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Authors:
Cátia Arieira, Francisca Dias de Castro, Pedro Boal Carvalho, Bruno Rosa, Maria João Moreira, José Cotter

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Small Bowel Transit Time in Capsule Endoscopy: a determinant factor for the diagnosis of small bowel bleeding

Arieira C.[1,2,3], Dias de Castro F.[1,2,3], Boal Carvalho P.[1,2,3], Rosa B.[1,2,3], Moreira MJ.[1,2,3], Cotter J.[1,2,3]

[1] Gastroenterology Department. Hospital da Senhora da Oliveira. Guimarães. Portugal

[2] Life and Health Sciences Research Institute. School of Medicine. University of Minho. Braga/Guimarães. Portugal

[3] ICVS/3B's. PT Government Associate Laboratory. Braga/Guimarães. Portugal

Correspondence: catia_arieira@hotmail.com

Hospital da Senhora da Oliveira, Guimarães, Portugal

Rua dos Cutileiros, Creixomil. 4835-044 Guimarães

ABSTRACT

Background

Small bowel capsule endoscopy (SBCE) is the gold standard in the study of small bowel bleeding (SBB). Recent studies suggested that longer small bowel transit times (SBTT) may be associated with higher diagnostic yield of SBCE..

Aim

The aim of the study is to investigate if longer SBTT is a predictive factor of positive findings on SBCE in a population that performed SBCE due to suspected SBB.

Methods

Retrospective single-center study, including consecutive SBCE between May 2012 and May 2019 due to suspected SBB. Positive SBCE was considered in the presence of lesions with high bleeding potential, such as ulcers, angioectasias and tumors (P2 lesions, according to the Saurin classification).

Results

We included 372 patients, 65.9 % female, with median age 67 (IQR: 19-97) years.

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We observed that patients with P2 lesions (n=131; 35.2 %) in SBCE presented longer SBTT (p=0.01), were older (p<0.001), more frequently male (p=0.019), suffered more frequently from arterial hypertension (p=0.011), diabetes (p=0.042), chronic kidney disease (p=0.003) and heart failure (p=0.001). In logistic analysis, the significant predictive factors for the presence of P2 lesions were age (OR1.027;IC 95 % 1.009-1.045;p=0.004), SBTT (OR1.002; IC95 % 1.001-1.005; p=0.029) and male gender (OR 1.588;IC95 %1.001-2.534;p=0.049).

Conclusions

Patients with longer SBTT presented higher rates of lesions with high bleeding potential (P2). SBTT along with previous well defined factors–age and male gender were the only independent predictor factors of the presence of P2 lesions. These findings may suggest that slower passage of the capsule in the small bowel may allow a better diagnostic yield for significant lesions.

Keywords

Capsule endoscopy; small intestine

BACKGROUND

Small Bowel Bleeding (SBB) accounts for 5 % of all intestinal bleeding and its source is defined as distal to the ampulla of Vater and proximal to the ileocecal valve.[1] Since 2001, small bowel capsule endoscopy (SBCE) constitutes the gold standard investigation for SBB.[1,2] It is a noninvasive tool with a direct visualization of the entire small bowel mucosa, with excellent diagnostic yield and high negative predictive value (83–100 %).[1] This tool can be used as a screening method in the identification of bleeding lesions, with the ability to guide future therapeutic endoscopic approaches, such as device assisted enteroscopy.[1,2]

Several small bowel lesions may be responsible for SBB, most commonly vascular lesions, predominantly angioectasias, while other sources include inflammation from Crohn's disease, nonsteroidal (NSAID) enteropathy, tumors, Meckel's diverticula and other rare etiologies.[3]

The diagnostic yield of SBCE may be influenced by multiple factors, with a higher likelihood of positive findings in patients with older age (>65 years), overt bleeding, anticoagulant,

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antiplatelet or non-steroidal anti-inflammatory drugs (NSAID) use, higher transfusion requirements and with chronic comorbidities such as dyslipidemia and hypertension.[4-7]

Recently, small-bowel transit time (SBTT) was pointed as a factor associated with the diagnostic yield of significant lesions in SBB.[8-10] Incomplete SBCE evaluation may impair the diagnostic yield and factors such as hospitalization, previous surgery or radiation, diabetes mellitus and very old age have been identified as potential risk factors. The combined strategy of checking the position of SBCE with real time viewer and the selective administration of prokinetics has been adopted to overcome this limitation.[11]

The aim of the study is to investigate if longer SBTT is a predictive factor of positive significant findings on SBCE in a population that performed SBCE due to suspected SBB.

