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Diagnostic accuracy of one sample or two samples quantitative fecal immunochemical tests for intestinal neoplasia detection

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ABSTRACT – **Background** – Rectal bleeding is the most important symptom of intestinal neoplasia; thus, tests of occult blood detection in stools are widely used for pre neoplastic lesions and colorectal cancer (CRC) screening. **Objective** – Evaluate the accuracy of OC-Sensor quantitative test (Eiken Chemical, Tokyo, Japan) at cut-off 10 µg Hb/g feces (50 ng/mL) in a cohort of subjects that had to undergo diagnostic colonoscopy, and if more than one sample collected in consecutive days would improve the diagnostic accuracy of the test. **Methods** – Patients (mean age 56.3±9.7 years) that underwent colonoscopy prospectively randomly received one (1-sample FIT, FIT 1) or two (2-sample FIT, FIT 2) collection tubes. They collected the stool sample before starting colonoscopy preparation. Samples were analyzed by the OC-Auto Micro 80 (Eiken Chemical, Tokyo, Japan). The performance of FIT 1 and FIT 2 were compared to the colonoscopy findings. **Results** – Among 289 patients, CRC was diagnosed in 14 (4.8%), advanced adenoma in 37 (12.8%), early adenoma in 71 (24.6%) and no abnormalities in 141 (48.8%). For FIT 1, the sensitivity for CRC was 83.3% (95%CI 36.5–99.1%), for advanced adenoma was 24% (95%CI 10.1-45.5%), with specificity of 86.9% (95%CI 77.3–92.9%). For FIT 2, the sensitivity for CRC was 75% (95%CI 35.6–95.5%), for advanced adenoma was 50% (95%CI 22.3–77.7%), with specificity of 92.9% (95%CI 82.2–97.7%). The positive likelihood ratios were 1.8 (95%CI 0.7–4.4 for FIT 1) and 7.1 (95%CI 2.4–21.4 for FIT 2) for advanced adenoma, and 6.4 (95%CI 3.3–12.3, for FIT 1) and 10.7 (95%CI 3.8–29.8, for FIT 2) for CRC. The negative likelihood ratio were 0.9 (95%CI 0.7–1, for FIT 1) and 0.5 (95%CI 0.3–0.9, for FIT 2) for advanced adenoma, and 0.2 (0.03–1.1, for FIT 1) and 0.3 (0.08–0.9, for FIT 2) for CRC. The differences between FIT 1 and FIT 2 performances were not significant. However, the comparison of the levels of hemoglobin in feces of patients of FIT 1 and FIT 2 showed that the differences between no polyp group and advanced adenoma and CRC were significant. **Conclusion** – The accuracy of OCR Sensor with 10 µg Hb/g feces cut-off was comparable to other reports and two-sample collection improved the detection rate of advanced adenoma, a pre neoplastic condition to prevent CRC incidence.

HEADINGS – Colorectal neoplasms, diagnosis. Intestinal polyps. Predictive value of tests. Occult blood. Colonoscopy.

INTRODUCTION

In 2018 in Brazil 36,360 new cases of colorectal (CRC) cancer were diagnosed, being 17,380 in men and 18,980 in women, and 16,697 deaths caused by CRC, being 8,163 of men and 8,533 of women (https://www.inca.gov.br/tipos-de-cancer/cancer-de-intestino). Bowel symptoms of constipation, diarrhea or abdominal pain had no significant association with CRC or precancerous polyps, in contrast, rectal bleeding and weight loss were mostly associated with CRC, and only rectal bleeding was associated with precancerous polyps[1]. Thus, positive detection of fecal occult blood would be, mostly indicated, to select patients for colonoscopy[1] for early detection of advanced adenoma to prevent CRC development[2].

Initially, the tests were an indirect measure of blood on the stools, based on the colorimetric assay of peroxidase activity of the hemoglobin, named guaiac test, but also using "in-house" solution of toluidine. Presence of peroxidase activity in foods and the necessity of a diet at least three days before stool collection, and the small amount of bleeding by polyps (52.7–71.9 ng Hb/mL) and cancer (86.6 ng Hb/mL)[3] restricted their use, due to a lack of sensitivity and specificity[3-5]. Although, guaiac-based fecal tests reduced mortality, detecting early neoplastic lesions, and if only guaiac test is available, is preferable to do the test for CRC screening than doing nothing[6].

