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Predictors for finding lesions in the small bowel by enteroscopy after a positive capsule endoscopy

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ABSTRACT

Introduction: studies have examined the agreement between capsule endoscopy and double-balloon enteroscopy, with varying results. The aim of this study was to identify factors that predict the visualization of lesions in the small bowel by double-balloon enteroscopy after a positive capsule endoscopy.

Methods: a retrospective, observational and comparative study was performed that evaluated patients that underwent double-balloon enteroscopy after a positive capsule endoscopy, between January 2017 and August 2019. The data studied included demographics, indications, comorbidities and the results of capsule endoscopy and double-balloon enteroscopy, which were evaluated by multiple logistic regression.

Results: 91 patients were included (age 58 ± 16.5 years, 53 female). Sixty-two double-balloon enteroscopy (68.1 %) found the same lesions as capsule endoscopy. Predictive factors for a positive double-balloon enteroscopy were multiple lesions (OR 8.10, 1.50-43.78; p = 0.015) and < 15 days between both studies (OR 5.31, 1.19-23.66; p=0.029). In the subgroup of patients with small bowel bleeding (70 patients), the results of 46 double-balloon enteroscopies (65.7 %) agreed with the capsule endoscopy. Predictive factors in this group were multiple lesions (OR 13.51, 1.78-102.22; p = 0.012), < 15 days between both studies (OR 13.51, 1.78-102.22; p = 0.012), > 60 years of age (OR 7.45, 1.51-36.75; p = 0.014) and ulcers (OR 4.67, 1.08-20.22; p = 0.039).

Conclusions: predictive factors for a positive double-balloon enteroscopy after a positive capsule endoscopy were multiple lesions and < 15 days between both procedures. In patients with small bowel bleeding, age over 60 years and the presence of ulcers were also predictive factors.

Key words: Enteroscopy. Small bowel bleeding. Capsule endoscopy.

INTRODUCTION

Endoscopic study of the small bowel (SB) is complex, due to its extension and location. The main tools available are capsule endoscopy (CE) and device-assisted enteroscopy (DAE) (1). Due to the fact that both procedures were introduced at the same time (CE in 2000 and double balloon enteroscopy (DBE) in 2001), multiple studies were performed to compare the diagnostic yield of both techniques (2). However, CE became the initial diagnostic study, since it is less invasive and has a lower rate of complications than DAE (3,4). Comparative studies have shown that the diagnostic yield of EC is 62 %, while that of DBE is 56 % in patients with small bowel bleeding (SBB), which is the main indication of both procedures (5). There are various studies of the agreement between CE and DAE, with varied results (6,7). It has been noted that only 66 % of the DAE studies identified the findings observed in CE. Thus, many lesions were missed (6). There is little evidence about the factors that might contribute to the identification of the lesions observed by CE in

DAE. The aim of this study was to identify the predictive factors of a positive enteroscopy after a positive CE.

MATERIAL AND METHODS

Study design

A retrospective, observational and comparative study was performed, which included all patients who underwent DBE after a positive CE in the Hospital de Especialidades del Centro Médico Nacional Siglo XXI of the Instituto Mexicano del Seguro Social. Those patients that underwent a push enteroscopy, with a negative CE or with extra-intestinal lesions were excluded.

CE Pillcam SB3 (Given Imaging Ltd, Yoqneam, Israel) was used and was considered positive when lesions were identified in the SB (angioectasias, ulcers, polyps or tumors and significant erosions). If a patient had more than one lesion, the most significant one was considered according to the indication of the CE. All patients were prepared before ingesting the CE with two liters of polyethylene glycol the day before ingestion and an 8-hour fast. DBE (Fujinon, Saitama, Japan) was used for enteroscopies and studies were considered positive when the same lesion was observed as in the CE. When DBE was performed via anterograde, patients were prepared with an 8-hour fast and with 4 liters of polyethylene glycol the afternoon before the study with an 8-hour fast for retrograde DBE. Access was decided according to the location of the lesion in the CE. If it was identified by CE in the first two thirds of the SB, the access was anterograde and if it was identified in the last third, it was retrograde. In cases of doubt about the location of the lesion, the access was anterograde.

Data analysis

The data collected for the study included demographics, indications of the studies, comorbidities, previous surgeries, date of the procedures, previous radiological studies and the results of the CE and DBE.

Statistical analysis

Quantitative variables were presented as the mean with the standard deviation or the median with the interquartile range, depending on normality. Qualitative variables are presented as frequencies with percentages. Differences were evaluated using the Mann-Whitney U test for quantitative variables with a free distribution and qualitative variables using the Chi^2 or the Fisher exact test. Statistical analysis of a subgroup included only patients with a suspicion of small bowel bleeding (SBB). Multiple logistic regression was performed including variables with $p < 0.2$ and those that were reported as significant in the literature. These included the time between studies and insertion depth, which explained a greater R^2 to identify predictive factors for positive enteroscopy using a confidence interval of 95 % (95 %CI). $p < 0.05$ was as considered statistically significant. The statistical program SPSS version 22 was used for the analysis (IBM, Chicago IL, USA).

