REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

Title:
Evaluation of a new composite score combining SPICE and Protrusion Angle scores to distinguish submucosal lesions from innocent bulges

Authors:
Edgar Afecto, Rolando Pinho, Catarina Gomes, João Paulo Correia, Manuela Estevinho, Ana Ponte, Adélia Rodrigues, João Carvalho

DOI: 10.17235/reed.2021.8080/2021
Link: PubMed (Epub ahead of print)

Please cite this article as:
Afecto Edgar, Pinho Rolando, Gomes Catarina, Correia João Paulo, Estevinho Manuela, Ponte Ana, Rodrigues Adélia, Carvalho João. Evaluation of a new composite score combining SPICE and Protrusion Angle scores to distinguish submucosal lesions from innocent bulges. Rev Esp Enferm Dig 2021. doi: 10.17235/reed.2021.8080/2021.

REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

Evaluation of a new composite score combining SPICE and Protrusion Angle scores to distinguish submucosal lesions from innocent bulges

Edgar Afecto, Rolando Pinho, Catarina Gomes, João Paulo Correia, Manuela Estevinho, Ana Ponte, Adélia Rodrigues, João Carvalho

Department of Gastroenterology, Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal

Corresponding Author:
Full name: Edgar Manuel Pontes Afecto
E-mail address: edgarafecto@gmail.com

KEYWORDS: Capsule endoscopy. Small bowel. Submucosal lesions.

ABBREVIATION LIST: CE – capsule endoscopy; CT – computed tomography; CTE - computed tomography enterography; MRE – magnetic resonance enterography; SBSL – small bowel submucosal lesion; SBT – small bowel tumor;

Abstract

Introduction/Aims

In capsule endoscopy (CE), small bowel subepithelial lesions (SBSL) are difficult to distinguishing from innocent mucosal protrusions. The SPICE score (smooth, protruding lesions index on CE) and a score that assesses the SBSL protrusion angle were developed.

We intend to determine if a composite score is superior to the proposed models.

Methods

All CE between 01/2010 and 12/2020 were included if a smooth, round protruding lesion was identified. Both scores and a composite score (SPICE>2 and Angle<90º)

were calculated after video review. Mucosal protrusions were defined as SBSL if they had a histological/imaging diagnosis and innocent protrusions if otherwise. All patients without at least one appointment and an additional diagnostic exam after CE were excluded.

Results

A total of 34 CE included, 64.7% men, age 65.4±14.7 years. The most common indication for CE was anemia (52.9%). SBSL were identified in 17 cases, with lipomas (14.7%) being the most frequent diagnosis.

Both the SPICE (AUROC 0.90, p<0.001) and protrusion angle scores (AUROC 0.74, p=0.019) accurately distinguished SBSL from innocent protrusions. Applying a 90º cut-off, the protrusion angle has a sensitivity of 52.9% and specificity of 88.2%. Applying a cut-off of >2 points, the SPICE score has a sensitivity of 64.7% and specificity of 94.2%. The composite score had a sensitivity, specificity, positive and negative predictive value of 47.0%, 100%, 100% and 65.4%.

Conclusion

We propose that in cases where both a SPICE>2 and angle of <90º are obtained, additional follow-up investigation should always be undertaken, as the likelihood of SBSL is high.

Introduction and Aims

Small bowel tumors (SBT) are a rare form of primary neoplasia, accounting for only 2% of all gastrointestinal cancers (1) but the overall incidence of SBT seems to be increasing, both in the United States and in Europe (2-4). The diagnosis of the SBT is usually delayed and performed only at a late phase, when metastatic disease and lymph node is present in a significant amount of patients, due to non-specific symptoms in early stages. The most common presentation is bleeding or small bowel obstruction (5, 6).

The advent of capsule endoscopy (CE), which visualizes the whole small bowel, dramatically improved our diagnostic capacity for SBT, with incidence rates ranging from 2.4% to 6.3% of all exams in retrospective studies (7-9). Nevertheless, CE has several limitations, due to the nature of the exam such as the inability to take biopsies, the inability to steer the capsule or perform any other procedure. Additionally, the distinction between true small bowel submucosal lesions (SBSL) from innocent bulges covered by normal looking mucosa isn't always simple. A small prospective study by Shyung L et al (10) proposed a score based on "alarm" features such as bleeding, mucosal disruption, an irregular surface, color, and white villi. This proposed score can help in the setting of mucosal alterations but the problem of SBSL with normal overlying mucosa still remains. To address this issue, two scores by Girelli C et al (11) and Min M et al (12) were proposed.

