


## ENDOSCOPIC POLYPECTOMY OF PRECURSOR LESIONS AS A PREVENTION FOR THE DEVELOPMENT OF COLORECTAL CANCER – INTEGRATIVE REVIEW

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### ABSTRACT

Colorectal Cancer (CRC) is the third most frequent neoplasm in the world, screening is based on early detection and prevention, colonoscopy is an exam that allows biopsy and subsequent removal of these lesions. The objective of the present study was to identify the importance of endoscopic polypectomy in the literature. Methodology: the study is carried out using the integrative literature review method, searching the Pubmed, Cochrane, and Scielo databases, using the descriptors ("colon" OR "colorectal") AND ("cancer" OR "polyp") AND ("polypectomy" OR "colonoscopy") in the period from 2017 to 2023. From a selection with two screenings, with a subsequent qualitative evaluation of what was found. Results: the sample used was 8 published articles, in which many benefits were observed in performing screening colonoscopy and polypectomy of precursor lesions, compared to other means of screening. Conclusion: the study shows the importance of polypectomy of these precursor lesions of CRC, with new advances that facilitate screening and prevention, consequently reducing the mortality rate of this disease so prevalent in the world.

**Keywords:** Colonoscopy. Colorectal Cancer. Polyps. Polypectomy.

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## INTRODUCTION

Colorectal Cancer (CRC) is one of the main public health problems worldwide. It is among the four leading causes of death, with about 1.8 million new cases and 0.88 million deaths per year. In Brazil, it is the second most common neoplasm in women and the third most frequent in <sup>1 2 men,3</sup>.

The estimated incidence of CRC in Brazil in 2023 was 45,630 cases, corresponding to an estimated risk of 21.10 cases per 100 thousand inhabitants, with 21,970 cases among men and 23,660 cases among women, corresponding to an approximate risk of 20.78 new cases per 100 thousand men and 21.41 per 100 thousand women. <sup>3</sup> Its etiology is multifactorial. <sup>4</sup>

Colorectal cancer (CRC) can be classified into sporadic, hereditary, and familial. Sporadic lymphomas, which account for 70% of cases, begin with a mutation in the Adenomatous Polyposis Coli (CAP) suppressor gene, leading to the formation of adenomas and, later, adenocarcinomas. Hereditary cancers, which represent 5%, are divided into polypoid, such as Familial Adenomatous Polyposis (FAP), which causes multiple malignant polyps, and non-polypoid, such as Hereditary Nonpolyposis Colorectal Cancer (HNPCC), associated with mutations in DNA repair mechanisms<sup>6</sup>.

Polyps can be precursor lesions of RCC, depending on their subtype, formed by the abnormal growth of mucosal cells, whose unregulated cell expansion can develop in cancer. Size is an independent predictive factor for dysplasia, larger polyps are at higher risk for advanced dysplasia and CRC. <sup>7 8</sup>

Colorectal polyps can be classified into sessile inflammatory, hyperplastic, serrated adenoma (SSAP), and adenoma. Adenomas and SSAP have the highest risk of progression to CRC, while hyperplastic and inflammatory polyps rarely become malignant. Accurate polyp classification is crucial for endoscopists and patients alike, as it reduces unnecessary resections, surgical complications, medical costs, and workload. Adenomas, with malignant potential, require early surveillance by colonoscopy. Factors such as size ( $\geq 10$  mm), villous elements, high-grade dysplasia, or the presence of three or more adenomas are strongly associated with advanced neoplasia<sup>10,11,12,13</sup>.

Serrated polyps are often difficult to detect during colonoscopy, as they can be flat and inconspicuous. All of these require early follow-up colonoscopy; Those who have cytologic dysplasia, are 10 mm or larger, or are located near the sigmoid colon may be associated with a higher risk of developing cancer <sup>13,14</sup>.

Cancer screening is based on early detection and prevention. Early detection allows early treatment and can reduce its mortality. Preventive screening consists of detecting and removing precursor lesions of cancers. Since CRC arises from precursor lesions and the survival of neoplastic patients depends largely on the stage of the disease at the time of diagnosis, screening is a form of secondary prevention<sup>15</sup>.

