 (±17)
Female sex	104 (60.1%)
Type of OGIB	
Occult	116 (67.1%)
Overt	
Ongoing-overt	23 (13.3%)
Past-overt	34 (19.7%)
Antiplatelet drugs	31 (17.9%)
NSAID	20 (11.6%)
Anticoagulation	25 (14.5%)
Number of units PRBC before CE	2.8 (±6.4)
Hemoglobin level (g/dl) before CE	11.2 (±9.4)
Follow up duration (months)	27 (±20)

Therapeutic strategy after CE

After CE, specific treatments were done in almost 56.9% of patients with positive CE and in three patient with negative CE (56.9% *vs.* 3.2%, p < 0.001). In patients with positive CE, 22% (n = 39) received endoscopic treatments, which included argon plasma coagulation of angiodysplasias (59%, n = 23), polypectomy (10.2%, n = 4) and hemostatic clipping in a Dieulafoy lesion (0.6%, n = 1); 6.3% (n = 11) underwent surgery, with a final diagnosis of small bowel tumors or subepithelial lesions; and in 3.4% (n = 6) anticoagulation or antiplatelet/anti-inflammatory drugs were stopped. Specific treatments were associated with a decrease in rebleeding rate in patients with positive findings -38% who received specific treatment rebleed *vs.* 62% who did not received specific treatment rebleed, p = 0.03).

Table III. Comparison between rebleeding rate in negative and positive CE

	Negative CE (n = 94)	*Positive CE (n = 79)*	*p*
Rebleeding	15 (16%)	24 (30.4%)	0.02

Table II. Factors associated with positive and negative capsule endoscopy findings

	Negative CE (n = 94)	*Positive CE (n = 79)*	*Univariate analysis, p*	*Multivariate analysis, p*
Age (mean)	58.8 (±18.6)	65 (±14.3)	0.004	0.021
Female sex	63 (67%)	52% (41)	0.04	0.21
Antiplatelet use	11 (11.7%)	20 (25.3%)	0.02	0.93
NSAID	6 (6.4%)	14 (17.7%)	0.02	0.068
Anticoagulation	10 (10.6%)	15 (19%)	0.12	
Units PRBC before CE (mean)	1.2 (±2.2)	4.7 (±8.5)	< 0.001	0.020
Level of hemoglobin (mean) (g/dl)	10.8 (±1.8)	11.7 (±13.8)	0.1	
Type of OGIB				
Occult	76 (80.8%)	40 (50.6%)	< 0.001	
Overt				
Previous overt	19 (20%)	15 (19%)	0.2	
Ongoing overt	2 (2.1%)	22 (27%)	< 0.001	0.020
Follow up time	25.8 (±19.6)	28.3 (±27)	0.48	
Complete SB examination	88 (94%)	71 (90%)	0.24	

In the 3 patients with negative CE, specific treatment included stopping NSAID; none of these patients received endoscopic/surgical treatment.

Rebleeding rates and factors associated with rebleeding

The global rebleeding rate was 22.5% (n = 39). Most rebleeding occurred within 10 months (±10.3 months). In patients with positive CE, a specific treatment was associated with a lower rebleeding rate (62% *vs.* 16.4%, p = 0.03).

Patients with OGIB and negative CE have a low probability of rebleeding (16%, n = 15). In the univariate analysis of patients with negative CE, the rebleeding rate is higher in patients who need more transfusions of PRBC units before CE (3.0 *vs.* 0.9, p = 0.024) and have overt OGIB (46% *vs.* 13.9%, p = 0.03) (Table IV). Age, sex, type of medication, hemoglobin level before CE treatment with antiplatelet drugs, percentage of complete small bowel examination, NSAID or anticoagulation and specific treatment after CE did not influence rebleeding rate. Furthermore, the type of overt-OGIB did not influence the rebleeding rate in patients with negative CE.