The development of fecal immunochemical tests (FITs) with polyclonal or monoclonal antibodies against human hemoglobin showed promising results with higher sensitivity and specificity than the chemical test[3-7]. FITs may be qualitative immunochromatographic with a visual reading, and pre-determined detection limit that varies from 25 ng/mL to 50 ng/mL, declared by the manufacturer, usually with similar performances[4]. However, other studies observed great variability, comparing the performance of six different qualitative FITs, when the sensitivity was highest, specificity was lowest, and vice versa[2]. Probably, due to the different detection limits that are fixed in the qualitative test.

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Several brands of quantitative FITs that measures the hemoglobin concentration with preset threshold that stratifies the positive cases are available on the market. The most important advantage of quantitative tests is to adjust the threshold of hemoglobin concentration that defines positive tests. In fact, the comparison of nine different quantitative FITs showed that adjusting the cutoff would overcome the heterogeneity amongst them[8]. At preset cutoff 15µg hemoglobin/g feces, two quantitative FITs: FOB-Gold (Sentinel, Milan, Italy) and OC-Sensor (Eiken Chemical, Tokyo, Japan), had similar accuracy to detect advanced adenoma, precursor of CRC[9]. Another issue to be considered is the number of fecal samples collected. The collection of two samples in consecutive days improved the diagnostic outcome with no effect on attendance[10]. Although bleeding is the main symptom of advanced neoplasia[1] and immunochemical test is far too superior to guaiac[4,5], neoplasia may not bleed every day, then bleeding may be missed with one sample collection[10].

Thus, the purpose of this study was to evaluate the accuracy of one quantitative test: OC-Sensor (Eiken Chemical, Tokyo, Japan) in a cohort of subjects that had to undergo diagnostic colonoscopy at cut-off 10 µg Hb/g feces, and if more than one sample collected in consecutive days would improve the diagnostic accuracy of the test.

METHODS

Study population

Patients that attended the Gastrointestinal Endoscopy Division from January 2015 to December 2016 to undergo colonoscopy for diagnostic purpose, were invited to participate. Patients randomly received one (1-sample FIT) or two (2-sample FIT) collection tubes and had to collect the stool sample before starting colonoscopy preparation of the same bowel movement. The two-sample collections were one sample per FIT of two bowel movements on consecutive days. Among 474 that were invited, 333 brought the stool samples the day that underwent colonoscopy, forty-four were excluded due to: colectomy (n=5), inadequate bowel preparation (n=4), incomplete colonoscopy (n=6), colon stenosis (n=2), and twenty-seven inflammatory bowel disease. 289 were eligible for the study, 172 one-sample FIT and 117 two-sample FIT (FIGURE 1). The mean age was 56.3±9.7 years and range of 27 to 77 years, 191 (66.1%) were women.

Ethical statement

Ethics Committee of the Hospital approved this study protocol through http://plataformabrasil.saude.gov.br. Patients gave written informed consent to participate.

OCR FIT test

According to the manufacturer the sample collection tube may be stored at room temperature for 7 days. Patients were instructed to keep the sample collection tube at room temperature, and after delivering to the lab on the same day of colonoscopy, the samples were analyzed using the OC-Auto Micro 80 (Eiken Chemical, Tokyo, Japan). The calibration curve was performed every 15 days. The test was considered positive at ≥50 ng Hb/mL (10µg Hb/g feces), and for 2-sample FIT if one sample tested positive, was considered positive.

Colonoscopy

Colonoscopy was performed according to the routine of the Gastrointestinal Endoscopy Division. Patients were instructed to cleanse the colon with bisacodyl the day before the exam and 1 liter of oral 10% mannitol solution 4 hours before the exam. The quality of the bowel preparation was assessed using the Boston Preparation Score (BBPS) and a score of 6 or more was considered adequate preparation and the patient was excluded if the BBPS scale was <6[11]. The colonoscopes used were high definition Olympus CF-H180 (Olympus Optical, Tokyo, Japan) and Fujinon EC 590 (Fujifilm Co., Tokyo, Japan). Sedation with intravenous midazolam, fentanyl and propofol was used for all the patients, and the dose was titrated according to each patient. After cecal intubation, the colonoscope was withdrawn, and the mucosa was carefully evaluated. The duration time of colonoscope withdrawal was longer than 6 minutes, regardless of the time of therapeutic procedures. All polyps were removed and sent for histological analysis. The polyp size measurement was based on opened biopsy forceps (7mm in diameter), and classified according to the size: <5 mm, 5–9 mm and ≥10 mm. The right-sided polyp was defined when its location was proximal to the splenic flexure and the left-sided polyp when distal to the splenic flexure.