METHODS

This study was a single-center retrospective study. All patients referred to our center for SBCE for suspected SBB between May 2012 and May 2019 were reviewed. SBB was characterized as overt in the presence of melena or hematochezia or as occult if manifested as iron deficiency anemia or as a positive fecal occult blood test.

All patients underwent nondiagnostic esophagogastroduodenoscopy and total colonoscopy with adequate bowel preparation prior to SBCE. Furthermore, women were evaluated to exclude abnormal gynecological bleeding. Patients' clinical information was collected from medical records, including gender, age, presentation (overt vs. occult) of SBB and comorbidities, namely hypertension, dyslipidemia, diabetes, chronic kidney disease, heart failure and medical therapy.

SBCE procedure

SBCE was performed using PillCam® SB2 and SB3 (Given® Imaging Ltd. Yoqneam, Israel).

Patients that performed SBCE between May 2012 and February 2018, underwent a 24 h clear liquid diet and 12 h fasting prior to SBCE and were advised not to eat for 4 h after swallowing the capsule – Protocol A. From February 2018 and May 2019, patients followed a 24 h clear liquid diet and 12 h fasting prior to SBCE and 1L of Moviprep® was administered after real time confirmation of SBCE arrival at small bowel –Protocol B. For all procedures, patients were given 100 mg of Simethicone 30 min before capsule ingestion and 1 h after

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ingestion they returned to our unit for real time visualization using the real time viewer; at this point, if the capsule remained in the stomach, the patient was given 10 mg of oral Domperidone. Thirty minutes after prokinetic administration, if the capsule remained in the stomach, it was placed into the duodenum by upper gastrointestinal endoscopy.

Every patient that performed SBCE signed informed consent and all the data collected were coded to ensure anonymity. The ethical committee of Gastroenterology Department of Hospital da Senhora da Oliveira - Guimarães approved the study.

Exclusion criteria

Patients with incomplete SBCE or inadequate small bowel preparation were excluded.

Inadequate small bowel preparation was defined if the mucosa could be observed in < 50 % of the recording time with the presence of significant amounts of fluid, bubbles or debris that compromised the interpretation of the examination.[12]

Findings

Findings were classified using the Capsule Endoscopy Standard Terminology. Positive SBCE was considered in the presence of lesions with high potential bleeding, or luminal blood-P2, according to the Saurin classification.[13]

Small Bowel Transit time

SBTT was calculated in minutes and was defined as the time elapsed from the first frame of duodenal bulb to the first frame of the cecum.

Statistical Analysis

Statistical analysis was performed with SPSS®, version 22.0 (IBM, Armonk, New York, USA). The categorical variables are presented as frequencies and percentages, and continuous variables as means, medians, standard deviations and range. All reported p values are two tailed, with a p value inferior to 0.05 indicating statistical significance. The distribution of categorical variables between groups was evaluated by $\chi 2$-analysis and continuous variables by Mann Whitney U test.

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Multivariate analysis was performed using binomial regression to identify potential independent predictive factors of positive SBCE. Spearman's rank correlation coefficient was used to calculate the correlation between the factors that could influence SBTT. Receiver operating characteristic (ROC) analysis was performed to evaluate the performance of SBTT in predicting positive SBCE and Youden index was used to find the optimal cut off of SBTT.

RESULTS

Four hundred and seven patients performed SBCE during this period, 35 were excluded due to incomplete SBCE (n=24) or inadequate small bowel preparation (n=11). We included 372 patients, 65.9 % female with median age 67 (IQR: 19-97) years. From this population 16.4 % (n=61) performed SBCE during hospitalization. Regarding the type of small bowel preparation, 80.1 % (n=298) performed the protocol A and 19.9 % (n=74) the protocol B.