The rebleeding in patients with negative CE occurred in a mean of 9.8 months (±5.4). In 53% of these patients, the rebleeding occurs more than 12 months after CE. The causes of rebleeding were not found in 53.3% (n = 8), with spontaneous resolution of the OGIB with non-specific therapy. In the remaining, the diagnosis were: Gastrointestinal stromal tumor (n = 1) diagnosed by CT enterography, Cameron´s lesions (n = 1), gastric varices (n = 1), myelodisplastic syndrome (n = 1), uterine fibromioma (n = 1) and chronic use of NSAID (n = 2).

Table IV. Factors associated with rebleeding in negative CE (univariate analysis)

	Rebleeding (n = 15)	*No-rebleeding (n = 79)*	*p*
Age (mean)	56 (±18.1)	59 (±18.8)	0.84
Female sex	9 (60%)	54 (68%)	0.5
Antiplatelet use	3 (20%)	8 (10.1%)	0.27
NSAID	1 (6.7%)	6.3% (5)	0.96
Anticoagulation	2 (13%)	10% (8)	0.7
Units PRBC transfused before CE (mean)	3.0	0.9	0.024
Level of hemoglobin (mean) (g/dl)	10.4 (±3)	10.8 (1.5)	0.4
Type of OGIB			0.003
Occult	8 (53%)	68 (86%)	
Overt	7 (46%)	11 (13.9%)	
Overt OGIB			0.39*
Ongoing-overt	0 (0%)	3 (3.8%)	
Past-overt	7 (46.7%)	8 (10%)	
Specific treatment	0% (0)	3 (3.8%)	0.51
Complete small bowel examination	14 (93%)	76 (96%)	0.64

*Chi2 with Yates correction.

DISCUSSION

Although it is generally accepted that CE is the first line examination for OGIB (1), the impact of a negative CE on the patients' outcome, as well as the factors associated with rebleeding after a negative CE remain poorly investigated and controversial.

In our data, 54.3% of CE examinations are negative, which is in accordance with other studies (9,13). The rebleeding rate after a negative CE is low (16%), with a mean time of follow up of 25.8 months and is significantly lower than in patients with positive CE findings (16% *vs.* 30.2%). This is in accordance with previous reports (10,14). A short time of follow up and a small number of patients have been pointed as a cause of a lower rebleeding rate after a negative CE in some series. However, our study presents one of the largest series reported in patients with OGIB and a negative CE, with a mean time of follow up of more than 24 months.

Overall rebleeding rates range from 6% to 31% (14). The discrepancies found on rebleeding rates in the literature can also be explained by differences in patient´s selection and subsequent management. Macdonald et al. report a rebleeding rate of 11% after a negative CE with more than a year of follow-up (14), with a negative predictive value of 89%. In a more recent study, Riccioni et al. showed that patients with negative CE had a significantly lower rebleeding rate (16.4% *vs.* 45%) (10). All these data demonstrated that a negative CE can predict a favorable prognosis in patients with OGIB.

In univariate analysis, patients with positive CE findings were older, had a higher ingestion of NSAID and antiplatelet drugs, transfusion of PRBC before CE and presented with ongoing-overt OGIB. This is in accordance with other reports (15-17). However, in multivariate analysis, only age, type of OGIB and the number of transfusion of PRBC were significantly different between negative and positive CE.

The association of advanced age and positive CE can be explained by the more frequent occurrence of angiodysplasia in elderly patients, which is one of the main bleeding lesion found in our series (17).

Another factor associated with a higher diagnostic yield was an increasing number of PRBC. Presumably the transfusion requirement may be a marker of ongoing or severe pathology within the gastrointestinal tract. Lai et al. con-

cludes that a positive CE is associated with a longer hospital stays and more units of blood transfused than those observed after a negative CE and that these findings further support that patients with a positive CE would benefit from further interventions to identify and treat the site of bleeding (16). Additionally, in patients with overt OGIB, CE and endoscopic interventions have higher diagnostic and therapeutic yield when performed early in the clinical presentation, supporting the role of CE and deep enteroscopy in the urgent setting to improve their accuracy and utility (17,18).