Histological examination

Colon removed lesions were fixed in 10% formalin, stained with hematoxylin and eosin, and assessed by two pathologists for histo-

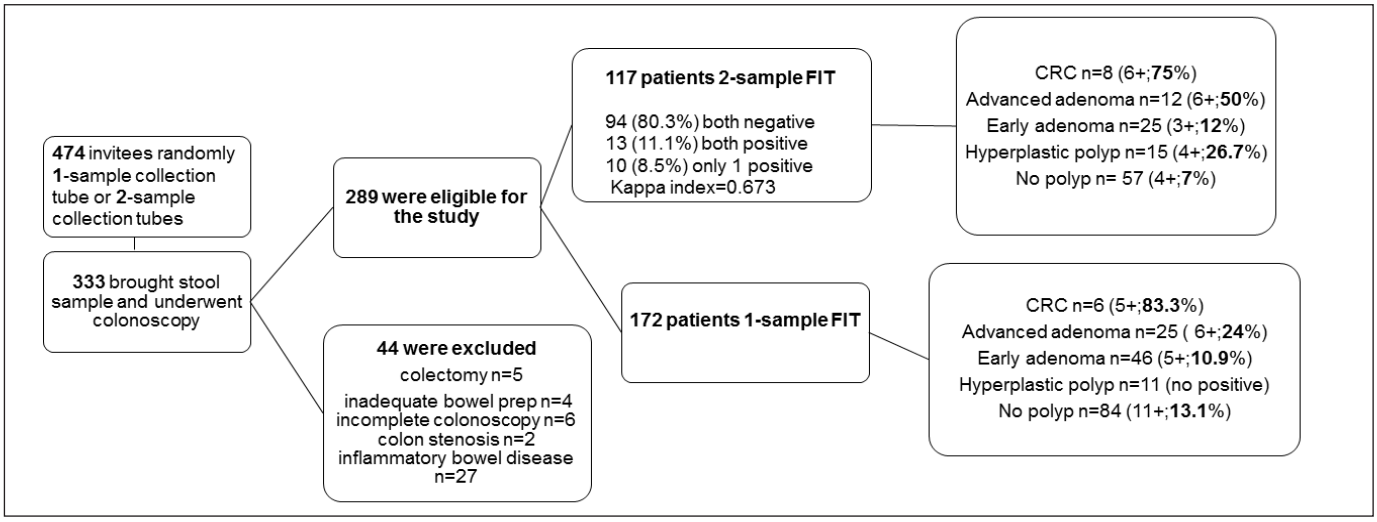

FIGURE 1. Flow diagram of the diagnostic accuracy of FIT for CRC screening.

logical diagnosis. According to the WHO classification of tumours of the colon and rectum[12], the biopsies were stratified as no polyp, serrated polyp (hyperplastic polyp, serrated adenoma), adenoma (tubular, tubulovillous, or villous), or adenocarcinoma. Dysplasia was defined as low grade or high grade. Early adenoma was defined as tubular with size <10 mm and low-grade dysplasia. Advanced adenoma was defined as either large (with size ≥10 mm), villous, tubulovillous (>25% villous) or high-grade dysplasia. Advanced neoplasia included advanced adenoma and adenocarcinoma.

Statistical analyses

The statistical analysis was performed with IBM SPSS 25 (Statistical Package for the Social Sciences) and Excel 2010® (Microsoft Office). Descriptive statistics characterized the findings of colonoscopy and the study patients. Sensitivity, specificity, positive predictive value, negative predictive value, and positive and negative likelihood ratios with 95% confidence interval (95%CI) were calculated using an online program (http://vassarstats.net/). The Kolmogorov-Smirnov test evaluated the normality of the variables distribution. The associations of 1-sample FIT (FIT 1), 2-sample FIT (FIT 2), and the higher value FIT of the group FIT 2 and the findings of colonoscopy were performed by Kruskal-Wallis test, and the significant values adjusted by Bonferroni correction for multiples tests. All the statistical tests considered two-sided α of 0.05 and 95% confidence interval. In the present study, G* Power version 3.1.9.4 (Franz Faul, Universität Kiel, Germany) was used to for post hoc power analysis. The effect size was calculated with the means and standard deviations between the no polyp group with either hyperplastic polyp, early adenoma, advanced adenoma, and CRC for FIT 1, FIT 2 and higher value FIT. The result of effect size was transferred to main window to calculate power (1- β error probability) for each one of the analysis of the study by means: Wilcoxon-Mann Whitney test (two groups). The input parameters were the effect size d, α=0.05, sample size of group 1 and sample size of group 2 to calculate power for each one of the analysis. Results are reported in accordance with the Standards for the Reporting of Diagnostic accuracy studies (STARD) checklist (2015)[13].

