ORIGINAL PAPERS

Participation in clinical trials increases the detection of pre-malignant lesions during colonoscopy

Alexandre Oliveira Ferreira[1,2], Maria Pia Costa-Santos[3], Catarina Gomes[1], Bárbara Morão[1], Luisa Glória[1], Marília Cravo[1,2], Mário Dinis-Ribeiro[4,5], and Jorge Canena[6,7,8]

[1]Department of Gastroenterology. Hospital Beatriz Ângelo. Loures, Portugal. [2]Department of Gastroenterology. Hospital da Luz. Lisboa, Portugal. [3]Department of Gastroenterology. Hospital do Divino Espirito Santo. Ponta Delgada, Portugal. [4]Department of Gastroenterology. Instituto Português de Oncologia. Porto, Portugal. [5]Cintesis, Center for Health Technology and Services Research. Porto, Portugal. [6]Department of Gastroenterology. Nova Medical School/Faculty of Medical Sciences. Lisbon, Portugal. [7]University Center of Gastroenterology. Hospital Cuf Tejo. Lisbon, Portugal. [8]Department of Gastroenterology. Professor Doutor Fernando Fonseca Hospital. Amadora, Portugal

Received: 14/06/2021 · **Accepted:** 26/09/2021

Correspondence: Alexandre O. Ferreira. Department of Gastroenterology. Hospital Beatriz Ângelo. Av. Carlos Teixeira, 3. 2674-514 Loures, Portugal. **e-mail:** Alex.gastrohep@gmail.com

ABSTRACT

Background: colorectal adenoma detection has been associated with the effectiveness of cancer prevention. Clinical trials have been designed to determine the role of several interventions to increase the detection of pre-malignant lesions. We hypothesized that colonoscopy in the setting of clinical trials has a higher pre-malignant lesion detection rate.

Methods: a cross-sectional study was performed that compared the detection of pre-malignant lesions in 147 randomly sampled non-research colonoscopies and 294 from the control group of two prospective trials. Outpatients aged 40-79 years, with no personal history of colorectal cancer (CRC) were included.

Results: baseline characteristics were similar between the two groups. The pre-malignant lesion detection rate in the trial *vs* control group was 65.6 % *vs* 44.2 % (OR 2.411; 95 % CI: 1.608-3.614; p < 0.001), the polyp detection rate was 73.8 % *vs* 59.9 % (OR 1.889; 95 % CI: 1.242-2.876; p = 0.003), the adenoma detection rate was 62.6 % *vs* 44.2 % (OR 2.110; 95 % CI: 1.411-3.155; p < 0.001) and the sessile serrated lesion detection rate was 17 % *vs* 4.1 % (OR 4.816; 95 % CI: 2.014-11.515; p < 0.001). The mean number of pre-malignant and sessile serrated lesions was 1.70 *vs* 1.06 (p = 0.002) and 0.32 *vs* 0.06 (p = 0.001) lesions per colonoscopy, respectively. There was no significant change in any of the study outcomes according to the multivariate analysis with each single potential confounder.

Conclusions: patients involved in colonoscopy trials may benefit from higher quality examinations, as shown by the higher detection rates. Institutions should consider supporting clinical research in colonoscopy as a simple means to improve colonoscopy quality and colorectal cancer prevention.

Keywords: Colonoscopy. Quality. Research. Adenoma.

INTRODUCTION

Colorectal cancer is one of the leading cancers and accounts for over 860,000 deaths worldwide (1). Colonoscopy has been shown to decrease both CRC incidence (2) and mortality by detecting and allowing the removal of adenomas (3-8).

Conflict of interest: the authors declare no conflict of interest.

Author´s contribution:
AOF was responsible for the study design, data collection and analysis and manuscript writing.
MPCS collaborated in the study design analysis and manuscript critical review.
CG and BM collaborated in data collection and manuscript critical review.
LG collaborated in the study design and manuscript critical review.
MC collaborated in the study design and manuscript critical review.
JC collaborated in the study design and manuscript critical review.
MDR collaborated in the study design and manuscript critical review.