From this population, 79.3 % performed SBCE due to occult bleeding and 20.7 % overt bleeding and P2 lesions were present in 131 (35.2 %) patients. These patients presented a median SBTT of 267 (55-670) minutes.

Regarding patients with P2 lesions on SBCE, 85.5 % (n=112) presented angioectasias, 9.9 % (n=13) ulcerations, 3.8 % (n=5) tumors and 0.76 % (n=1) varices.

We observed that patients with P2 lesions in SBCE presented longer SBTT, were older, more frequently males, suffered more frequently from hypertension, diabetes, chronic kidney disease and heart failure. Concerning the presentation of SBB (occult vs overt), no differences were observed between the two groups. No differences were observed between patients under anticoagulants (p=0.598) and antiplatelet agents (p=0.553).

Regarding the factors that influence SBTT, we found a significant correlation between SBTT and age (rs 0.136;p=0.008) - Graph 1. SBCE with SBTT ≥ 321min presented higher rate of P2 lesions (47.0 % vs 29.8 %; p=0.001), with a Sensitivity of 41,98 % and Specificity 74,27 %. In Graph 2 we present the ROC curve of SBTT in predicting the presence of P2 lesion with AUROC of 0.581 (CI 95 % 0.52-0.642). Concerning, small bowel preparation, the administration of purgatives (Protocol B) did not influence the SBTT (median: 283 [86-619] versus 263[55-670] min; p=0.255), as well as gender (p=0.979) or the presence of diabetes (p=0.963), and the inpatient status (median: 279 [86-670] versus 261 [55-653] years; p<0.616), which also did not interfere with SBTT.

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In a logistic regression, the significant predictive factors of the presence of P2 lesions were age (p=0.004), SBTT (p=0.029) and male gender (p=0.049). Univariate and Logistic regression are presented in Table 1.

DISCUSSION

Over the years several studies have assessed risk factors associated with positive SBCE in SBB. Older age, overt bleeding, anticoagulant use, antiplatelet use, NSAID use, lower hemoglobin, higher transfusion requirements and patients with chronic comorbidities such as chronic kidney disease, dyslipidemia and hypertension are associated with higher diagnostic yield in SBB.[4-7]

Recent investigation have hypothesized that longer SBTT could be a factor associated with higher rates of lesion detection in SBB.[8-10]

In our cohort, in univariate analysis we found in accordance to previous studies that older patients, male gender, and with chronic comorbidities such as hypertension, diabetes, CKD and HF presented more frequently with P2 lesions in SBCE. [4-7] Moreover, in our study, patients with P2 lesions in SBCE presented longer SBTT, suggesting that slower passage of the capsule in the small bowel allows for a better inspection of the small bowel mucosa and it is associated with higher diagnostic yield for significant lesions.[8]

Furthermore, beyond male gender and older age, in logistic regression, SBTT constitutes an independent predictor factor of the presence of P2 lesions. In addition, older patients presented a longer SBTT, likely due to the reduced motility that occurs with aging, which partially explains the higher diagnostic yield of P2 lesions in this population, being is in line with previous series.[8,14]

In accordance to our results, Girelli C. et al found that longer SBTT along with older age were associated with higher rates of P2 lesions.[8] Blanco-Velasco and coworkers suggested that SBTT ≥4 hours were associated with an improved diagnostic yield with a odds ratio of 3.13.[10]

Despite Egea-Valenzuela J. et al having found a positive correlation between prolonged SBTT and higher diagnostic yield of SBCE, this study included all types of indication for SBCE and not only SBB.[9] Oppositely, Velayos Jiménez B et al. found no differences in SBTT with regard to age, gender or body mass index, despite this study being limited by sample size (n=89) and younger mean age of the patients (59.20 ±17.27). [15]

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Regarding the presence of comorbidities, a study of 29 patients found that diabetics had a prolonged gastric transit time and shorter SBTT, however in our study we did not find such association, and the SBTT did not correlated with the diabetes status.[16] This finding may be explained by our preparation protocol which includes the administration of prokinetics to overcome the long standing of SBCE in the stomach.