RESULTS

Patients that were eligible for the study totalized the number of 289, with 172 in the 1-sample FIT and 117 in the 2-sample FIT group. The analysis of agreement between the results of 2-sample FIT showed that 94 (80.3%) patients had both FIT negative, 13 (11.1%) had both FIT positive and 10 (8.5%) had only one FIT positive, with a kappa index = 0.673 (substantial).The STARD flow diagram is depicted in FIGURE 1.

The endoscopic findings according to the size of the polypoid lesion, number of adenomas, location of polypoid lesion, and histological based diagnosis are depicted in TABLE 1. The comparisons according to the size and the number of polyps were not significant (Kruskal-Wallis test), TABLE 1.

In the advanced adenoma, FIT 1 had a sensitivity of 24% (95%CI: 10.1–45.5%) and FIT 2 of 50% (95%CI: 22.3–77.7%) with positive predictive value of 15.6% (95%CI: 9.6–24%) and 14.5% (7.5–25.5%), respectively. The negative predictive value was 84.4% (95%CI: 75.9–90.3 for FIT 1 and 85.5% (95%CI: 74.5–92.5%) for FIT 2. The positive likelihood ratio of FIT 1 was 1.8 (0.7–4.4) and of FIT 2 was 7.1 (2.4–21.4). The negative likelihood ratio was 0.9 (95%CI: 0.7–1) and 0.5 (95%CI: 0.3–0.9) for FIT 1 and FIT 2, respectively (TABLE 2).

TABLE 1. The findings of colonoscopy of 289 patients that entered the study.

Variables	Number	%	95%CI
Size of polyp (mm)			
Non-polypoid lesion	157	54.3%	48.6–60%
<5	69	23.9%	19.2–29%
5–9	43	14.9%	11.1–19.3%
≥10	20	6.9%	4.4–10.3%
Number of adenomas			
No adenoma	182	63.0%	57.3–68.4%
1–2	80	27.7%	22.8–33%
3 or more	27	9.3%	6.4–13.1%
Location of polyp			
Left-sided	61	41.8%	34–49.9%
Right-sided	61	41.8%	34–49.9%
Bilateral	24	16.4%	11.1–23.1%
Histology			
No polyp	141	48.8%	43.1–54.5%
Hyperplasic polyp	26	9.0%	6.1–12.7%
Early adenoma	71	24.6%	19.9–29.8%
Advanced adenoma	37	12.8%	9.3–17%
CRC	14	4.8%	2.8–7.8%

TABLE 2. The performance of FIT 1 and FIT2 (two samples, positive if either one was positive) for advanced adenoma, advanced neoplasia and CRC detection with 95% confidence interval.

Parameters	FIT 1	FIT 2
Sensitivity		
Advanced adenoma	24% (10.1–45.5%)	50% (22.3–77.7%)
Advanced neoplasia	35.5% (19.8-54.6%)	60% (36.4-80%)
CRC	83.3% (36.5–99.1%)	75% (35.6–95.5%)
Specificity	86.9% (77.3–92.9%)	92.9% (82.2–97.7%)
PPV		
Advanced adenoma	15.6% (9.6–24%)	14.5% (7.5–25.5%)
Advanced neoplasia	19.1% (12.6-27.7%)	20.8% (12.7-31.8%)
CRC	17.8% (10.8–27.5%)	15.4 (8–26.9%)
NPV		
Advanced adenoma	84.4% (75.9–90.3%)	85.5% (74.5–92.5%)
Advanced neoplasia	80.9% (72.2-87.3%)	79.2% (68.1-87.3%)
CRC	82.2% (72.4–89.2%)	84.6 (73–91.9%)
+ Likelihood ratio		
Advanced adenoma	1.8 (0.7–4.4)	7.1 (2.4–21.4)
Advanced neoplasia	2.7 (1.3-5.6)	8.6 (3.1-23.5)
CRC	6.4 (3.3–12.3)	10.7 (3.8–29.8)
Negative Likelihood ratio		
Advanced adenoma	0.9 (0.7–1)	0.5 (0.3–0.9)
Advanced neoplasia	0.7 (0.6-1)	0.4 (0.2-0.7)
CRC	0.2 (0.03–1.1)	0.3 (0.08–0.9)