The first score, entitled SPICE (smooth, protruding lesions index on capsule endoscopy), encompasses 4 criteria: a clear defined boundary with surrounding mucosa, height larger than diameter, visible lumen in the frames in which the lesion appears and image of the lesion lasting more than 10 minutes. One point is attributed per criteria, with lesions scoring >2 points being diagnosed as SBSL. The score fared well overall, with a sensitivity of 83 % and a specificity of 89% in the inception study. In a subsequent external validation study by Rodrigues J et al (13), a sensitivity of 67% and a specificity of 100%, corresponding to four false-negative and zero false-positive findings was demonstrated.

The score proposed by Min M et al is simpler and evaluates only the lesion protrusion angle in relation to the surrounding mucosa. A cut-off of <90º was found to predict the presence of SBSL with a sensitivity of 92% and specificity of 88.9%.

This work intends to externally validate the mucosal protrusion score and to determine the accuracy of a novel composite model (combining the SPICE and mucosal protrusion scores).

Methods

Study design

All consecutive CE exams performed between January 2010 and December 2020 were analyzed for the purpose of this study. All exams in which a round, smooth, protruding lesion was identified in the small bowel were included. For all patients we collected information regarding sex, age, indication for exam, timing (urgent vs. elective) and exam reader.

Mucosal protrusions with definitive histological, endoscopic and/or radiological diagnosis of subepithelial lesions were considered as such. If no lesion was identified in follow-up studies, they were defined as innocent bulges.

Absence of additional follow-up study such as small bowel enteroscopy, computerized tomography (CT), CT enterography (CTE), magnetic resonance enterography (MRE) and/or surgery was considered an exclusion criteria. Other exclusion criteria were poor small bowel visualization and the presence of suspicious features for SBSL (ulcers or bleeding).

Capsule endoscopy protocol

All procedures were performed with the Mirocam™ CE platform, after an appropriate informed consent. All patients are instructed to follow a liquid diet in the day before the procedure and to perform an overnight fast. A bowel preparation of polyethyleneglycol + ascorbic acid is administered (1 liter in the previous night). All iron supplements are suspended in the previous 8 days.

After capsule ingestion, a 10mg metoclopramide pill is taken by the patient. The exam is interrupted after the capsule reaches the colon (as seen in real-time) or the battery ends.

SPICE and protrusion angle scores

All studies were analyzed by an experience reader. Subsequently, another reader observed the studies and calculated the SPICE score and the mucosal protrusion angle.

The SPICE score was calculated as described in the original work. Points were attributed if the suspected lesion had a well-defined border with the surrounding mucosa, if the height was larger than its diameter, if the small bowel lumen was visible in the frames the lesion appears and lastly if the images of the lesion lasts longer than 10 minutes. If a total score of 3 or 4 points was obtained, the lesion was defined as a

SBSL.

The mucosal protrusion angle was defined as the angle between the protruding lesion and the surrounding mucosa. The angle was measured by placing a protractor on the screen, after selecting the frame that allowed for the best characterization. A cut-off point of <90º was utilized, as in the original paper, to define true SBSL. The angle measurement is demonstrated on figure 1.

Statistics

All continuous variables were expressed as mean±standard deviation or median+IQR, as appropriate. Normal distribution of the variables was tested with Shapiro-Wilk tests or with skewness/kurtosis analysis. Categorical variables were expressed as percentages and frequencies. The Chi-square test was used to assess the association between categorical variables while Mann-Whitney or t-student tests were used for continuous variables, as appropriate. All presented p-values are two tailed and were considered significant if <0.05.