Ferreira AO, Costa-Santos MP, Gomes C, Morão B, Glória L, Cravo M, Dinis-Ribeiro M, Canena J. Participation in clinical trials increases the detection of pre-malignant lesions during colonoscopy. Rev Esp Enferm Dig 2022;114(6):323-328

DOI: 10.17235/reed.2021.8104/2021

The magnitude of this effect is related to the detection rate of pre-malignant colorectal lesions, especially the adenoma detection rate (ADR), which is highly variable (9-13). Sessile serrated lesions are another subset of colorectal lesions that also have malignant potential (14) and are more difficult to detect, with an even higher variability between endoscopists (15).

Quality in colonoscopy is therefore a major issue in digestive endoscopy, with significant efforts being made by international societies such as the European Society of Gastrointestinal Endoscopy (ESGE) (16) and the American Society of Gastrointestinal Endoscopy (ASGE) (17) to set standards. Both societies set the adenoma detection rate as one of the most important indicators of colonoscopy quality.

In the last few decades, endoscopists and researchers have tried to improve the detection of pre-malignant lesions through technological advances, such as high-definition imaging, electronic chromoendoscopy (18), wide view lenses (19), devices (20,21) or artificial intelligence (22). Furthermore, simple interventions such as educational sessions, feedback (23), benchmarking, changing the patient position (24), performing the colonoscopy underwater (25) and administering butylscopolamine (26) or simethicone (27) have also been examined. Several trials of these interventions reported ADRs above 50 % in some groups, including the "placebo" arms (18,28,29). These results are well over the proposed threshold of 25 % and above our department's own indicators, with an ADR of 36 % and a sessile serrated lesion detection of 1 %, as reported in 2017 (30).

We hypothesized that patients whose colonoscopy was performed in a clinical trial setting may have higher pre-malignant lesion detection rates (adenomas and SSL) than patients under routine care. To our knowledge, there are no data to assess the impact of clinical research projects on quality performance in endoscopy units. The aim of this study was to assess the colonoscopy quality indicators in patients who were included in a control group for an endoscopic clinical trial at our institution and compare them with a sample group from the same institution.

MATERIALS AND METHODS

Patients and setting

A retrospective cross-sectional study was performed, comparing colonoscopies performed in a clinical trial setting with a group of "routine" colonoscopies.

Inclusion criteria

The inclusion criteria for the control group were similar to those for the trials with registered protocols, which included patients aged from 40 to 79 years undergoing outpatient colonoscopies. Bowel preparation quality was determined with the Boston Bowel Preparation Score (BBPS) and deemed adequate if at least two points were reached in each segment. One of the trials excluded patients with one or more segments with a BBPS below 2, but the other trial randomized patients before colonoscopy preparation and preparation quality was not an exclusion criterion. To control for bowel preparation quality, only cases with BBPS scores of at least 2 in each segment were included. Patients with polyposis syndromes, primary sclerosing cholangitis, inflammatory bowel disease, a personal history of colorectal cancer or surgery or failure to reach the caecum were excluded.

All patients provided written informed consent before the procedure and a specific consent form was completed for those who were participants in the trials. The Institutional Review Board approved the collection of data for this observational study.

Case selection

Routine colonoscopies for the control group were randomly selected from our department's database of routine colonoscopies. For the "trial group", colonoscopies were randomly selected from the control arms of two trials performed at our institute (NCT03856957 and NCT02876133). A computer-generated algorithm was created for case selection. Cases were selected from our 2019 colonoscopy database of outpatient colonoscopies performed in subjects aged 40-79 years during 2019. Cases that did not meet the study criteria were excluded from the selection.

A cut-off of 300 colonoscopies was defined in the clinical trials, which allowed the participation of senior endoscopists and two senior residents. In the control group, colonoscopies from nine senior endoscopists and the same two senior residents were included.

Study outcomes

The primary outcome was the pre-malignant lesion detection rate and the secondary outcomes were the polyp detection rate, ADR, sessile serrated lesion (SSL) detection rate, number of pre-malignant lesions, adenomas and SSL per colonoscopy and number of serrated lesions > 9 mm.