Some authors raised the question about the use of prokinetics and purgatives during the SBCE, since, in theory, some of those products may reduce the SBTT and consequently impact the diagnostic yield. [8]

Adler et al presented conflicting results regarding the use of small bowel preparation, and using a post-ingestion purge-based cleansing protocol (Picolax®) found a better visibility of the small bowel, however with a shorter SBTT.[17] On the contrary, in our study and in accordance to a previous study of our center, the administration of bowel preparation (PEG 1L) did not shorten the SBTT, having no influence on diagnostic yield.[18]

Additionally, several authors reported that inpatient status is inversely correlated with completion rate of SBCE mainly because hospitalized patients represent a population with reduced mobility and overall health.[19-21] Notably, in our study we did not find significant longer SBTT in hospitalized patients and it could be explained due to a population selection bias since we excluded patients with incomplete SBCE.

Regarding study limitations, this is a retrospective study, and we were unable to identify the proportion of patients who needed prokinetic administration during the procedure and, therefore, we cannot compare the SBTT between these groups. Even though, a previous study from our group found that the selective administration of prokinetics namely domperidone guided by the position of capsule in real-time viewer is a valid approach towards reducing incomplete examinations, with no effect on SBTT or diagnostic yield.[11]

In conclusion, we found that longer SBTT in SBB is independently associated with higher diagnostic yield, namely in the identification of lesions with higher potential bleeding. Age is the main determinant influencing the SBTT. It does not seem to be influenced by prokinetics or purgative solutions, which therefore can be safely used increasing the proportion of complete examinations and the quality of the small bowel preparation, while not compromising the SBTT and consequently the diagnostic yield of SBCE in patients presenting with SBB.

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AUTHOR CONTRIBUTIONS

Arieira C. and Dias de Castro F. designed the study, interpreted the data ar
manuscript.

Arieira C., Boal Carvalho P., Rosa B. and Moreira MJ reviewed the small b
endoscopies.

Arieira C. participated on the acquisition of data and performed the statistica

Dias de Castro F., Boal Carvalho P., Rosa B. and Moreira MJ. critically
manuscript.

Cotter J. critically revised and approved the final version of the manuscript.

DISCLOSURES

Rosa B. has consulting services agreement with Medtronic®.

Other authors have no conflict of interest to declare.

REFERENCES

1. Gerson LB, Fidler JL, Cave DR, Leighton JA. ACG Clinical Guideline: Diagnosis and Management of Small Bowel Bleeding. Am J Gastroenterol 2015;110:1265-87; quiz 88.

2. Rondonotti E, Spada C, Adler S, et al. Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Technical Review. Endoscopy 2018;50:423-46.

3. Gunjan D, Sharma V, Rana SS, Bhasin DK. Small bowel bleeding: a comprehensive review. Gastroenterol Rep (Oxf) 2014;2:262-75.

4. Boal Carvalho P, Rosa B, Moreira MJ, Cotter J. New evidence on the impact of antithrombotics in patients submitted to small bowel capsule endoscopy for the evaluation of obscure gastrointestinal bleeding. Gastroenterol Res Pract 2014;2014:709217.

5. Cúrdia Gonçalves T MJ, Boal Carvalho P, Moreira MJ, Rosa B, Cotter Is It Possible to Predict the Presence of Intestinal Angioectasias? Diagn Ther Endosc 2014;461602.

6. Katsinelos P, Kountouras J, Chatzimavroudis G, et al. Factors predicting a positive capsule endoscopy in past overt obscure gastrointestinal bleeding: a multicenter

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retrospective study. Hippokratia 2016;20:127-32.

7. Ribeiro I, Pinho R, Rodrigues A, Marques J, Fernandes C, Carvalho J. Obscure gastrointestinal bleeding: Which factors are associated with positive capsule endoscopy findings? Rev Esp Enferm Dig 2015;107:334-9.

8. Girelli CM, Soncini M, Rondonotti E. Implications of small-bowel transit time in the detection rate of capsule endoscopy: A multivariable multicenter study of patients with obscure gastrointestinal bleeding. World J Gastroenterol 2017;23:697-702.