The sensitivity, specificity, positive predictive value, negative predictive value and the area under the ROC curve were calculated for SPICE and mucosal protrusion angle scores. Subsequently, a dichotomic composite score combining the previous two (SPICE > 2 and Mucosal protrusion angle <90º) was tested in our population and the same parameters previously described in this paragraph were calculated. ROC curve comparison was performed using DeLong's method on MedCalc® (MedCalc Software Ltd, Ostend), v14.8. All other statistical analysis was performed with IBM® SPSS® Statistics software (SPSS Inc., Chicago), version 20.0.

Results

Between January 2010 and December 2020, a total of 1204 capsule endoscopy examinations were performed in our department, 6.7% (81 cases) of which had a protruding lesion. Of these, 47 were excluded (characteristics suspicious for lesions, n=26; inability to calculate the protrusion angle, n=12; no adequate follow-up, n=3; staging of polyposis syndromes, n=3; poor visualization, n=2; technical failure, n=1). A total of 34 capsule endoscopies, from 31 patients, were included in the analysis. Of these, 19 patients had been previously included in another study from our group (13).

Patient analysis

The mean age of the included patients was 65.4+14.7 and 64.7% were male. There was no statistical difference between groups (SBSL vs. innocent bulges) in terms of sex (p=0.15) or age (p=0.25). Most exams (79.4%) were performed on an elective basis while 20.6% were urgent and SBSL were not more commonly found on either group (p=0.20). The most common indication for capsule endoscopy was iron deficient anemia (52.9%) followed by obscure gastrointestinal bleeding (32.4%). All patient data is summarized in table 1.

Capsule findings

Most protruding lesions were identified in the ileon (50%) or the jejunum (47.1%) with only 1 being identified in the duodenum. A total of 17 (50%) true SBSL were confirmed after follow-up examinations (CTE, MRE or enteroscopy) were performed.

The most common SBSL diagnoses were lipomas (14.7%), gastrointestinal stromal tumors (11.8%) and neuroendocrine tumors (11.8%). All definitive diagnosis were confirmed via enteroscopy (due to pathognomonic characteristics) or by histological analysis after surgery was performed. All patient and CE data is summarized in table 1.

Score assessment

The mean SPICE score was significantly higher in the true SBSL group (2.71±0.58 vs. 1.24±0.90, p<0.001). The sensitivity, specificity, positive predictive value and negative predictive value for the diagnosis of SBSL was 64.7%, 94.1%, 91.7% and 72.7%, respectively. When going by the four different components of the SPICE score, we found that well-defined borders was an accurate predictor for the presence of SBSL (n=13 vs. n=4, p=0.002); likewise, bulge diameter being inferior to its height was a predictor for SBSL (n=14 vs. n=2, p<0.001); on the other hand, a visible lumen in the same frames as the lesion (n=16 vs. n=13, p=0.146) and the lesion being visible for more than 10 minutes (n=3 vs. n=2, p=0.628) were not found to be accurate predictors for SBSL.

The mean mucosal protrusion angle value was significantly lower in the SBSL group (85.29±46.62 vs. 122.35±34.92, p=0.018). The sensitivity, specificity, positive predictive value and negative predictive value for the diagnosis of SBSL was 58.8%,

88.2%, 83.3% and 68.2%, respectively.

The ROC curves for both scores can be seen on figure 2. Overall, the SPICE score was superior to the mucosal protrusion angle score, with an AUROC of 0.9 (CI 0.79-1.0) vs. 0.74 (CI 0.56-0.91), although the difference was not statistically significant (p=0.06).

A combined score of mucosal protrusion angle <90º and SPICE>2 was tested (table 2) and was found to significantly predict the presence of SBSL (n=8 vs. n=0, p=0.001). The sensitivity, specificity, positive predictive value and negative predictive value for the diagnosis of SBSL was 47.1%, 100.0%, 100.0% and 65.4%, respectively.