In the CRC, FIT 1 had a sensitivity of 83.3% (95%CI: 36.5–99.1%) and FIT 2 of 75% (95%CI: 35.6–95.5%) with positive predictive value of 17.8% (95%CI: 10.8–27.5%) and 15.4 (95%CI: 8–26.9%), respectively. The negative predictive value was 82.2% (95%CI: 72.4–89.2%) for FIT 1 and 84.6 (95%CI: 73–91.9%) for FIT 2. The positive likelihood ratio of FIT 1 was 6.4 (95%CI: 3.3–12.3) and of FIT 2 was 10.7 (95%CI: 3.8–29.8). The negative likelihood ratio was 0.2 (95%CI: 0.03–1.1) and 0.3 (95%CI: 0.08–0.9) for FIT 1 and FIT 2, respectively. The specificity was 86.9% (95%CI: 77.3–92.9%) and 92.9% (95%CI: 82.2–97.7%) for FIT 1 and FIT 2, respectively.

The performance of FIT 1 and FIT 2, considering advanced adenoma and CRC altogether as advanced neoplasia, is depicted in TABLE 2. The comparison of the performance of FIT 1 and FIT 2 to indicate advanced adenoma, advanced neoplasia and CRC were not significant (TABLE 2).

The comparison of the levels of hemoglobin in feces of patients of FIT 1 according to the colonoscopy findings showed that the differences between no polyp group and advanced adenoma and among CRC and all the other groups were significant (FIGURE 2).

The comparison of the levels of hemoglobin in feces of patients of FIT 2 according to the colonoscopy findings showed that the differences between hyperplastic polyp and advanced adenoma, and among CRC, no polyp and hyperplastic polyp were significant (FIGURE 3).

The comparison of the levels of hemoglobin in feces of patients of FIT 2, considering the higher value FIT, according to the colonoscopy findings showed that the differences among CRC and all the other groups were significant (FIGURE 4). The post hoc power analysis of FIT 1, FIT 2 and higher value FIT showed that power 1-β err probability was high (0.99, 0.94, 0.99, respectively) only for CRC.

DISCUSSION

The importance of occult blood in stools, indicating the presence of a serious disorder in the gastrointestinal tract, usually cancer[14], dates back to the beginning of the 20th century[15]. The chemical tests by guaiac and benzidine for occult blood detection considered the simplest among the other options had a relative specificity and sensitivity[15]. These assays depend upon the peroxidase like activity of heme of hemoglobin and hydrogen peroxide (the developer) to oxidize some chromogenic substances, yielding a color[15]. The addition of an enhancer to the developer to detect low levels of peroxidase improved the high-sensitive guaiac fecal occult blood tests; however, some immunochemical tests (FIT) had a better performance[16].

The basis of FIT is the reaction of monoclonal or polyclonal antibodies against the globin molecule of human hemoglobin. The assays may be qualitative by lateral-flow immunochromatography[2,4,5], or quantitative by immune-turbidimetry and ELISA[8,9,17]. In the qualitative test, a band of different intensities of color visually detected, resulting from the preset positive threshold designed by the manufacturer indicates two possible results: positive or negative[4]. Different from chemical tests[15], FITs had no interference from diet and medications[17]; however, globin may degrade easier at high temperatures than heme[18,19], turning out the winter the best season for CRC screening[19].

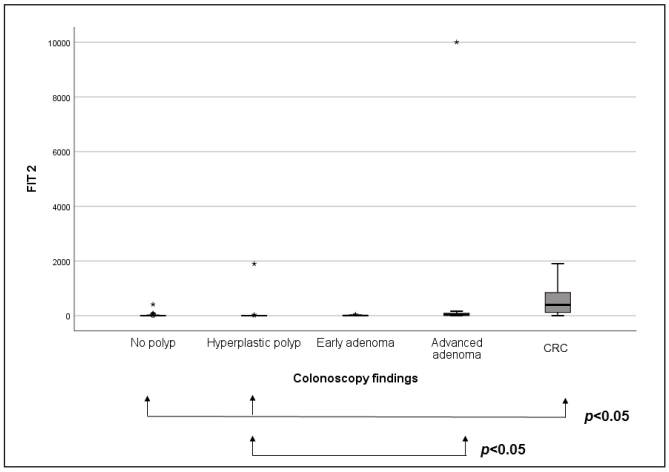

FIGURE 3. The levels of hemoglobin in feces of the patients of FIT 2 according to the colonoscopy findings. The boxes indicate 25–75% quartiles. The horizontal lines on the bottom of the figure indicate the comparisons of each group with one another that were significant (Kruskal-Wallis test).