Sample size calculation and statistical analysis

A 2:1 trial group to control group ratio was used as our trial database has over 1,000 cases. A sample size of 294 trial colonoscopies and 147 control colonoscopies was calculated to have 80 % power to detect a difference based on our own preliminary data. For the control group, we assumed 36 % ADR from our own series (30) and 60 % ADR for the study group, based on our Endocuff trial (NCT03856957) and the recently published ADENOMA trial that was an RCT of Endocuff (31).

The study endpoints were adjusted for age, sex, bowel preparation, sedation depth and personal history of polyps using multivariate logistic regression analysis to determine the "clinical trial" effect more accurately. Each confounder was adjusted individually and then all variables were tested in a single model.

The mean and standard deviation are shown for continuous variables with a normal distribution. These were compared using an independent t-test. Categorical variables are pre-

sented as proportions (%) and compared using the Fisher's exact or χ^2 test. Logistic regression was used to determine the effect estimates, which are presented as odds ratios and 95 % confidence intervals. Missing data were resolved by pairwise deletion. Statistical analysis was performed with the SPSS software package, version 21 (Statistical Package for the Social Sciences, IBM Corporation, Armonk, NY, USA). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in *a priori* approval by the institution's human research committee.

RESULTS

Patients

A total of 441 colonoscopies were selected, of which 294 were included in the clinical trial group and 147 were included in the control group. Baseline characteristics are shown in table 1. Most baseline characteristics (age, sex, colorectal cancer family history and personal history of polyps) were similar between the two groups. Sedation was significantly different because all procedures were performed under deep sedation in the clinical trials group.

Outcomes

The study outcomes are summarized in table 2. All lesion types were more frequently detected in the trial group. The pre-malignant lesion detection rate was 65.6 % *vs* 44.2 % (OR 2.411; 95 % CI: 1.608-3.614; p < 0.001), the polyp detection rate was 73.8 % *vs* 59.9 % (OR 1.889; 95 % CI: 1.242-2.876; p = 0.003), the adenoma detection rate was 62.6 % *vs* 44.2 % (OR 2.110; 95 % CI: 1.411-3.155; p < 0.001) and the sessile serrated lesion detection rate was 17 % *vs* 4.1 % (OR 4.816; 95 % CI: 2.014-11.515; p < 0.001). The mean number of pre-malignant and sessile serrated lesions was higher in the research group, with 1.70 *vs* 1.06 (p = 0.002) and 0.32 *vs* 0.06 (p = 0.001) lesions per colonoscopy, respectively. The mean

Table 1. *Baseline characteristics of the study population*

	Trial group (n = 294)	Control group (n = 147)	p-value
Age, y	62.16 (9.81)	61.97 (9.97)	0.802
Male sex, n (%)	161 (54.8)	70 (47.6)	0.157
CRC family history, n (%)	65 (22.4)	26 (18.1)	0.294
Previous colonoscopy, n (%)	133 (45.4)	74 (50.7)	0.295
Personal history of polyps, n (%)	87 (29.7)	44 (30.3)	0.888
Deep sedation, n (%)	294 (100)	65 (44.2)	0.001
Conscious sedation, n (%)		62 (42.2)	
No sedation, n (%)		20 (13.6)	
Indication			0.050
Screening	53 (17.3)	24 (16.3)	
FOBT/diagnostic	214 (69.9)	89 (60.5)	
Surveillance	39 (12.7)	34 (23.1)	

CRC: colorectal cancer; FOBT: fecal occult blood test.

Table 2. *Primary and secondary outcomes*

	Trial group (n = 316)	Control group (n = 182)	p-value
Mean polyp number (se)	2.21 (0.14)	1.74 (0.12)	0.062
Mean pre-malignant lesion number (se)	1.70 (0.12)	1.06 (0.16)	0.002
Mean adenoma number (se)	1.38 (0.10)	1.00 (0.15)	0.032
Mean SSL number (se)	0.32 (0.02)	0.06 (0.02)	0.001
Mean number of serrated lesions > 9 mm (se)	0.06 (0.019)	0.02 (0.015)	0.158
Polyp detection rate, %	73.8	59.9	0.003
Pre-malignant lesion detection rate, %	65.6	44.2	< 0.001
Adenoma detection rate, %	62.6	44.2	0.0002
Sessile serrated lesion detection rate, %	17.0	4.1	0.0001

SSL: sessile serrated lesion.