Discussion

Although CE revolutionized the way we can observe the small bowel, there are still unaddressed limitations. The absence of direct videocapsule control, the limited field of vision, non-continuous image capture, folds and angulations, incomplete exams and poor bowel cleansing are still severe limitations to this diagnostic method. While the first 4 parameters cannot be intervened upon as of yet, several authors have tried to identify predicting factors for incomplete examinations (14) and how to optimized bowel cleansing (15). Additionally, the operator sometimes only has a few still frames to reach a diagnosis and with everything added, up to 18.9% of SBSL may be missed by this method (16). While false negatives carry the risk of missing a potentially curable neoplastic lesion, false positives also carry the risk of unnecessary interventions and co-morbidity. SBT may be easier to identify if they show suspicious features, such as bleeding, mucosal disruption, an irregular surface, color and white villi, as proposed by Shyung L et al (10). The problem still remains for smooth protruding lesions covered by normal appearing mucosa and in this sense two scores were proposed to help make the distinction from SBSL and innocent bulges (11, 12).

In our study, both proposed scores accurately distinguished true SBSL from innocent bulges, with SPICE score being more robust, with a sensitivity of 64.7% vs 58.8% and a specificity of 94.1 vs. 88.2%. Our study also confirmed the findings of a previous work by our group, that the presence of well-defined borders and bulge diameter inferior to its height are better predictors of SBSL than the other two components of this score (13). While the mucosal protrusion angle falsely identified 7 cases as innocent protrusions, the SPICE score only did so on 6 cases. On the other

hand, the SPICE score was also superior in terms of false positives, incorrectly classifying one case as a SBSL vs. 2 cases when the mucosal protrusion angle was used. We can conclude that both scores still aren't perfect and probably suffer from the limitations associated with CE.

When a composite score was created by combining a SPICE>2 and a mucosal protrusion angle of <90º, a better specificity was obtained – 100%. This translates to diminishing false positives, reducing the number of diagnostic exams that are unnecessarily performed. This comes at a trade-off for sensitivity, with a superior number of false negatives when compared to SPICE (n=9 vs. n=6) or mucosal protrusion angle (n=9 vs. n=7). The reduction in sensitivity is bound to the limitations in the original scores, as a composite score demands that both previous scores correctly identify a lesion as a SBSL in order for it to consider it as such. The main strength of the composite score is, therefore, to identify the subset of patients with a positive composite score who will have with high certainty a SBSL and possibly requiring a specific intervention.

This study has its limitations. The retrospective nature is subject to confounding and selection bias and our patient sample is small. Nevertheless, this study design is in line with most of works performed in this line of investigation (7,8,10,12,13,17). This is explained by the low incidence of small bowel tumors and the very nature of capsule endoscopy, in which retrospective review of the studies is possible and readily accessible.

In conclusion, we propose than in cases where both a SPICE >2 and an angle of <90º are obtained, additional follow-up investigation should be undertaken, as these lesions are likely SBSL, as demonstrated by our data, although these results should be further validated by larger, prospective studies.

References

1. Schottenfeld D, Beebe-Dimmer JL, Vigneau FD et al. The epidemiology and pathogenesis of neoplasia in the small intestine. Ann Epidemiol 2009;19(1):58–69.

2. Søreidea K, Sandvika O, Søreide J et al. Global epidemiology of gastrointestinal stromal tumours (GIST): A systematic review of population-based cohort studies. Cancer Epidemiology 2016; 40:39-46

3. Lu Y, Frobom R, Lagergren J et al. Incidence patterns of small bowel cancer in a population-based study in Sweden: Increase in duodenal adenocarcinoma. Cancer Epidemiol 2012;36:e158-63

4. Bilimoria KY, Bentrem DJ, Wayne JD, et al. Small bowel cancer in the United States: Changes in epidemiology, treatment, and survival over the last 20 years. Ann Surg 2009;249:63-71

5. Dabaja BS, Suki D, Pro B et al. Adenocarcinoma of the small bowel: presentation, prognostic factors, and outcome of 217 patients. Cancer 2004;101:518–26

6. Talamonti MS, Goetz LH, Rao S, et al. Primary cancers of the small bowel: analysis of prognostic factors and results of surgical management. Archives of Surgery 2002; 137:564–70.

7. E Rondonotti, M Pennazio, E Toth, et al. Small-bowel neoplasms in patients undergoing video capsule endoscopy: a multicenter European study. Endoscopy 2008;40(6):488-95

8. Urbain D, De Looze D, Demedts I, et al. Video capsule endoscopy in small-bowel malignancy: A multicenter Belgian study. Endoscopy 2006;38:408-11

9. Bailey A, Debinski HS, Appleyard MN, et al. Diagnosis and outcome of small bowel tumors found by capsule endoscopy: A three-center Australian experience. Am J Gastroenterol 2006;101:2237-43.

