Artificial intelligence in the characterization of colorectal polyps: A prospective study in a clinical setting using CAD EYE®

STUDY PROTOCOL

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Brief summary

Current guidelines recommend resection and histopathological analyses of all colorectal polyps. Real-time optical diagnosis can obviate non-neoplastic polyp resection ("diagnose-and-leave-behind") and histopathological analyses of diminutive polyps ("predict-resect-and-discard") reducing healthcare and cost burden. The investigators aimed to evaluate the diagnostic accuracy of computer-aided diagnosis using CAD EYE® (Fujifilm,Germany) in real-time optical characterization of colorectal polyps compared to endoscopic diagnosis with histopathology as the gold-standard. For this purpose, a single-centre prospective study of diminutive/small colorectal polyps is ongoing.

Introduction

Worldwide, colorectal cancer (CRC) is the 4th most frequent cancer and the 3rd cause of cancer-related death. In Portugal, CRC is the 3rd most common cause and the 2nd leading cause of cancer-related mortality. In colorectal carcinogenesis, colorectal polyps (adenomatous or serrated polyps) are considered premalignant lesions. The detection of colorectal polyps and subsequent resection is effective in reducing CRC incidence and mortality and the risk of interval CRC, and is the crucial aspect of CRC prevention. Considering the detection of colorectal polyps, there is a wide variation among endoscopists in terms of skills for the detection of adenomas, the major premalignant lesions of CRC, translated into the detection rate of adenomas (ADR). ADR is considered a marker of careful inspection of colorectal mucosa, translating quality in colonoscopy, which is inversely associated with the risk of interval CRC or cancer-related death. In the context of screening colonoscopy, the minimum ADR is 25% to reduce the risk of interval

CRC and death, being predictably higher if a positive fecal occult blood test is found, although the exact value still remains to be elucidated. The detection rate of serrated polyps has been strongly correlated with ADR.

About 50% of small polyps are non-adenomatous and these polyps have no malignancy potential, especially for small polyps, whose cancer risk is extremely low (0-0.6%). The resection of these non-adenomatous polyps may increase medical costs and risks related to post-polypectomy complications (bleeding, perforation).

Real time optical diagnosis by artificial intelligence can improve the cost-benefit and efficiency of colonoscopy as an auxiliary tool in the decision making of which polyps should be resected and which polyps should be recovered for histological characterization. However, its practical application implies a negative predictive value ≥ 90% in optical diagnosis in order to don´t have implications in terms of interval CRC and medico-legal issues.

CAD EYE® (Fujifilm, Europe, Gesellschaft mit beschränkter Haftung, Dusseldorf, Germany) is a fully-automated computer program, which allows the detection of colorectal polyps as well as their histological classification using the artificial intelligence technology using deep learning, so-called REiII. When applied in a high-quality colonoscopy, it seems to improve the detection rate of polyps and the ADR in real time, during colonoscopy course. In fact, the detection of difficult lesions remains one of the major challenges in the endoscopy field in last years, particularly for flat lesions, multiple polyps and polyps located at the image periphery. The detection of colorectal polyps is shown by 3 simultaneous identifiers, 2 visual and 1 auditory. The visual identifiers correspond to a detection box in the area of suspected polyps and a semicircle at the periphery of the image, corresponding to the quadrant where the suspect polyps are located. The auditory stimulus corresponds to a volume adjustable sound signal emitted when a suspect polyps is detected. Regarding the optical characterization of histopathology, colo-rectal polyps are classified into 2 types, hyperplastic (green colour), which include hyperplastic and serrated polyps, and neoplastic (yellow colour), for adenomas and adenocarcinomas. In addition, it allows to perform this characterization in 3 confidence levels and the mapping of the position of the suspected area.

This system allows the storage of videos related to both detection and characterization of colorectal polyps, one of the recognized quality tools in colonoscopy.

The detection mode of colorectal polyps is performed in white light imaging (WLI) or Linked Colour Imaging (LCI), while the optical characterization is performed in Blue Light Imaging (BLI)

mode, without the need to fix or zoom the image. This tool is user-friendly, simple, intuitive and does not interfere with colonoscopy images.

Objectives

Primary objectives

- To evaluate the diagnostic accuracy of computer-aided diagnosis using CAD EYE® system in real-time optical characterization of colorectal polyps compared to digital chromoendoscopy;

- To evaluate the diagnostic accuracy of computer-aided diagnosis using CAD EYE® system in real-time optical characterization of colorectal polyps by comparison with histopathological analysis.

Secondary objectives

- To evaluate the diagnostic accuracy of computer-aided diagnosis using CAD EYE® system in real-time optical characterization of colorectal polyps in terms of dimension (≤5, 6-9mm and ≥10mm), location and histological type (hyperplastic, serrated sessile lesion, adenoma, adenocarcinoma);

- To evaluate the diagnostic accuracy of computer-aided diagnosis using CAD EYE® system in real-time optical characterization of colorectal polyps according to the experience of the endoscopist.

Population and methodology

Type of study

Prospective observational cohort study

Type of sample

The total number of consecutive patients who underwent elective colonoscopy with high quality of bowel preparation (at least two points per segment and at least of six points at the total score of Boston Bowel Preparation), performed at the Gastroenterology Department of the Centro

Hospitalar e Universitário de Coimbra, E.P.E., Coimbra, Portugal, with at least one identified colorectal polyp, regardless the indication for its performance.