Table 3. *Logistic regression to control for potential confounders for pre-malignant lesion detection*

Variables	Odds ratio	Robust standard errors	p
Trial group	2.316 (1.307-4.102)	0.292	0.004*
Age	1.043 (1.021-1.065)	0.011	0.0001*
Sex:			
Female	0.478 (0.315-0.725)	0.213	0.001*
Sedation:			
No	0.892 (0.447-1.779)	0.352	0.745
Polyp history:			
Yes	1.610 (1.005-2.578)	0.240	0.048†
Wald χ^2 test	*54.436**		
Pseudo R^2	*0.158*		

*Denote p-values < 0.01. †Denotes p-value < 0.05.

number of lesions (overall) was not significantly different between the groups. There was no significant change in any of the study outcomes according to a multivariate analysis with each single potential confounder.

The effects on the main quality indicators (ADR, SSL and pre-malignant lesion detection rate) were adjusted in a single model including age, sex, sedation depth and history of polyps (Table 3). In this model, the detection odds ratios were kept at a significant level for pre-malignant lesions (OR 2.316; 95 % CI: 1.307-4.102; p = 0.004), SSL detection rate (OR 6.810; 95 % IC: 1.588-29.210; p = 0.010) and ADR (OR 2.002; 95 % IC: 1.129-3.549; p = 0.018).

DISCUSSION

Our study compared the main colonoscopy quality indicators in two separate groups comprising 441 colonoscopies performed at our institution. One group comprised patients that underwent routine colonoscopy and were not participants in any clinical trial. They were later selected and associated data were retrospectively recorded, without any prior knowledge of the experimental group by the intervening clinical team. In the second group, colonoscopies were selected from the control groups of clinical trials, where the clinical team was aware that the outcomes would be systematically recorded and analyzed.

In this study, higher ADR, sessile serrated lesion detection rate (SSLDR) and lesion detection rates were observed in colonoscopies that were performed in a clinical trial setting. The results showed high lesion detection rates in both groups and these rates were well above the thresholds proposed by the leading endoscopy societies (ESGE and ASGE).

CRC is a common cancer in the Western world. Effectively increasing the ADR by just 1 % has been shown to decrease CRC incidence by 3 %. However, there is a remarkable inter-endoscopist variability in this metric, with rates ranging between 7.4 % and 52.5 % (9). There have been significant efforts to establish quality indicators to guide endoscopy practitioners in their quest to maximize the effectiveness of colorectal cancer screening. Although it can be argued that the best current indicators of quality are probably adenoma detection rate and mean adenomas per colonoscopy (16,17). The ADR is the most studied and widely accepted quality measure (17,32) but the mean adenoma number may be more discriminative and more resistant to gaming. The SSLDR shows more variability between endoscopists, as these lesions may be more difficult to detect than conventional adenomas (33,34). In one study, this variability was 20-fold, ranging from 0.3 % to 6.7 % among endoscopists from the same group (34). Furthermore, evidence is also increasing to support sessile serrated lesion detection as an important quality metric, especially for the proximal colon, due to their association with interval cancer due to missed lesions (35,36).

Studies have shown that when endoscopists are audited, publicly report their indicators and receive feedback, their performance increases by up to 45 % (37-39). This type of intervention, if effective, is potentially more cost-effective than using artificial intelligence, single-use devices such as the third eye or the Endocuff cap. In our department, we were interested in determining our own quality indicators and published them as a benchmark reference (30). We have also performed several trials on colonoscopy quality in the last few years (40), one of which is currently recruiting participants (NCT02876133). This study was initiated after we noticed high rates of detection in these trials.

We acknowledge some important limitations inherent to the study design. The endoscopists in the trial group were not aware of this particular study, but they were not blinded to the research protocols, as they were aware of the trial in which they were involved. The control group data were retrospectively collected. Thus, some potentially relevant confounders, such as family history of CRC or withdrawal time, were not accounted for as the data were not available. The electronic reporting system only started to automatically record the withdrawal time in 2019. Moreover, the groups were not properly matched, even though the baseline characteristics were quite similar. We tried to overcome this limitation by adjusting the outcomes for known potential confounders such as age, sex and sedation. Bowel preparation was controlled by including only colonoscopies with at least two BBPS points in each bowel segment. Furthermore, according to the multivariate analysis, there was an association with age, male sex and personal history of polyps and higher lesion detection. The model also allowed us to confirm that the association of being in a trial with higher lesion detection rates is independent of age, sex, personal history of polyps and sedation depth.

