RESEARCH PROJECT

TITLE: “The use of artificial intelligence to improve adenoma detection during Gastroenterology training”

A. STUDY INVESTIGATORS

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B. RESEARCH PROPOSAL

1. Specific aims and hypotheses

Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the second leading cause of cancer death, with more than 1.9 million new diagnoses and 935,000 deaths in 2020.[1] Endoscopic removal of colonic polyps through polypectomy has been shown to contribute to a reduction in the incidence and death from CCR.[2-4] However, the prevalence of cancer after a negative colonoscopy, referred to as interval cancer, is still as high as 7%.[5] Therefore quality in colonoscopy is crucial, being the number of colorectal adenomas detected during endoscopy - the adenoma detection rate (ADR) – the main quality indicator, which is inversely related to the risk of interval cancer.[6-8]

Recent studies have demonstrated a benefit of computer-aided diagnosis (CADe) and artificial intelligence (AI) on the improvement of quality in colonoscopy, by increasing the ADR, the polyp detection rate (PDR), the mean number of adenomas detected per colonoscopy (MAP) and the mean number of polyps detected per colonoscopy.[9-11] However, there seems to be a difference in ADR variation with the use of AI-assisted colonoscopy according to the baseline ADR, with less experienced endoscopists benefiting the most from this device, as opposed to gastroenterologists with high ADR.[12] Moreover, previous studies have demonstrated that there is an increase in ADR with training and there seems to be a difference according to the baseline experience of the endoscopist. [13]

However, it is unknown what is the impact of AI in the process of training Gastroenterologists, namely if it helps increase ADR, if it accelerates the learning curve or if otherwise, it may be detrimental. Our **global aim** is to determine what **is the impact of AI-assisted colonoscopy in Gastroenterology training and if it can be considered a future quality indicator in the training process.**

Specific aim 1: To compare trainees' colonoscopy quality parameters (such as the mean number of adenomas detected per colonoscopy, adenoma detection rate and polyp detection rate) between AI-assisted colonoscopy versus high-definition white light (HD-WL) colonoscopy.

Specific aim 2: To compare the difference in trainees' colonoscopy quality parameters with AI-assisted colonoscopy and HD-WL colonoscopy, according to the years of experience in Gastroenterology training.

Specific aim 3: To compare the evolution of the learning curve during training with the use of AI-assisted colonoscopy with a retrospective group of trainees that only performed colonoscopy with HD-WL.

Our global **hypothesis** is that the use of AI-assisted colonoscopy during Gastroenterology training could be a quality indicator, improving trainees' adenoma and polyp detection skills, which may contribute in the future to a global increase in the effectiveness of colonoscopy screening and in the long-term to a reduction on the incidence of interval CRC.

2. Background and significance

CRC s still one of the leading causes of mortality due to cancer, being one of the most frequently diagnosed cancers worldwide.[1]

Recent trials on the use of AI in colonoscopy have demonstrated a significant benefit of this technique on the increase of adenoma and polyp detection rate. Particularly, in Europe, *Repici et al.* have demonstrated a relative risk of ADR of 1.30 and an incidence rate ratio for the mean number of adenomas detected per colonoscopy of 1.46 with the use of AI-assisted colonoscopy. This increase was most significant for adenomas less than 10 mm.[9] In this trial, like in the study by *Wang et al*. only senior endoscopists were included and there seemed to exist a smaller variation in ADR with the use of AI versus standard colonoscopies comparing to the other studies where non-experienced endoscopists were also included.[10] However, in a recent study comparing two trials of AI-assisted colonoscopy in experienced and non-experienced endoscopists, the use of AI (RR 1.29; 95% CI: 1.16 to 1.42) but not the level of endoscopist's experience (RR 1.02; 95% CI: 0.89 to 1.16) seem to be associated with the variation in ADR between groups.[14]

Although it is not clear if endoscopists' experience influences the increase in ADR with the use of AI-assisted colonoscopy, it is believed that there is a ceiling effect in adenoma and polyps detection and, therefore, AI-assisted colonoscopy may be more useful in less experienced endoscopists, contributing to an improvement in their colonoscopy performance. However, the utility of AI-assisted colonoscopy during Gastroenterology training is yet to be determined. Our aim is to evaluate if AI-assisted colonoscopy may help increase quality in colonoscopy early during Gastroenterology training.