According to the Bethesda guidelines, screening for colorectal cancer (CRC) is targeted at individuals with a higher predisposition, including: people from families that meet the Amsterdam Criteria; those with synchronous or metachronic cancer related to HNPCC; subjects with CRC and a first-degree relative with CRC or associated extracolonic cancer; cases of cancer diagnosed before the age of 45 or adenomas before the age of 40; and individuals with right-sided RCC with an undifferentiated pattern on histopathology or signet ring, both diagnosed before the age of 45<sup>16</sup>.

The signs and symptoms of colorectal cancer (CRC) vary according to the growth and location of the tumors. Before symptoms manifest, RCC can cause occult bleeding, detectable by fecal blood tests such as the guaiac Fecal Occult Blood Test (gFOBT) and the Fecal Immunochemical Test. However, early RCC is usually asymptomatic. Colonoscopy allows direct visual inspection of the intestinal tract, enabling the detection, biopsy, and removal of lesions in the same session<sup>17</sup>.

Colonoscopy is the standard technique for exploring the colon and rectum, widely used in colorectal cancer (CRC) screening due to its high sensitivity in detecting CRC and precancerous adenomatous polyps. It allows complete examination of the colon, removal of polyps and diagnosis of small polyps, smaller than 5 mm. Endoscopic polypectomy, with low morbidity and mortality, is the main form of treatment. As the lesions can be multiple, it is essential to evaluate the entire colon up to the cecum when finding a polyp<sup>18</sup>.

Due to the development and promotion of endoscopic techniques, and increased awareness of endoscopic examination for the prevention and treatment of CRC, polyps <10 mm in size account for 90% of all colorectal polyps detected. However, tiny, small polyps are rarely highly dysplastic, while large, especially non-pedicated polyps tend to be high-grade neoplasms and are at high risk of being cancerous. Therefore, the removal of these lesions is of significant importance for the prevention of CRC and reduction of related mortality. For endoscopic resection of lesions without signs of submucosal invasion, Cold Polypectomy is recommended for lesions smaller than 10 mm, and Warm Polypectomy is suggested for pedicled lesions larger than 10 mm. In addition, Endoscopic Mucosal

Resection (EMR) or mucosectomy is a less invasive, effective and safe technique, recommended for non-pedicated lesions with 10 to 20 mm. <sup>19</sup>

Endoscopic Submucosal Dissection (ESD) is an effective and safe treatment that allows the removal of neoplastic lesions, especially sessile or flat adenomatous lesions, and large colonic lesions (>2 cm). Endoscopic resection of colorectal polyps reduces the risk and mortality of colorectal cancer (CRC). Hot loop polypectomy is commonly used for small lesions ( $\leq 9$  mm), but it carries risks such as bleeding and perforation. Endoscopy societies recommend cold loop polypectomy for lesions <10 mm. The effectiveness of the procedure depends on complete resection, as residual lesions are associated with post-colonoscopy interval cancer, with rates of 3% to 14% of residual tissue. The objective is to ensure complete resection, minimizing complications<sup>22</sup>.

Tomography Colonography (CTC) is a minimally invasive and sedation-free imaging technique comparable to colonoscopy in detecting clinically significant polyps and colorectal cancer (CRC). It offers less invasion, greater comfort, safety, high precision and cost-effectiveness, in addition to allowing the detection of extracolonic lesions and complete evaluation of the colon. However, its disadvantages include exposure to ionizing radiation and the need for later colonoscopy for resection, which increases costs. Although CTC is an option for screening in asymptomatic patients, it should not replace colonoscopy, which remains the gold standard<sup>15</sup>.

## **METHODOLOGY**

### **SELECTION CRITERIA**

#### **Types of studies**

All types of studies investigating the association of intestinal polyps with the development of CRC were included.

#### **Participants**

The study population is composed of patients over eighteen years of age who underwent colonoscopy without a previous diagnosis.

#### **Intervention**

Colonoscopic polypectomy (removal of intestinal polyps) for the prevention of CRC.

## Comparator

Individuals who did not undergo colonoscopic polypectomy did not participate in any/minimal intervention or conservative treatment.

## Defects

Identify its signs and symptoms, risk factors, as well as the evolution of intestinal polyps to CRC, and its screening through colonoscopy, in addition to other possible tests. CRC incidence and mortality, all-cause mortality, harm (bleeding, perforation, screening-related death), and burden (need for additional diagnostic work-up, including colonoscopy, procedure) will also be included.