RESULTS

Ninety-one patients were included in the study with a mean age of 62 years (51-70) and 53 (58.2 %) were females. Indications for CE were manifest SBB (68.1 %), Crohn's disease (14.3 %), non-manifest SBB (8.8 %) and suspicion of an intestinal tumor or polyp (8.8 %). The main findings in CE were ulcers (50.5 %), angioectasias (30.8 %), tumors or polyps (9.9 %) and significant erosions (8.8 %). The same findings were identified by DBE as CE in 62 cases (68.1 %). The DAE route was anterograde in 68 cases (74.7 %). The mean time between both procedures was 32 days (9, 64). When demographic, background and findings among the DBE that agreed with CE and those that did not were compared, statistically significant differences were only observed for age ($p = 0.025$) and the presence of multiple lesions ($p = 0.015$) (Table 1). Statistically significant differences were also seen in the case of active hemorrhage ($p = 0.016$). However, it was more common when there was no agreement between the two procedures (34.5 % *vs* 12.9 %). According to the multiple logistic regression, the variables that were statistically significant were multiple lesions (OR 8.10, 95 % CI 1.50-43.78) and less than 15 days between CE and DBE (OR 5.31, 95 % CI 1.19-23.66; $p = 0.029$) (Table 2). Therapy by DBE was performed in 21

patients (plasma argon coagulation in 16 and placement of hemoclips in 5), tattooing was also performed in 5 patients and biopsies were taken in 43 cases.

The subgroup of patients with suspected SBB included 70 patients, divided into manifest (88.6 %) and non-manifest (11.4 %) groups. The main lesions identified were ulcers (45.7 %), angioectasias (40 %), tumors (8.6 %) and significant erosions (5.7 %). The same findings were observed by CE and DBE in 65.7 % of the cases. 78.5 % of DBE were anterograde and the time between both studies was 32 days (9, 66). When the groups were divided according to agreement between CE and DBE, age (p = 0.009), multiple lesions (p = 0.016) and active hemorrhage in CE (p = 0.027) showed differences. According to the multiple logistic regression, the variables with statistically significant differences were patients over 60 years (OR 7.45, 95 % CI 1.51-36.75; p = 0.014), multiple lesions (OR 10.42, 95 % CI 1.37-79.30; p = 0.024), less than 15 days between CE and DBE (OR 13.51, 95 % CI 1.78-102.22; p = 0.012) and ulcers (OR 4.67, 95 %CI 1.08-20.22; p = 0.039).

DISCUSSION

The agreement identified between CE and DBE is variable, ranging from weak (Kappa 0.17) (8) to moderate (Kappa 0.46) (9), which depends on the indication and the lesions identified. The main indication for CE in our population was manifest SBB, which is the most common indication for CE (10) and DBE (11), followed by Crohn's disease and tumors and polyps.

Decker et al. (12) found more lesions by DBE in older patients when they were previously observed by CE. In our study, a difference was found in age by univariate analysis. In the multivariate analysis, which covered patients in dichotomy that were over and under 60 years of age, a significant p value was noted. However, the confidence interval overlapped with the unit and therefore was not considered as significant. One variable that had a significant difference according to both the univariate and multivariate analysis was the presence of multiple lesions. This was due to the fact that while the patient had more lesions by CE, there was a greater probability of identifying them by DBE compared to a unique lesion. Active hemorrhage was also significant according to the univariate analysis

and was more common in the group that did not show lesions by enteroscopy. This differs from the report by Pérez-Cuadrado-Robles, et al. (13), where the cause of the hemorrhage was not identified in only 8 (21 %) of 37 patients with active hemorrhage by CE. However, upon introducing this variable into the multivariate analysis, no significant difference was observed, demonstrating that the difference seen in the univariate analysis was random.

According to the multivariate analysis, the time between CE and DBE also showed a statistically significant difference. The variable became dichotomic when less than or over 15 days were considered (14). A time over 15 days may associate with curing of the lesion, such as ulcers or erosions.

When the subgroup of patients with an indication of manifest SBB were analyzed, the variables that showed significant differences were the same as in the study of all patients, both for the univariate and multivariate analysis. In addition, age over 60 years and the presence of ulcers were also significant in the univariate and multivariate analysis. This was a predictive factor for having a positive DBE after a positive CE. This is in accordance with the article published by Marmo et al. (9), which noted that the lesion with a greater agreement between both procedures were ulcers, with a Kappa of 0.78.

The main limitation of our work is that it is a retrospective study. We may conclude that multiple lesions and less than 15 days between CE and DBE are predictive factors for detecting lesions by enteroscopy when there is a positive CE. In addition, age over 60 years and the presence of ulcers are factors for a positive DBE in patients whose indication is SBB. Although, more studies are required with more patients to confirm the results reported in this article.