Significance: CCR is still one of the leading causes of death due to cancer and training in adenoma detection and resection is crucial to reduce the incidence of this cancer. AI is an emerging field in endoscopy with promising results. The use of AI-assisted colonoscopy during Gastroenterology training may contribute to an increase in quality in colonoscopy, which may lead to a global decrease in CCR incidence and, particularly, a decrease of interval CCR.

3. Feasibility and preliminary data

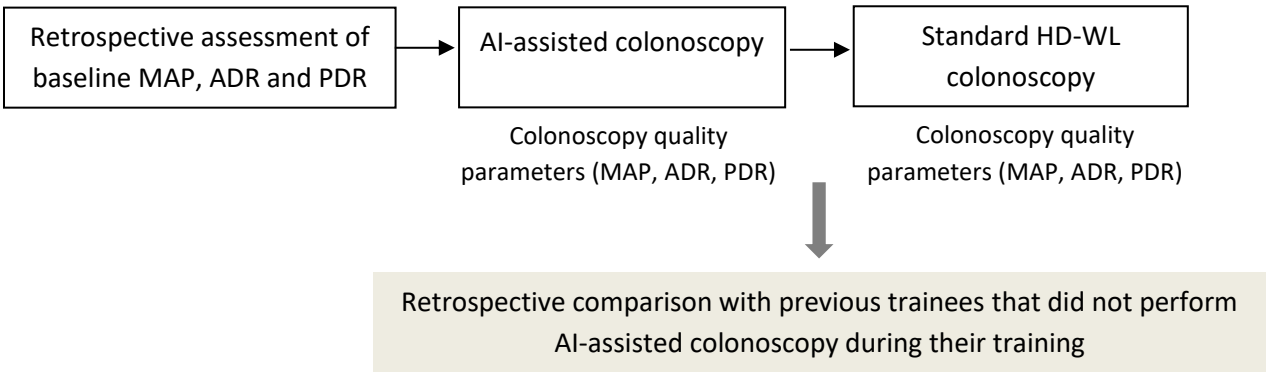
Our centre performs more than 3000 colonoscopies annually and we have a group of experts with extensive knowledge in colonoscopy and 5 residents in training that will help in our study. We also have experience in performing RCTs and we are one of the most active centres in endoscopic clinical research in Portugal. Since AI is a new field that is emerging in endoscopy there are few studies, particularly in western countries. Therefore, we do not have any preliminary data on this subject. However, previous international studies have demonstrated that there is a variation in ADR with AI-assisted colonoscopy according to the baseline ADR. Thus, we strongly believe that AI-assisted colonoscopy will also have a significant impact on young Gastroenterologists' training. For the implementation of this study, we will count on the collaboration of Medtronic®, which will allow the use of their CADe system named GI Genius®.

4. Research design and methodology

Study design. We will perform an exploratory prospective cohort study comparing the use of AI-assisted vs HD-WL colonoscopy during Gastroenterology training on trainees' colonoscopy quality parameters. **Study population.** Our population will include Gastroenterology trainees, >18 years old, with less than 1000 colonoscopies. **Endpoints.** The primary endpoint will be the mean number of adenomas detected per colonoscopy (MAP). Secondary endpoints will be the adenoma detection rate (number of patients with at least 1 adenoma/total number of participants) and the polyp detection rate (number of patients with at least 1 polyp/total number of participants). **Study Protocol.** Written and oral informed consent will be obtained before the initiation of the study. Only patients >40 years old, able to give informed consent, admitted for diagnostic or screening colonoscopy (including clarification of gastrointestinal symptoms/signs, post-polypectomy surveillance and positive faecal occult blood test) will be selected for performing colonoscopy. Exclusion criteria will be known polyposis syndromes, primary sclerosing cholangitis, inflammatory bowel disease, personal history of colorectal cancer, previous colonic resection, inadequate bowel preparation (defined as Boston Bowel Preparation Scale < 2 in any colonic segment) or any contraindication for polypectomy (eg, use of anticoagulants). An artificial intelligence-based medical device (GI Genius, Medtronic®) developed on a deep-learning architecture with the aid of endoscopists and modellers will be used. This CADe system will be connected to the endoscope and monitor, and the output images will be presented in real-time, on the endoscopy screen, as a green box surrounding the target polyp. All colonoscopies will be performed with Olympus™ 180 and 190 series colonoscopes. A minimum withdrawal time of 6 min will be required. All detected lesions will be removed on withdrawal of the colonoscope, and histopathology findings will be used as the reference standard. For the comparison of the quality parameters in colonoscopy during training with AI-assisted and HD-WL colonoscopy, each selected trainee will be asked to perform 75 colonoscopies with the use of AI followed by 75 colonoscopies with standard HD-WL colonoscopy. Colonoscopies with and without AI will be performed sequentially to evaluate the impact of the use of AI during training on future adenoma detection without the use of AI. In both groups, only inputs from the trainees will be recorded. Quality parameters such as MAP, ADR and PDR will be recorded. Information regarding baseline MAP, ADR and PDR (previous to the inclusion in the study), will also be retrospectively collected, in order to be included in this comparison (Figure 1). Other variables that will be collected include endoscopists and patients' baseline demographic characteristics, endoscopists' years of training and number of colonoscopies, patients' personal and family risk factors for colon cancer, colonoscope withdrawal time, Boston Bowel Preparation Scale score, any polyp's location, size, and morphological features according to the Paris classification and any complication during the procedure. During AI-assisted colonoscopy, false detections from the CADe system, defined as specific areas traced consistently by the device but not deemed as polyps after close inspection, will be recorded, alongside missed detections, defined as polyps detected by the operating