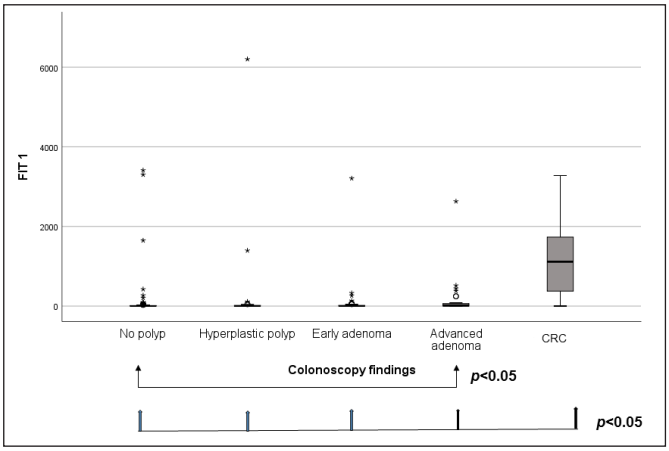

FIGURE 2. The levels of hemoglobin in feces of the patients of FIT 1 according to the colonoscopy findings. The boxes indicate 25–75% quartiles. The horizontal lines on the bottom of the figure indicate the comparisons of each group with one another that were significant (Kruskal-Wallis test).

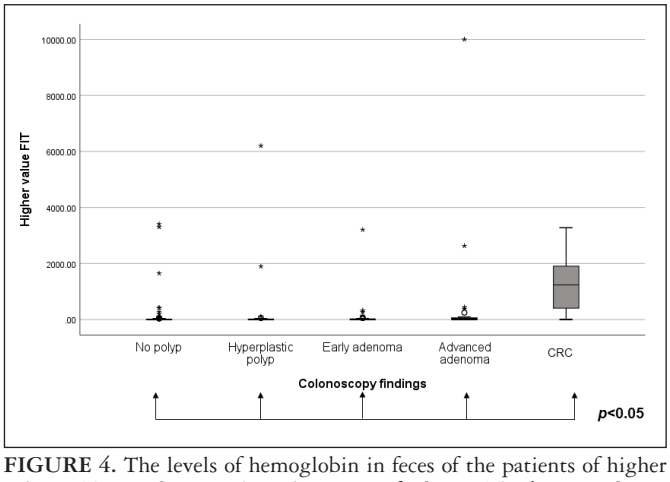

FIGURE 4. The levels of hemoglobin in feces of the patients of higher value FIT according to the colonoscopy findings. The boxes indicate 25–75% quartiles. The horizontal lines on the bottom of the figure indicate the comparisons of each group with one another that were significant (Kruskal-Wallis test).

In the light of that, Brazil is a tropical country with higher temperatures than the north continents; nonetheless, the qualitative FITs had similar performances and more sensitive than the chemical test, making qualitative FITs suitable for the clinical practice in spite of the weather[4]. In the present study, we sought to analyze the accuracy of a quantitative FIT (quantified by OC-Auto Micro 80), which principle is the immune reaction between hemoglobin and monoclonal anti-hemoglobin latex-adsorbed antibodies. The measure of optical absorbance of the turbid solution at 660 nm against a calibration curve indicating the concentration of hemoglobin[19]. The analysis was with predefined cut-off 10 µg Hb/g feces.

One of the advantages of the OC-Auto Micro 80 is the closed automated system, being the technique of choice at this time of SARS-CoV-2 threat. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that emerged in China at the end of 2019[20], spread worldwide, causing the COVID-19 pandemic disease with 257,405 confirmed deaths and 3,726,292 confirmed cases, involving 215 countries, areas or territories at this point (https://www.who.int/emergencies/diseases/novel-coronavirus-2019). Although the infection is characterized by respiratory symptoms, indicating droplet transmission, several cases presented gastrointestinal symptoms, suggesting another possible route the fecal-oral transmission. Patients had positive rectal swabs even after nasopharyngeal tests were negative[21]. OC-Auto Micro 80 is safe for the lab personnel, as there is no risk of aerosol transmission from patients' feces. The individual collects the stools in the sampling bottle, closes the bottle, delivers to the lab, a bar code is attached, and the closed sampling bottle is placed into the instrument where the needle of the probe perforates the sampling bottle, pipettes the sample, the reaction solutions, and after some minutes prints the result with the respective bar code.