Park et al. (9) demonstrated that specific treatment decreases long term rebleeding after CE, suggesting that vigorous investigation to detect the bleeding source could reduce rebleeding. In the present study, more than half the patients with positive findings received specific treatment and it significantly decreased the rebleeding rate.

Because this is a retrospective study, we can not specify why some patients with positive findings did not receive specific treatment. However, most patients had multiple comorbidities adding increased sedation-related risks and little benefits for enteroscopy (19) in the treatment of angyodisplasias; others had a few small angyodisplasias or ulcers, and in these cases, the best treatment option was deemed to be iron therapy.

Few studies evaluated factors associated with rebleeding after a negative CE. This is a topic scarcely explored in the literature. Anticoagulation, younger age, male sex, and bleeding presentation with melena are reported to be risk factors of rebleeding (10,20,21). We found that a higher number of units of PRBC transfused before CE and an initial presentation in the form of overt OGIB are significantly associated with an increased rebleeding after a negative CE. These factors can be a marker of a more severe pathology in the gastrointestinal tract. However, in more than an half, the cause of rebleeding was not found. Unlike what has been previously reported, we found no association with age and anticoagulation. Also, there was no significant difference in the rebleeding rate in negative CE patients regardless of specific treatments. Only three patients had specific treatments that did not include endoscopic or surgical treatment.

The timing of rebleeding after a negative CE has also not been extensively investigated in the literature. According to Gonçalves et al. (21), the vast majority of rebleeding episodes occur within the first two years after CE. In concordance with Riccioni et al. (10), we also found that more than a half of patients rebleed more than 12 months after a negative CE.

Our study has some limitations. It has a retrospective design and all data was obtained from only one center. Because some exams were incomplete it was possible that some lesions might be missed. Also, the lack of a gold standard for small bowel diagnosis limits the evaluation the performance of CE.

In summary, patients with OGIB and a negative CE had a significantly lower rebleeding rate and can be safely followed with no further invasive investigations. However, we have to consider that, although the rebleeding is low, patients with a higher need of transfusion of PCRB previous to CE and presenting with an overt OGIB are associated with a higher rebleeding rate. So, in the absence of stringent guidelines for patients with OGIB and negative CE, it is reasonable to consider that these patients should be monitored closely. Only a careful clinical observation can help to identify a false negative CE. Although the time for follow up is not clear, we think that patients with these characteristics may benefit of a follow up of at least one year.