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Table 1. Demographic characteristics and findings by capsule endoscopy

	All indications			**Small bowel bleeding**		
	Agreement in DBE n = 62	**Without agreement in DBE n = 29**	***p***	**Agreement in DBE n = 46**	**Without agreement in DBE n = 24**	***p***
Age (years)*	66 (54.5, 72)	52 (39, 67)	0.025	67 (56, 74)	52 (39, 67)	0.009
Female†	36 (58.1 %)	17 (58.6 %)	0.960	27 (58.7 %)	15 (62.5 %)	0.758
Hospitalized†	14 (22.6 %)	7 (31 %)	0.387	11 (23.9 %)	8 (33.3 %)	0.400
Reason for study†			0.238			0.706
Manifest SBB	40 (64.5 %)	22 (75.9 %)		40 (87 %)	22 (91.7 %)	
Non-manifest SBB	6 (9.7 %)	2 (6.9 %)		6 (13 %)	2 (8.3 %)	
Tumor or polyps	5 (8.1 %)	3 (10.3 %)				
Crohn's disease	11 (17.7 %)	2 (6.9 %)				
Diabetes mellitus 2†	6 (9.7 %)	5 (17.2 %)	0.318	5 (10.9 %)	5 (20.8 %)	0.294
Abdominal surgery†	19 (30.6 %)	8 (27.6 %)	0.766	16 (34.8 %)	6 (25 %)	0.403

Consumption of NSAIDs†	14 (22.6 %)	7 (24.1 %)	0.869	12 (26.1 %)	5 (20.8 %)	0.627
Time between CE and DBE (days)*	31 (9. 57)	36 (10.5. 90.5)	0.317	31 (9. 57)	44 (9. 94)	0.242
Location†						
Duodenum	4 (6.5 %)	0	0.302	3 (6.5 %)	0	0.546
Jejunum	38 (61.3 %)	22 (75.9 %)	0.172	28 (60.9 %)	19 (79.5 %)	0.122
Ilium	12 (19.3 %)	6 (20.7 %)	0.882	9 (19.6 %)	5 (20.8 %)	0.900
Multiple	8 (12.9 %)	1 (3.43 %)	0.263	6 (13 %)	0	0.087
Multiple lesions†	*19 (30.6 %)*	*2 (6.9 %)*	*0.015*	*16 (34.8 %)*	*2 (8.3 %)*	*0.016*
Active hemorrhage†	*8 (12.9 %)*	*10 (34.5 %)*	*0.016*	*8 (17.4 %)*	*10 (41.7 %)*	*0.027*
Anterograde†	44 (71 %)	24 (82.8 %)	0.228	35 (76.1 %)	20 (83.3 %)	0.483
Positive radiological studies†	24 (38.7 %)	8 (10.2 %)	0.300	13 (28.3 %)	5 (20.8 %)	0.500
Angioectasias†	16 (25.7 %)	12 (41.4 %)	0.134	16 (34.8 %)	12 (50 %)	0.217
Ulcers†	35 (56.5 %)	11 (37.9 %)	0.100	*25 (54.3 %)*	*7 (29.2 %)*	*0.045*
Tumors†	5 (8.1 %)	4 (13.8 %)	0.459	3 (6.5 %)	3 (12.5 %)	0.406
Erosions†	6 (9.7 %)	2 (6.9 %)	0.662	2 (4.3 %)	2 (8.3 %)	0.603
Insertion depth (cm)*	235 (150, 250)	200 (150, 300)	0.593	235 (150, 272)	200 (150, 292)	0.242

*Median (interquartile range); Mann-Whitney U. †Frequencies (percentages); Chi^2. DBE: double-balloon enteroscopy; CE: capsule endoscopy; SBB: small bowel bleeding; NSAIDs: nonsteroidal anti-inflammatory drugs.

Table 2. Predictors to identify lesions in the small bowel by enteroscopy after a positive capsule endoscopy

	All indications			**Small bowel bleeding**		
	OR	**95 % CI**	***p***	**OR**	**95 % CI**	***p***
Over 60 years	3.00	1.00-9.02	0.049	*7.45*	*1.51-36.75*	*0.014*
Active hemorrhage in CE	2.77	0.72-10.66	0.136	1.82	0.39-8.53	0.442
Multiple lesions	*8.10*	*1.50-43.78*	*0.015*	*10.42*	*1.37-79.30*	*0.024*
Lesions in the jejunum	1.82	0.58-5.79	0.215	4.41	0.936-20.85	0.061
Ulcers	2.42	0.76-7.68	0.134	*4.67*	*1.08-20.22*	*0.039*
Less than 15 days between CE and DBE	*5.31*	*1.19-23.66*	*0.029*	*13.51*	*1.78-102.22*	*0.012*
Insertion depth greater than 200 cm in DBE	2.51	0.84-7.49	0.098	3.66	0.86-15.59	0.078

Nagelkerke R^2 for all indications: 0.355. Nagelkerke R^2 for small bowel bleeding: 0.491. OR: odds ratio; CI: confidence interval; CE: capsule endoscopy; DBE: double-balloon enteroscopy.

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