The qualitative tests are less cumbersome, easier to handle, fast, and cheap; however, the samples of feces are opened inside the lab with the risk of aerosolization of the virus[22], and contamination of the lab personnel. The comparison of FIT of several brands: qualitative and quantitative showed that the overall sensitivity was not much different among them, with the quantitative tests offering the advantage of positive threshold flexibility[8,9,23]. Another advantage of OCR-Auto Micro 80 in comparison to ELISA, is the possibility of placing the sampling bottle inside the equipment and analyzing as quickly as they are delivered to the lab.

The most important value of screening CRC is to detect advanced adenoma, rather than CRC itself. The analysis of the performance of OCR quantitative test at cut-off 10 µg Hb/g showed that collecting two samples improved the sensitivity to indicate advanced adenoma, although not significant that was different from previously described[10]. Otherwise, the high specificity and negative predictive value for both advanced adenoma and CRC indicated that collecting two samples would not increase the number of unnecessary colonoscopies.

In accordance with other authors[24-27], most of the patients (48.8%; 95%CI: 43.1–54.5%) had no polyps or early (<10 mm) adenoma (24.6%; 95%CI: 19.9–29.8%). Taking into account the size of the polyp (≥10 mm), the prevalence in the present study (6.9%; 95%CI: 4.4–10.3%) was similar to that in non-Hispanic whites of the Eastern states in the US[28]. The prevalence of advanced adenoma in 12.8% (95%CI: 9.3–17%) was comparable to that described in Europeans of Amsterdam and Rotterdam regions[25] and among colonoscopy-referral patients of a Cancer Hospital in Brazil[26]. However, the prevalence of CRC (4.8%; 95%CI: 2.8–7.8%) was higher than previous reported in asymptomatic individuals of The Netherlands (0.6%)[25]; nonetheless, was comparable to that described in symptomatic patients of mid-Sweden (5.4%)[27], but half among colonoscopy-referral patients of a Cancer Hospital in Brazil (10.1%)[26].

The more recent guideline of CRC surveillance[29] proposes that screening to adults aged 50–79 should be based on the risk of CRC for the next 15 years, by answering the QCancer® calculator that takes into account age, gender, ethnicity, BMI, smoking, and medical and family history. Screening is suggested with one of the four options: FIT every year, FIT every two years, single sigmoidoscopy, or a single colonoscopy for individuals with risk of 3% or higher. Below 3% of risk, screening is not recommended based on benefits, harms, and burdens of screening.

The specificity of FIT in the present study (86.9% for one sample- FIT1 and 92.9% for two sample- FIT2) was similar (between 88–95%) to other reports[2,8,16,23,25,30], except for the qualitative ColonView (Hb/Hp) with 65% specificity[26], and the quantitative QuikRead go®FIT with 77%[27]. The sensitivity varied among the different tests and the colonoscopy findings, being higher for those with CRC than the ones with advanced adenoma, as adenoma bleeds less than CRC and does not bleed every day. For advanced adenoma the sensitivity varied from 18% with OC Sensor[8], 25% ImmoCare-C^2 to 33% automated ELISA[23]; however, with two sample FIT (FIT2) the sensitivity for advanced adenoma in this study increased from 24% (One-sample FIT) to 50% (two-sample FIT). For a developing country with a tropical weather, a lesion that bleeds less than CRC, and considering the simplicity of the test in relation to the colonoscopy, the sensitivity of collecting two consecutive samples is more reliable. The sensitivity for advanced neoplasia was from 15.1 % (OC FIT-CHEK)[15], 21.8% (OC Sensor)[8], 26.3% (InSure FIT)[16], 35.2% (FOB Gold)[30] and the present study for one-sample FIT, to 38% (OC- Sensor)[25]. However, the sensitivity for advanced neoplasia increased to 60% with two-sample FIT. The sensitivity for CRC was 68.8 % (OC Sensor)[8], 88 % (OC Sensor)[25], 92.3% (QuikRead go®FIT) one-sample FIT to 100% two-sample FIT[27]. In the present study two-sample FIT did not increase the sensitivity (75%), as with one-sample FIT for CRC was 83.3%.