The strengths of our study are being the first to analyze the impact of participating in an endoscopy trial and showing a significant benefit of participating in clinical trials. There have been a few other studies on the impact of research in other areas, such as cancer (41,42) and women's health (43), although these studies show conflicting results (44).

In conclusion, this study shows for the first time that being involved in research, specifically in colonoscopy clinical trials, may lead to significant improvements in the detection of pre-malignant lesions, even if the subjects are allo-

cated to control/placebo groups. These results should be confirmed in other centers/study groups, which could help to foster clinical research in colonoscopy quality with the added clinical benefit of decreasing CRC burden.

ACKNOWLEDGEMENTS

The authors acknowledge the support of the Portuguese Society of Gastroenterology through the free access to Research Electronic Data Capture (REDCap). Study data were collected and managed using REDCap electronic data capture tools hosted at Sociedade Portuguesa de Gastrenterologia. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing: a) an intuitive interface for validated data capture; b) audit trails for tracking data manipulation and export procedures; c) automated export procedures for seamless data downloads to common statistical packages; and d) procedures for data integration and interoperability with external sources.

REFERENCES

1. Ferlay J, Colombet M, Soerjomataram I, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. Int J Cancer 2019;144:1941-53. DOI: 10.1002/ijc.31937

2. Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med 1993;329:1977-81. DOI: 10.1056/NEJM199312303292701

3. Loberg M, Kalager M, Holme O, et al. Long-term colorectal-cancer mortality after adenoma removal. N Engl J Med 2014;371:799-807. DOI: 10.1056/NEJMoa1315870

4. Nishihara R, Wu K, Lochhead P, et al. Long-term colorectal-cancer incidence and mortality after lower endoscopy. N Engl J Med 2013;369:1095-105. DOI: 10.1056/NEJMoa1301969

5. Schoen RE, Pinsky PF, Weissfeld JL, et al. Colorectal-cancer incidence and mortality with screening flexible sigmoidoscopy. N Engl J Med 2012;366:2345-57. DOI: 10.1056/NEJMoa1114635

6. Shaukat A, Mongin SJ, Geisser MS, et al. Long-term mortality after screening for colorectal cancer. N Engl J Med 2013;369:1106-14. DOI: 10.1056/NEJMoa1300720

7. Zauber AG, Winawer SJ, O'Brien MJ, et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med 2012;366:687-96. DOI: 10.1056/NEJMoa1100370

8. Kaminski MF, Wieszczy P, Rupinski M, et al. Increased rate of adenoma detection associates with reduced risk of colorectal cancer and death. Gastroenterology 2017;153:98-105. DOI: 10.1053/j.gastro.2017.04.006

9. Corley DA, Jensen CD, Marks AR, et al. Adenoma detection rate and risk of colorectal cancer and death. N Engl J Med 2014;370:1298-306. DOI: 10.1056/NEJMoa1309086

10. Leung WK, Lo OS, Liu KS, et al. Detection of colorectal adenoma by narrow band imaging (HQ190) vs. high-definition white light colonoscopy: a randomized controlled trial. Am J Gastroenterol 2014;109:855-63. DOI: 10.1038/ajg.2014.83

11. Ng SC, Tsoi KK, Hirai HW, et al. The efficacy of cap-assisted colonoscopy in polyp detection and cecal intubation: a meta-analysis of randomized controlled trials. Am J Gastroenterol 2012;107:1165-73. DOI: 10.1038/ajg.2012.135

12. Gralnek IM, Siersema PD, Halpern Z, et al. Standard forward-viewing colonoscopy versus full-spectrum endoscopy: an international, multicentre, randomised, tandem colonoscopy trial. Lancet Oncol 2014;15:353-60. DOI: 10.1016/S1470-2045(14)70020-8