10. Shyung L, Lin S, Shih S et al. Proposed Scoring System to Determine Small Bowel Mass Lesions Using Capsule Endoscopy. J Formos Med Assoc 2009; 108(7):533–538

11. Girelli CM, Porta P, Colombo E, et al. Development of a novel index to discriminate bulge from mass on small-bowel capsule endoscopy. Gastrointest Endosc 2011; 74:1067-74

12. Min M, Noujaim M, Green J et al. Role of Mucosal Protrusion Angle in Discriminating between True and False Masses of the Small Bowel on Video Capsule Endoscopy. J Clin Med 2019; 8(418)

13. Rodrigues J, Pinho R, Rodrigues A et al. Validation of SPICE, a method to differentiate small bowel submucosal lesions from innocent bulges on capsule endoscopy. Rev. Esp. Enferm. Dig. 2017, 109, 106–113

14. Ponte A, Pinho R, Rodrigues A et al. Predictive factors of an incomplete examination and inadequate small-bowel cleanliness during capsule endoscopy. Rev Esp Enferm Dig 2018:110(10):605-611

15. Ponte A, Pinho R, Rodrigues A et al. Review of small-bowel cleansing scales in capsule endoscopy: A panoply of choices. World J Gastrointest Endosc 2016 September 16; 8(17): 600-609

16. Lewis BS, Eisen GM, Friedman S et al. A pooled analysis to evaluate results of capsule endoscopy trials. Endoscopy 2005;37:960-5

17. Cobrin GM, Pittman RH, Lewis BS et al. Increased diagnostic yield of small bowel tumors with capsule endoscopy. Cancer 2006;107:22-7

Table 1 – Patient and videocapsule information

Patient age		65.4±14.7
SBSL group		68.4±10.8
Innocent bulge group		62.5±17.6
Patient sex		64.7% male
SBSL group		52.9% male
Innocent bulge group		76.5% male
Indication for VCE		
Anemia		52.9%
Obscure GI bleeding		32.4%
IBD (suspected/confirmed)		14.7%
Modality of VCE		
Urgent		20.6%
Elective		79.4%
Protrusion location		
Duodenum		2.9%
Jejunum		47.1%
Ileum		50.0%
Diagnosis		
SBSL	50%	
Lipoma		14.6%
GIST		11.8%
NET		11.8%
Adenoma		5.9%
Lymphangiectasia		5.9%
Innocent bulges	50%	

SBSL – small bowel submucosal lesion; VCE – videocapsule endoscopy; GI – gastrointestinal; IBD – inflammatory bowel disease; GIST – gastrointestinal stromal tumor; NET – neuroendocrine tumor

Table 2 – Composite score performance

	True SBSL	Innocent bulge
Positive for SBSL	8	0
Negative for SBSL	9	17
Sensitivity 47.1%, Specificity 100.0%, PPV 100.0%, NPV 65.4%		
SBSL – small bowel submucosal lesion; PPV – positive predictive value; NPV – negative predictive value		