9. Egea Valenzuela J, Sanchez Martinez A, Garcia Marin AV, Alberca de Las Parras F. Influence of demographic and clinical features of the patient on transit times and impact the on the diagnostic yield of capsule endoscopy. Rev Esp Enferm Dig 2019;111:530-6.

10. Blanco Velasco G PRM, Álvarez Licona NE. Small bowel transit time of capsule endoscopy as a factor for the detection of lesions in potential small bowel bleeding. Rev Esp Enferm Dig 2019;111(9):696-8.

11. Cotter J, de Castro FD, Magalhaes J, Moreira MJ, Rosa B. Finding the solution for incomplete small bowel capsule endoscopy. World J Gastrointest Endosc 2013;5:595-9.

12. Rosa BJ, Barbosa M, Magalhaes J, Rebelo A, Moreira MJ, Cotter J. Oral purgative and simethicone before small bowel capsule endoscopy. World J Gastrointest Endosc 2013;5:67-73.

13. Saurin JC, Delvaux M, Gaudin JL, et al. Diagnostic value of endoscopic capsule in patients with obscure digestive bleeding: blinded comparison with video push-enteroscopy. Endoscopy 2003;35:576-84.

14. Fireman Z, Kopelman Y, Friedman S, et al. Age and indication for referral to capsule endoscopy significantly affect small bowel transit times: the given database. Dig Dis Sci 2007;52:2884-7.

15. Velayos Jiménez B FSL, Aller de la Fuente R, de la Calle Valverde F, Del Olmo Martínez L, Arranz Santos T, González Hernández J. Study of gastronitestinal transit times with capsule endoscopy. Gastroenterol Hepatol 2005;28(6):315-20.

16. Triantafyllou K, Kalantzis C, Papadopoulos AA, et al. Video-capsule endoscopy gastric and small bowel transit time and completeness of the examination in patients with diabetes mellitus. Dig Liver Dis 2007;39:575-80.

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17. Adler SN, Farkash S, Sompolinsky Y, Gafanovich I, Goldin E, Bar-Gil Shitrit A. A novel purgative protocol for capsule endoscopy of the small bowel produces better quality of visibility than 2 l of PEG: Timing is of the essence. United European Gastroenterol J 2017;5:485-90.

18. Xavier S, Rosa B, Monteiro S, et al. Bowel preparation for small bowel capsule endoscopy - The later, the better! Dig Liver Dis 2019;51:1388-91.

19. Yazici C, Losurdo J, Brown MD, et al. Inpatient capsule endoscopy leads to frequent incomplete small bowel examinations. World J Gastroenterol 2012;18:5051-7.

20. Westerhof J, Weersma RK, Koornstra JJ. Risk factors for incomplete small-bowel capsule endoscopy. Gastrointest Endosc 2009;69:74-80.

21. Robinson CA, Jackson C, Condon D, Gerson LB. Impact of inpatient status and gender on small-bowel capsule endoscopy findings. Gastrointest Endosc 2011;74:1061-6.

Table 1. Factors associated with positive SBCE (P2 lesions)

	univariate analysis			**binomial regression**		
	P2 lesions	**no P2 lesions**	**p**	**OR**	**IC 95%**	**p**
SBTT (min)	295	256	**0.01***	1.002	1.001-1.005	**0.029***
Age	73.0	60.0	**<0.001 ***	1.027	1.009-1.045	**0.004***
Male Gender	42.0%	29.9%	**0.019***	1.588	1.001-2.534	**0.049***
Hypertension	69.5%	56.0%	**0.011***			*0.399*
Diabetes	38.2%	28.6%	**0.042***			*0.712*
CKD	34.4%	20.3%	**0.003***			*0.245*
HF	38.2%	21.6%	**0.001***			*0.369*
Overt vs Occult	44.2%	32.9%	0.065	---	-----	----
Anticoagulants	21.4%	19.1%	0.598	---	-----	----
Antiplatelets	35.1%	32.1%	0.553	---	-----	----