## RESEARCH STRATEGY

The databases selected for the search of studies were scientific articles in PubMed, Cochrane Library and Scielo, using Health Sciences Descriptors, defined according to the research question. Thus, a search was carried out using the descriptors related to endoscopic polypectomy and its repercussion on the reduction of the incidence of CRC, with the objective of identifying its signs and symptoms, risk factors, as well as the evolution of intestinal polyps to CRC, and its screening through colonoscopy, in addition to other possible tests.

Items from the *Extension for Scoping Reviews (PRISMA-ScR)*<sup>24</sup> will be followed to perform this study. The basic line of research will be with the use of the descriptors ("colon" OR "colorectal") AND ("cancer" OR "polyp") AND ("polypectomy" OR "colonoscopy"). Articles in English and Portuguese will be used as inclusion criteria, from 2017 to 2024, and then, those that do not meet the pre-established requirements will be excluded.

In the search, the titles and abstracts of the articles will be considered for a broad selection of probable works of interest using the following terms as keywords: colorectal cancer, polyps, colonoscopy and polypectomy, as well as filters for systematic review and meta-analysis.

## STUDY SELECTION

The main aspects analyzed in the studies included: author and year of publication, type of study, sample size and origin, evaluation methods, and main variables in each study. Subsequently, this information was organized into spreadsheets, categorized

according to specific characteristics of each study, such as main limitations, sources of funding, and declarations of interest. While two of the three researchers were responsible for collecting the data, the third was in charge of summarizing the information to understand the differences in the results.