The limitations of the study were the small number of the individuals with advanced adenoma, as the post hoc power analysis was high only for CRC and no assessment of symptoms and correlation with the findings of colonoscopy and OCR FIT- tests. Future study may evaluate a higher number of patients with advanced adenoma and symptoms to indicate intestinal neoplasia diagnosis.

CONCLUSION

In conclusion, the accuracy of OCR Sensor with 10 µg Hb/g feces cut-off was comparable to other reports and two-sample collection improved the detection rate of advanced adenoma, a pre neoplastic condition to prevent CRC incidence.

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Authors' contribution

PS: study design, kits donation management. SBM: study design, writing the research project, writing the article, patient inclusion, colonoscopy, collection of biopsy samples, data management. MKM: colonoscopy, collection of biopsy samples. JMKSE: OCR FIT performance. RM: writing the article, statistical analyses, OCR FIT performance, data management. EGHM and all the authors read and approved the final version of the manuscript.

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Mattar R, Marques SB, Minata MK, Silva-Etto JMK, Sakai P, de Moura EGH. Acurácia diagnóstica de teste quantitativo imunoquímico fecal com uma amostra ou com duas amostras para detectar neoplasia intestinal. Arq Gastroenterol. 2020;57(3):316-22.

RESUMO – **Contexto** – Sangramento retal é o sintoma mais importante de neoplasia intestinal; portanto, testes para detecção de sangue oculto nas fezes são amplamente usados para rastreamento de lesões pré-neoplásicas e de câncer colorretal (CCR). **Objetivo** – Avaliar a acurácia do teste quantitativo OC-Sensor (Eiken Chemical, Tokyo, Japan) com o valor de corte de 10 µg Hb/g fezes (50 ng/mL) numa coorte de indivíduos que se submeteram à colonoscopia diagnóstica, e se mais de uma amostra coletada em dias consecutivos melhoraria a acurácia diagnóstica do teste. **Métodos** – Pacientes (idade média 56,3±9,7 anos) que se submeteram à colonoscopia prospectivamente, randomicamente, receberam tubos de coleta: um (1-amostra FIT, FIT 1), ou dois (2-amostra FIT, FIT 2). Eles coletaram as amostras de fezes antes de iniciar o preparo da colonoscopia. As amostras foram analisadas pelo OC-Auto Micro 80 (Eiken Chemical, Tokyo, Japan). As performances do FIT 1 e do FIT 2 foram comparadas com os achados da colonoscopia. **Resultados** – Entre 289 pacientes, CCR foi diagnosticado em 14 (4,8%), adenoma avançado em 37 (12,8%), adenoma precoce em 71 (24,6%) e sem anormalidades em 141 (48,8%). Para FIT 1, a sensibilidade para CCR foi 83,3% (95%IC 36,5–99,1%), para adenoma avançado foi 24% (95%IC 10,1–45,5%), com especificidade de 86,9% (95%IC 77,3–92,9%). Para FIT 2, a sensibilidade para CCR foi 75% (95%IC 35,6–95,5%), para adenoma avançado foi 50% (95%IC 22,3–77,7%), com especificidade de 92,9% (95%IC 82,2–97,7%). A razão de verossimilhança positiva foi 1,8 (95%IC 0,7–4,4 para FIT 1) e 7,1 (95%IC 2,4–21,4 para FIT 2) para adenoma avançado, e 6,4 (95%IC 3,3–12,3, para FIT 1) e 10,7 (95%IC 3,8–29,8, para FIT 2) para CCR. A razão de verossimilhança negativa foi 0,9 (95%IC 0,7–1, para FIT 1) e 0,5 (95%IC 0,3–0,9, para FIT 2) para adenoma avançado, e 0,2 (0,03–1,1, para FIT 1) e 0,3 (0,08–0,9, para FIT 2) para CCR. As diferenças de performance entre FIT 1 e FIT 2 não foram significantes. Entretanto, a comparação dos níveis de hemoglobina nas fezes dos pacientes de FIT 1 e FIT 2 mostraram que as diferenças entre sem pólipo e adenoma avançado e CCR foram significantes. **Conclusão** – A acurácia do OCR Sensor com valor de corte de 10 µg Hb/g de fezes foi comparável a outras publicações e a coleta de duas amostras melhorou a taxa de detecção de adenoma avançado, lesão pré-neoplásica, para prevenir CCR.

DESCRITORES – Neoplasias colorretais, diagnóstico. Pólipos intestinais. Valor preditivo dos testes. Sangue oculto. Colonoscopia.

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