Inclusion criteria

- Age ≥18 years
- The presence of at least one polyp in an elective colonoscopy

Exclusion criteria

- Poor bowel preparation (Boston Bowel Preparation Score <6 at the total score or <2 at one of colorectal segment)
- No recovery of excised polyps for histopathological analysis
- The presence of polyps not amenable to endoscopic excision or with contraindication for their excision at the time of colonoscopy
- The absence of explicit indication for colonoscopy

Study design

All colonoscopies will be performed by the endoscopist (trainee and experienced endoscopist) using CAD EYE® in detection mode (WLI or LCI), during colonoscopy retrieval. When a suspected polyp is identified by the endoscopist, optical characterization is performed by the endoscopist in WLI and BLI modes, in a first phase and by the CAD EYE® with BLI, in a second phase.

Methods plan

Phase 1. Brief virtual chromoendoscopy training on the characterization of colorectal polyps (WLI, LCI and BLI)

Phase 2. CAD EYE® system applied during colonoscopy retrieval:

2.1. CAD EYE® system OFF: Virtual chromoendoscopy (BLI) – independently characterization of a suspected polyp in WLI and BLI by the first endoscopist and by the second endoscopist (iconographic record)

2.2. CAD EYE® system ON: Characterization mode (BLI): Characterization of a suspected polyp by CAD EYE® and respectively level of characterization (1 to 3) (iconographic record)

Phase 3. Histopathological evaluation (pathologist with gastrointestinal expertise): Resection and recovery of a suspected polyp for anatomopathological characterization

Detailed explanation of Methods phases

Phase 1. Brief virtual chromoendoscopy training on the characterization of colorectal polyps (WLI, LCI and BLI)

Virtual chromoendoscopy training should be performed online through the BASIC e-learning platform (bli.eu/category/e-learning/). This training should be carried out by all participants enrolled in the project (trainees and experienced endoscopists) before its practical application, which will allow skills acquisition on the characterization of virtual chromoendoscopy of colorectal polyps using BLI. Additionally, a brief review of the Kudo classification of pit pattern of colorectal polyps should be carried out.

Phase 2. Evaluation of colorectal polyps in real-time - Optical characterization of colorectal polyps

The first approach on optical characterization of an identified polyp consists in the evaluation of the polyp, first in WLI mode and then in BLI mode, with CAD EYE® OFF. This evaluation should be systematically performed by two independent endoscopists in the exam room, and the evaluation of both should be recorded on a separate record sheet by the endoscopist who is not performing the examination. The two endoscopists should preferably (but not necessarily) be an experienced endoscopist and a trainee from the last few years, and the presence of at least one experienced endoscopist is mandatory. The independent evaluation is guaranteed by a phased and recorded approach: 1st step - The 1st endoscopist (endoscopist performing colonoscopy) request the polyp evaluation and written record by the 2nd endoscopist (the one who is not performing the colonoscopy) - blinded evaluation because the 1st endoscopist doesn't verbalize his evaluation); 2nd moment - when the 2nd endoscopist signals that he has completed his record, the 1st endoscopist verbally explicit his classification, which is recorded by the 2nd endoscopist. This evaluation should include the histopathological type of polyp (hyperplastic, adenoma, sessile serrated lesion or other type) and the level of confidence of the

evaluation performed (high or low). Kudo classification of pit pattern can also be recorded (optional).

Afterwards, optical characterization mode of CAD EYE® (CAD EYE® ON) in BLI mode should be activated for the evaluation of CAD EYE® optical characterization, in hyperplastic or neoplastic polyps, as well as the level of characterization (graduated from 1 to 3). The evaluation of the CAD EYE® should also be recorded by the endoscopist in the exam room who is not performing the colonoscopy, on its own record sheet.

The iconographic record of evaluated polyps in WLI and BLI modes and the evaluation video using CAD EYE® in BLI characterization mode should be done.

Phase 3. Histopathological evaluation (by pathologist with gastrointestinal expertise)

After detection and optical characterization of identified colorectal polyps, their resection should be performed by the most appropriate technique according to the size and type of polyp (cold forceps polypectomy if dimensions <3mm), cold snare polypectomy if dimension between 3-10mm and diathermic snare polypectomy/endoscopic mucosal resection if lesions >10mm) and recovery of colorectal polyp for anatomopathological characterization. Each colorectal polyp should be recovered to a separate vial. Unrecovered polyps will not be counted for comparative evaluation of optical characterization.

Statistical analysis

The diagnostic performance of CAD EYE® will be evaluated by comparison with the gold standard (histological characterization in the optical characterization phase), in terms of diagnostic accuracy, sensitivity, specificity, positive predictive value and negative predictive value. Sub-analysis can be performed regarding the size, location and histological type of polyp, as well as the expertise of the endoscopist.

Sample size calculation

For an alpha risk of 0.05 and beta risk of 0.2 for a bilateral test, it will be necessary to include 197 colorectal polyps assuming the initial pre-intervention diagnostic ratio is 0.7 and the final after-intervention ratio is 0.82.

Expected Results

It is expected that the new CAD EYE® system will have a diagnostic accuracy in the optical characterization of colorectal polyps around 78.4%, comparable to experienced endoscopists (78.4% vs 79.6%) and superior to less experienced endoscopists (70.7% vs 79.6%).(14) Thus, the new CAD EYE® system will allow optical characterization with high accuracy impacting as a decision making tool for the endoscopist in strategies based on optical diagnosis such as "diagnosis and leave behind" for diminutive polyps from sigmoid colon and rectum with high degree of confidence in hyperplastic histology and "predict, resect and discard" for diminutive polyps.

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Links

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Description: World Health Organization International Agency for Research on Cancer (IARC). Global Cancer Observatory 2018: estimated cancer incidence and mortality worldwide in 2018. [homepage on the internet]. Available from: https://gco.iarc.fr

URL: https://www.fujifilm.eu/eu/cadeye
Description: CAD EYE® (Fujifilm,Germany)

URL: https://www.fujifilm.eu/fileadmin/content/medical_systems/download/CADEYE/CAD_EYE_brochure_detection.pdf
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