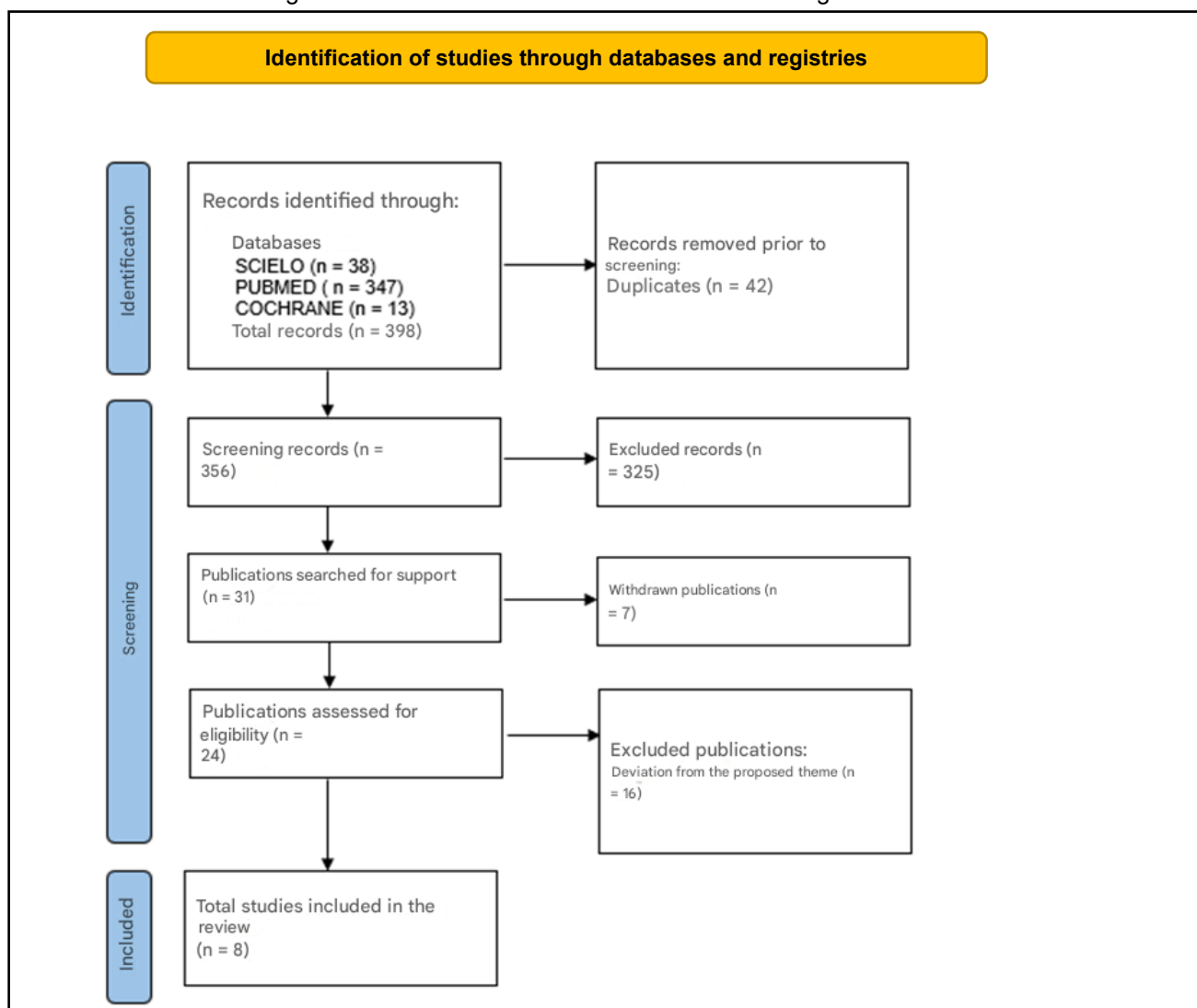
## DATA ANALYSIS

Initially, a characterization of each study was made, analyzing the main results, such as the evolution of intestinal polyps to colorectal neoplasia, based on the colonoscopic examination (gold standard) and the importance of their removal to prevent their progression. Based on the findings in each study, the diagnostic method used, the results were gathered in a table, so that the discussion could be written based on it.

## RESULTS

Using the descriptors, the search was carried out and a total of 398 articles were selected, 347 from the Pubmed database, 38 from Scielo and 13 from the Cochrane Library. 42 duplicate articles found in the different databases and a balance of 356 pre-selected articles were excluded. From this, two evaluators read the titles and abstracts of the articles, as a first screening, where articles that did not address the theme or objective of the study were excluded. From this first selection, 31 articles remained that went to a second screening, in which the evaluators did an in-depth reading of the full text and 16 publications that escaped the research question were excluded. Finally, a third reviewer resolved points of divergence in order to arrive at the 8 articles selected for review. The steps in the article selection process for this review are demonstrated in detail in flowchart PRISMA24 (Figure 1).

Figure 1 – Flowchart for the selection and screening of studies.



Source: Translated and adapted from Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al., 202024.

The studies included in this review are full literature reviews, and compare the role of endoscopic polypectomy in the prevention of CRC under different approaches, analyzing different screening tests and surgical techniques for polyp removal. In addition to the articles selected for review, there was a detailed search in the literature of recent studies, which did not meet the inclusion criteria, for a comparison of evidence with the selected articles.

Overall, the reviewed literature shows that while there are several screening methods available, colonoscopy stands out as the gold standard option for identifying and removing polyps. This is due to the fact that colonoscopy not only allows for the early diagnosis of precursor lesions, but also allows for the immediate treatment of these lesions.

## DISCUSSION

The evaluation of the results of the studies, in general, makes evident the positive impact of polypectomy on the incidence of Colorectal Cancer. Colorectal polyps are abnormal growths that form in the mucosa of the colon or rectum, which can vary in size or shape, and some have the potential to become malignant over time<sup>9</sup>. That said, through the analysis of several studies, endoscopic polypectomy has been shown to be a procedure that not only treats symptomatic polyps but also plays a crucial role in preventing CRC.

It is estimated that the use of colonoscopy in screening reduces the risk of colorectal cancer by 31% and a 50% reduction in death related to colorectal cancer, by making an early diagnosis of initial lesions. There is a significant difference in incidence and mortality rates between groups that underwent screening and those that did not, after a period of 10 years or more. The effectiveness of screening can vary based on factors such as age, family history of colorectal cancer, and adherence to screening guidelines. In general, the recommendation is to start colonoscopy screening at age 45 by the American Society of Colon and Rectal Surgeons or 50 years based on the Brazilian Society of Coloproctology, and for individuals with a family history, it should be performed 10 years before the age of diagnosis of the first-degree relative<sup>25,26</sup>.