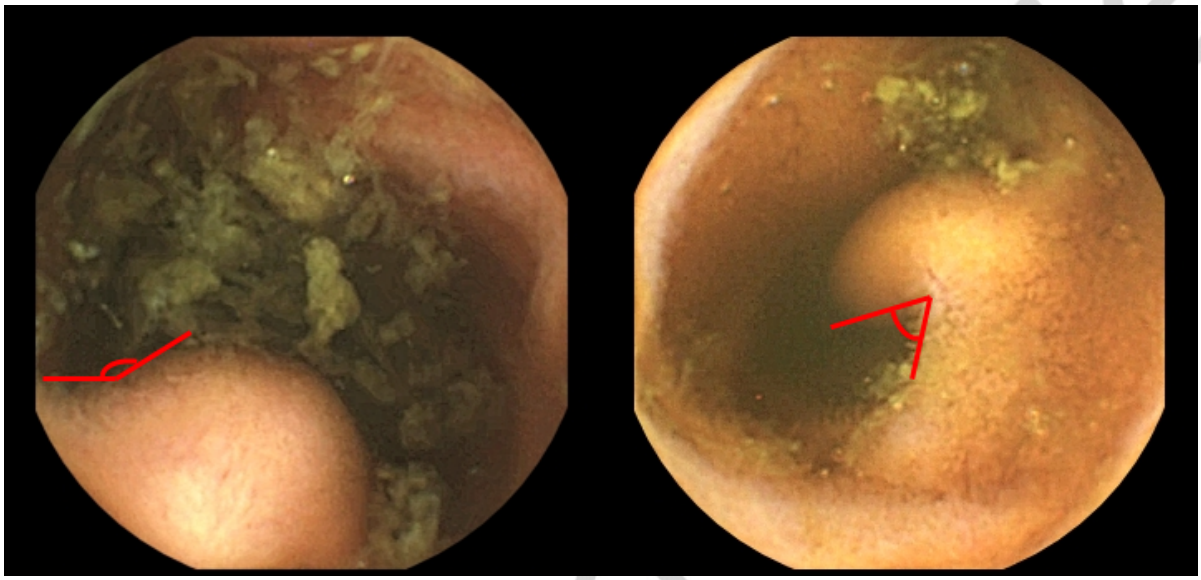

Figure 1 – Angle measurement

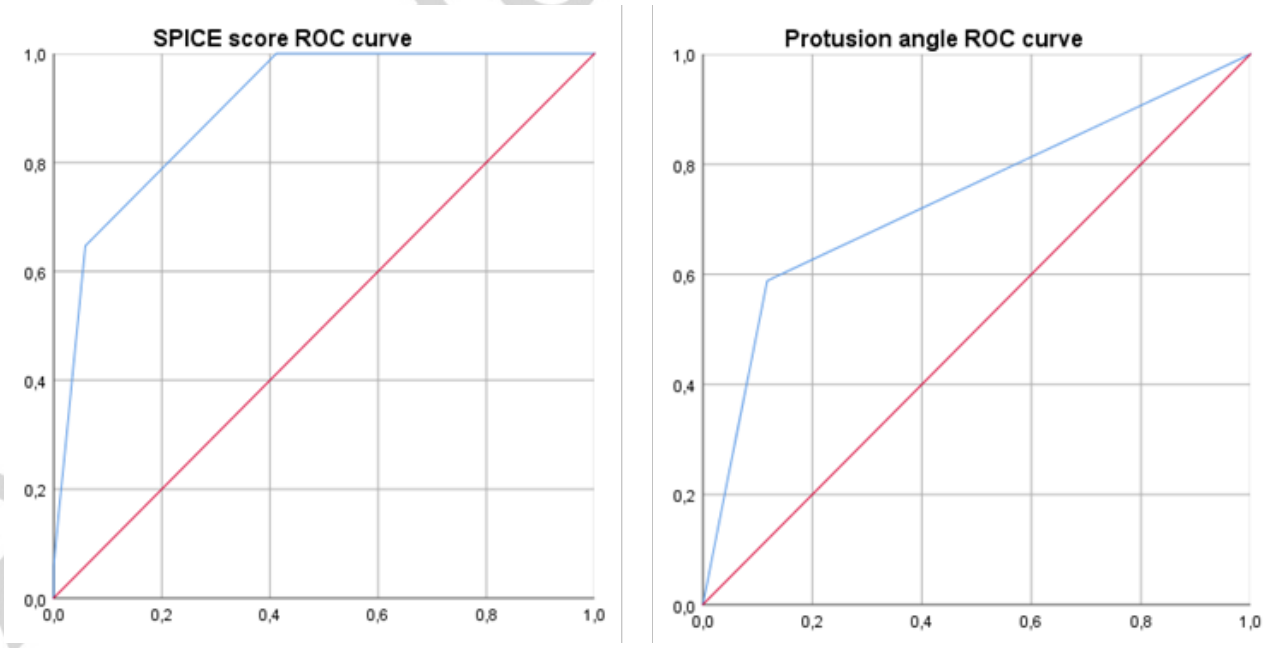

Figure 2 – ROC curves for the SPICE and mucosal protrusion scores