REFERENCES

1. Raju GS, Gerson L, Das A, et al. American Gastroenterological Association. American Gastroenterological Association medical position statement: Evaluation and management of occult and obscure gastrointestinal bleeding. Gastroenterology 2007;133:1694-6. DOI: 10.1053/j.gastro.2007.06.008
2. Raju GS, Gerson L, Das A, et al. American Gastroenterological Association (AGA) Institute technical review on obscure gastrointestinal bleeding. Gastroenterology 2007;133:1694-6 ID: 17983812] DOI: 10.1053/j.gastro.2007.06.007
3. Prakash C, Zuckerman GR. Acute small bowel bleeding: a distinct entity with significantly different economic implications compared with GI bleeding from other locations. Gastrointest Endosc 2003;58:330-5. DOI: 10.1016/S0016-5107(03)00003-8
4. Saurin JC, Delvaux M, Vahedi K, et al. Clinical impact of capsule endoscopy compared to push enteroscopy: 1-year follow-up study. Endoscopy 2005;37:318-23. DOI: 10.1055/s-2005-861114
5. Costamagna G, Shah SK, Riccioni ME, et al. A prospective trial comparing small bowel radiographs and video capsule endoscopy for suspected small bowel disease. Gastroenterology 2002;123:999-1005. DOI: 10.1053/gast.2002.35988
6. Hara AK, Leighton JA, Sharma VK, et al. Small bowel: Preliminary comparison of capsule endoscopy with barium study and CT. Radiology 2004;230:260-5. DOI: 10.1148/radiol.2301021535
7. Fisher L, Lee Krinsky M, Anderson MA, et al. The role of endoscopy in the management of obscure gastrointestinal bleeding. Gastrointestinal Endoscopy 2010;3:471-9. DOI: 10.1016/j.gie.2010.04.032
8. Ribeiro I, Rolando P, Rodrigues A, et al. The importance of alternative diagnostic modalities in the diagnosis of small bowel tumors after a negative capsule endoscopy. GE Portuguese Journal of Gastroenterology 2015;22:112-6. DOI: 10.1016/j.jpge.2015.01.008
9. Park J, Cheon J, Kim H, et al. Negative capsule endoscopy without subsequent enteroscopy does not predict lower long-term rebleeding rates in patients with obscure GI bleeding. Gastrointest Endosc 2010;71:990-7. DOI: 10.1016/j.gie.2009.12.009
10. Riccioni M, Urgesi R, Cianci R, et al. Negative capsule endoscopy in patients with obscure gastrointestinal bleeding reliable: Recurrence of bleeding on long-term follow-up. World J Gastroenterol 2013;19:4520-5. DOI: 10.3748/wjg.v19.i28.4520
11. Saurin JC, Delvaux M, Vahedi K, et al. Clinical impact of capsule endoscopy compared to push enteroscopy: 1-year follow-up study. Endoscopy 2005;37:318-23. DOI: 10.1055/s-2005-861114
12. Rondonotti E, Herrerias JM, Pennazio M, et al. Complications, limitations, and failures of capsule endoscopy: A review of 733 cases. Gastrointest Endosc 2005;62:712-6 DOI: 10.1016/j.gie.2005.05.002
13. Matsumura T, Arai M, Saito K, et al. Predictive factor of re-bleeding after negative capsule endoscopy for obscure gastrointestinal bleeding: Over 1-year follow-up study. Digestive Endoscopy 2014;26:650-8. DOI: 10.1111/den.12257
14. Macdonald J, Porter V, McNamara D. Negative capsule endoscopy in patients with obscure GI bleeding predicts low rebleeding rates. Gastrointest Endosc 2008;68:1122-7. DOI: 10.1016/j.gie.2008.06.054
15. Shahidi NC, Ou G, Svarta S, et al. Factors associated with positive findings from capsule endoscopy in patients with obscure gastroin-

testinal bleeding. Clin Gastroenterol Hepatol 2012;10:1381-5. DOI: 10.1016/j.cgh.2012.08.035
16. Lai LH, Wong GL, Chow DK, et al. Long-term follow-up of patients with obscure gastrointestinal bleeding after negative capsule endoscopy. Am J Gastroenterol 2006;101:1224-8. DOI: 10.1111/j.1572-0241.2006.00565.x
17. Ribeiro I, Pinho R, Rodrigues A, et al. Obscure gastrointestinal bleeding: Which factors are associated with positive capsule endoscopy findings? Rev Esp Enferm Dig 2015;107:334-9.
18. Pinto-Pais T, Pinho R, Rodrigues A, et al. Emergency single-balloon enteroscopy in overt obscure gastrointestinal bleeding: Efficacy and safety. United European Gastroenterol J 2014;2:490-6. DOI: 10.1177/2050640614554850.
19. Jackson CS, Gerson LB. Management of gastrointestinal angiodysplastic lesions (GIADs): A systematic review and meta-analysis. Am J Gastroenterol 2014;109:474-83. DOI: 10.1038/ajg.2014.19.
20. Koh S, Im J, Kim J, et al. Long-term outcome in patients with obscure gastrointestinal bleeding after negative capsule endoscopy. World J Gastroenterol 2013;19:1632-8. DOI: 10.3748/wjg.v19.i10.1632.
21. Curdia Gonçalves T, Dias de Castro F, Moreira MJ, et al. Small bowel capsule endoscopy in obscure gastrointestinal bleeding: Normalcy is not reassuring. Eur J Gastroenterol Hepatol 2014;26:927-32. DOI: 10.1097/MEG.0000000000000135.