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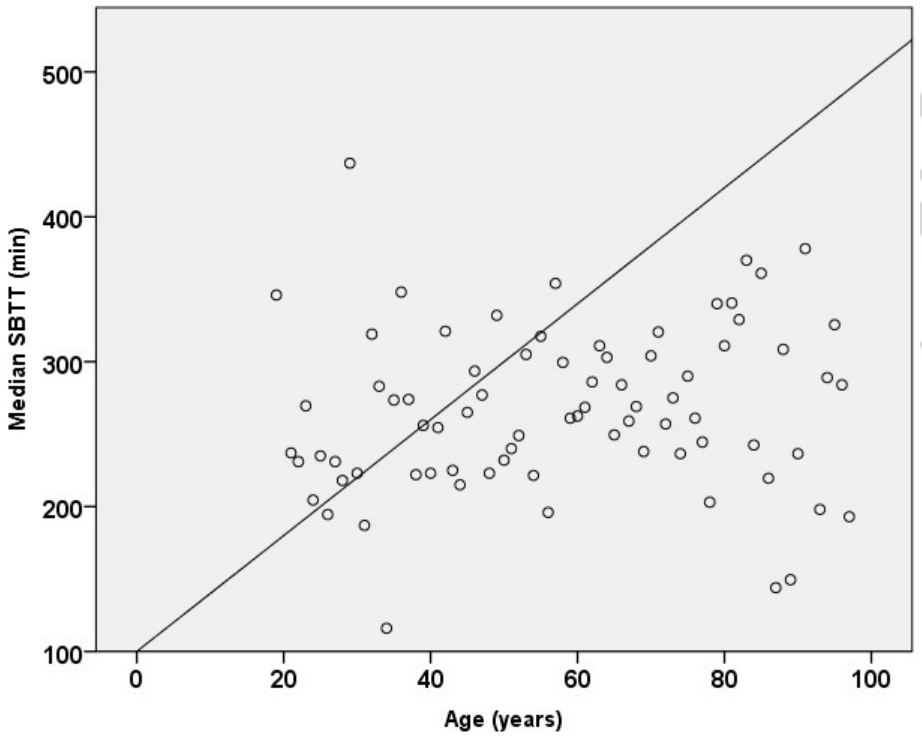

Figure 1. Spearman's correlation between SBTT (min) and Age (years).

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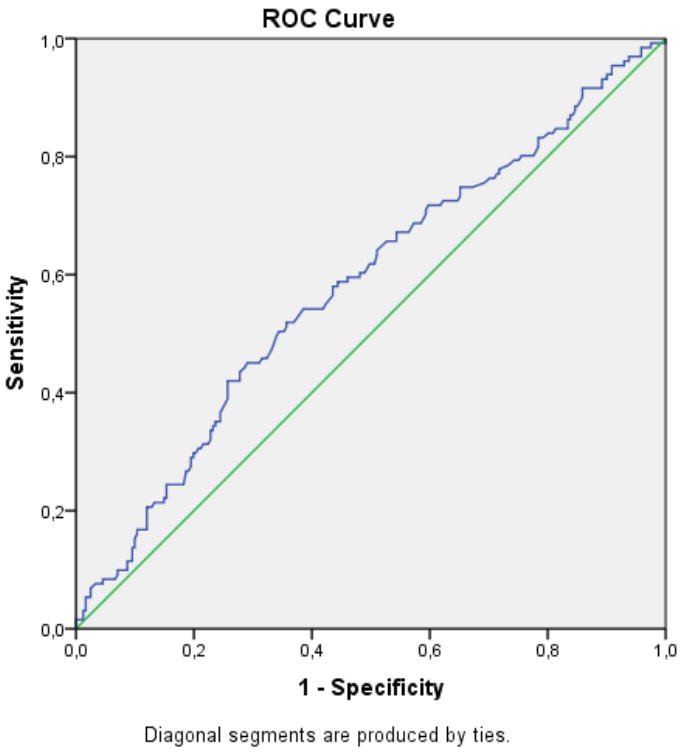

Figure 2. ROC curve of SBTT in predicting the presence of P2 lesions; AUROC=0.581; Cut Off=321min; Sensitivity 41.98 %; Specificity 74.27 %

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