endoscopist and confirmed by histology but not alerted by the CADe system (false positive). As a secondary objective, for the comparison of the learning curve during training, colonoscopy quality parameters of the trainees enrolled in the study will be compared with a historical cohort of previous trainees that only performed colonoscopy with HD-WL colonoscopes, within the same period.

Figure 1 – Study protocol



Statistical analysis and sample size calculation. Statistical analysis will be conducted using Stata Statistical Software 16.0 (StataCorp LP, Texas). Descriptive statistics for baseline characteristics will be performed, using unpaired t-test or Wilcoxon rank-sum test as appropriate for continuous variables and chi-square test for categorical variables. To compare colonoscopy quality parameters between AI-assisted and HD-WL colonoscopy, linear regression will be used. Multivariate analysis will be performed to adjust for potential confounders and to assess the impact of the number of years of training and previous colonoscopies on the role of AI in colonoscopy training. Comparison with the historical cohort will also be performed using linear regression. A p-value of <0.05 will be considered statistically significant. According to *Repici et al.,* the use of AI allowed an increase in MAP from 0.7 to 1.07.[9] Although this study was performed with senior endoscopists, assuming the same variation in MAP for young trainees, with a standard deviation of 0.8, a total of 150 colonoscopies per trainee (75 per group – AI-assisted colonoscopy vs HD-WL colonoscopy) will be needed to ensure 80% power, with a significance level (alpha) of 0.05. **Anticipated results and potential limitations.** We believe that with our study we will be able to demonstrate that the regular use of AI-assisted colonoscopy during Gastroenterology training will allow for an increase in quality in colonoscopy in an early phase of the career, which in the future may contribute to a more efficient training and ultimately to more effective screening and prevention of CRC. The increasing number of colonoscopies performed from the AI group to the non-AI group may be considered a limitation in our study to assess the effect of AI in the improvement of colonoscopy quality parameters. However, we do believe that an increase of 75 colonoscopies is small and, therefore, it is not a significant confounder on the assessment of the effect of AI in the variation in MAP. Moreover,

our centre has a small number of trainees that fulfil the inclusion criteria and therefore, only exploratory results regarding the effect of AI in colonoscopy training will be obtained. If needed further centres will be enrolled to further validate our results. Regarding sample size, we believe that our centre, with the number of colonoscopies performed per year, will be able to recruit the necessary patients to achieve our sample size.

With this project, we hope to define the role of AI-assisted colonoscopy in Gastroenterology training.

Timeline:

The study protocol follows the Declaration of Helsinki and the protocol has already been submitted for consideration and approval by the research ethics committee. We hope to start the study in November 2021.

	2021	2022	2023
Primary endpoint -Protocol preparation and ethical approval - Patients' recruitment and data collection - Data and statistical analyses -Public presentation and publication of the manuscript	 (2 months) (2 months)	 (8 months) (2 months) (2 months)	 (2 months)

Budget:

The CADe system GI Genius® will be sponsored by Medtronic® for the development of this study, so no costs will be imputed. Only patients with indications for performing screening and/or diagnostic colonoscopy will be include, so there will be no associated costs with the exam.

Description	**Costs**
Development and monitoring of eCase report Forms	1.500€
Study coordinator (10 months)	1.200€
Indirect costs (10%)	300€
Total	3.000€

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