13. Chung SJ, Kim D, Song JH, et al. Comparison of detection and miss rates of narrow band imaging, flexible spectral imaging chromoendoscopy and white light at screening colonoscopy: a randomised controlled back-to-back study. Gut 2014;63:785-91. DOI: 10.1136/gutjnl-2013-304578

14. He X, Hang D, Wu K, et al. Long-term risk of colorectal cancer after removal of conventional adenomas and serrated polyps. Gastroenterology 2020;158:852-61.e854. DOI: 10.1053/j.gastro.2019.06.039

15. JE IJ, de Wit K, van der Vlugt M, et al. Prevalence, distribution and risk of sessile serrated adenomas/polyps at a center with a high adenoma detection rate and experienced pathologists. Endoscopy 2016;48:740-6. DOI: 10.1055/s-0042-105436

16. Kaminski MF, Thomas-Gibson S, Bugajski M, et al. Performance measures for lower gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) quality improvement initiative. Endoscopy 2017;49:378-97. DOI: 10.1055/s-0043-103411

17. Rex DK, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy. Gastrointest Endosc 2015;81:31-53. DOI: 10.1016/j.gie.2014.07.058

18. Atkinson NSS, Ket S, Bassett P, et al. Narrow-band imaging for detection of neoplasia at colonoscopy: a meta-analysis of data from individual patients in randomized controlled trials. Gastroenterology 2019;157:462-71. DOI: 10.1053/j.gastro.2019.04.014

19. Pellisé M, Fernández-Esparrach G, Cárdenas A, et al. Impact of wide-angle, high-definition endoscopy in the diagnosis of colorectal neoplasia: a randomized controlled trial. Gastroenterology 2008;135:1062-8. DOI: 10.1053/j.gastro.2008.06.090

20. Karsenti D, Tharsis G, Perrot B, et al. Adenoma detection by Endocuff-assisted versus standard colonoscopy in routine practice: a cluster-randomised crossover trial. Gut 2020;69(12):2159-64. DOI: 10.1136/gutjnl-2019-319565:

21. Ngu WS, Bevan R, Tsiamoulos ZP, et al. Improved adenoma detection with Endocuff Vision: the ADENOMA randomised controlled trial. Gut 2019;68:280-8. DOI: 10.1136/gutjnl-2017-314889

22. Wang P, Berzin TM, Glissen Brown JR, et al. Real-time automatic detection system increases colonoscopic polyp and adenoma detection rates: a prospective randomised controlled study. Gut 2019;68:1813-9. DOI: 10.1136/gutjnl-2018-317500

23. Gurudu SR, Boroff ES, Crowell MD, et al. Impact of feedback on adenoma detection rates: Outcomes of quality improvement program. J Gastroenterol Hepatol 2018;33:645-9. DOI: 10.1111/jgh.13984

24. Lee SW, Chang JH, Ji JS, et al. Effect of dynamic position changes on adenoma detection during colonoscope withdrawal: a randomized controlled multicenter trial. Am J Gastroenterol 2016;111:63-9. DOI: 10.1038/ajg.2015.354

25. Aziz M, Sharma S, Fatima R, et al. How to increase proximal adenoma detection rate: a meta-analysis comparing water exchange, water immersion and air/CO2 insufflation methods for colonoscopy. Ann Gastroenterol 2020;33:178-86. DOI: 10.20524/aog.2020.0459

26. De Brouwer EJ, Arbouw ME, van der Zwet WC, et al. Hyoscine N-butylbromide does not improve polyp detection during colonoscopy: a double-blind, randomized, placebo-controlled, clinical trial. Gastrointest Endosc 2012;75:835-40. DOI: 10.1016/j.gie.2011.12.010

27. Bai Y, Fang J, Zhao SB, et al. Impact of preprocedure simethicone on adenoma detection rate during colonoscopy: a multicenter, endoscopist-blinded randomized controlled trial. Endoscopy 2018;50:128-36.

28. Triantafyllou K, Gkolfakis P, Tziatzios G, et al. Effect of Endocuff use on colonoscopy outcomes: a systematic review and meta-analysis. World J Gastroenterol 2019;25:1158-70. DOI: 10.3748/wjg.v25.i9.1158

29. Desai M, Viswanathan L, Gupta N, et al. Impact of electronic chromoendoscopy on adenoma miss rates during colonoscopy: a systematic review and meta-analysis. Dis Colon Rectum 2019;62:1124-34. DOI: 10.1097/DCR.0000000000001419

30. Oliveira Ferreira A, Fidalgo C, Palmela C, et al. Adenoma detection rate: I will show you mine if you show me yours. GE Port J Gastroenterol 2017;24:61-7. DOI: 10.1159/000450901

31. Ngu WS, Bevan R, Tsiamoulos ZP, et al. Improved adenoma detection with Endocuff Vision: the ADENOMA randomised controlled trial. Gut 2019;68:280-8. DOI: 10.1136/gutjnl-2017-314889

32. Ponugoti P, Lin J, Odze R, et al. Prevalence of sessile serrated adenoma/polyp in hyperplastic-appearing diminutive rectosigmoid polyps. Gastrointest Endosc 2017;85:622-7. DOI: 10.1016/j.gie.2016.10.022

33. Kahi CJ, Hewett DG, Norton DL, et al. Prevalence and variable detection of proximal colon serrated polyps during screening colonoscopy. Clin Gastroenterol Hepatol 2011;9:42-6. DOI: 10.1016/j.cgh.2010.09.013

34. Hetzel JT, Huang CS, Coukos JA, et al. Variation in the detection of serrated polyps in an average risk colorectal cancer screening cohort. Am J Gastroenterol 2010;105:2656-64. DOI: 10.1038/ajg.2010.315

35. Arain MA, Sawhney M, Sheikh S, et al. CIMP status of interval colon cancers: another piece to the puzzle. Am J Gastroenterol 2010;105:1189-95. DOI: 10.1038/ajg.2009.699

36. Farrar WD, Sawhney MS, Nelson DB, et al. Colorectal cancers found after a complete colonoscopy. Clin Gastroenterol Hepatol 2006;4:1259-64. DOI: 10.1016/j.cgh.2006.07.012

37. Kahi CJ, Ballard D, Shah AS, et al. Impact of a quarterly report card on colonoscopy quality measures. Gastrointest Endosc 2013;77:925-31. DOI: 10.1016/j.gie.2013.01.012

38. Abdul-Baki H, Schoen RE, Dean K, et al. Public reporting of colonoscopy quality is associated with an increase in endoscopist adenoma detection rate. Gastrointest Endosc 2015;82:676-82. DOI: 10.1016/j.gie.2014.12.058

39. Gurudu SR, Boroff ES, Crowell MD, et al. Impact of feedback on adenoma detection rates: outcomes of quality improvement program. J Gastroenterol Hepatol 2018;33:645-9. DOI: 10.1111/jgh.13984

40. Ferreira AO, Torres J, Barjas E, et al. Non-anesthesiologist administration of propofol sedation for colonoscopy is safe in low risk patients: results of a noninferiority randomized controlled trial. Endoscopy 2016;48:747-53. DOI: 10.1055/s-0042-105560

41. Medeiros BC, Othus M, Tallman MS, et al. The relationship between clinical trial accrual volume and outcomes in acute myeloid leukemia: a SWOG/ECOG-ACRIN study (S0106 and E1900). Leuk Res 2019;78:29-33. DOI: 10.1016/j.leukres.2019.01.007

42. Du Bois A, Rochon J, Lamparter C, et al. Pattern of care and impact of participation in clinical studies on the outcome in ovarian cancer. Int J Gynecol Cancer 2005;15:183-91. DOI: 10.1136/ijgc-00009577-200503000-00001

43. Nijjar SK, D'Amico MI, Wimalaweera NA, et al. Participation in clinical trials improves outcomes in women's health: a systematic review and meta-analysis. BJOG 2017;124:863-71. DOI: 10.1111/1471-0528.14528

44. Khoja L, Horsley L, Heesters A, et al. Does clinical trial participation improve outcomes in patients with ovarian cancer? ESMO Open 2016;1:e000057. DOI: 10.1136/esmoopen-2016-000057