The systematic review conducted by Jodal, et al.<sup>1</sup> in 2019, aims to evaluate and compare the efficacy of three screening methods for CRC: the fecal occult blood immunological test, sigmoidoscopy, and colonoscopy. Thus, the main findings were that the occult blood test has the lowest sensitivity compared to the other two endoscopic tests, with an ease of performance, as it is less invasive and has a lower cost. Sigmoidoscopy, on the other hand, examines only the rectum and lower colon, and is more effective in detecting cancers and polyps in the sigmoid colon and rectum, not evaluating the other segments. Finally, colonoscopy examines the entire colon and rectum, presenting itself as a more comprehensive and effective method in the detection of RCC and polypoid lesions that are precursors of this devastating disease, in addition to the removal of polyps during the procedure, being today the gold standard, however it is the most invasive and requires greater bowel preparation <sup>1</sup>.

Another diagnostic test that was compared to the effectiveness of colonoscopy was Computed Tomography Colonography. In a study conducted by Duarte et al.<sup>15</sup>, CTC is a viable alternative to colonoscopy, especially for patients who do not tolerate colonoscopy well. It can be used as a screening tool to detect CRC and assess the need for a complete



colonoscopy. However, despite being a non-invasive exam, it still does not replace colonoscopy, which in addition to detecting cancer, allows the removal of polyps and biopsies concomitantly with the diagnosis. The integration of the two techniques can bring benefits, with the initial use of CTC and colonoscopy only if necessary<sup>15</sup>.

A study by Sánchez-Peralta, et al.<sup>8</sup> investigated the use and benefits of advancing technology in a new form of screening for the detection of polyps. Deep learning is a technique that relies on the use of advanced artificial intelligence algorithms to analyze images and identify polyps during endoscopic examination, such as Convolutional Neural Networks (CNN). The NCRs showed high precision and sensitivity in the studies reviewed, especially in assisting in the analysis of difficult-to-visualize polyps that could be neglected by human examiners<sup>8</sup>. Also in the same vein, the authors Xu, et al. compared the use of CNN and the performance of the examination by human endoscopists. In direct comparison, NCRs often performed comparable to or better than human endoscopists, especially in terms of sensitivity to detect smaller or less visible polyps<sup>10</sup>.

In a review of cohort studies by authors IJspeert, et al.<sup>9</sup>, there is an analysis of the detection rate of serrated polyps and Serrated Polyp Syndrome (SPS) in screening programs for CRC in Europe. Although the prevalence of this disease is underestimated due to the difficulty in identifying these polyps, the study investigated how this subtype, less recognized compared to adenomatous polyps, is being identified during screenings with standard tests. Since both serrated polyps and SPS are associated with an increased risk of CRC, which highlights the importance of identifying them<sup>9</sup>.

Three cohorts were included in this review in which the screening test was fecal occult blood and two cohorts in which the screening was colonoscopy. The SPS rate was assessed in cohorts with known colonoscopy follow-up data and clinically relevant serrated polyps were defined as  $\geq 10$  mm and/or  $> 5$  mm in the proximal colon. From this review, the authors presented significant variations in the detection rate between the different screening programs, with the overview of the importance of improving screening strategies to identify and monitor these polyps. The conclusion of the study highlights the need to standardize and optimize screening protocols, such as better training for endoscopic detection and the global use of identical histopathological criteria to improve the clinical management of serrated polyps and facilitate more consistent practice, given the difficulty in identifying this subtype of polyps<sup>9</sup>.

Authors Iqbal et al.<sup>2</sup> pooled and analyzed data from several studies on Endoscopic Mucosal Resection (EMR) of large polyps in elderly patients, focusing on outcomes such as complication rates, procedure efficacy, and postoperative outcomes. The most common complications reported include bleeding and perforation, and most elderly patients who underwent RMS had good postoperative outcomes, with a low rate of polyp recurrence and adequate recovery<sup>2</sup>.

On the other hand, the study by Yuan et al.<sup>19</sup> compares the EMR technique and the Submucosal Endoscopic Resection (ESD) technique. From several studies analyzed, the authors reached the conclusion that EMR is effective for the removal of polyps of 10 to 20 mm and has a good rate of complete removal. However, there may be a risk of recurrence, especially in larger or more complex polyps. ESD has been shown to be more effective for larger and more complex polyps, providing a lower rate of relapse compared to EMR. However, it is a more complex technique and may have a higher risk of complications such as perforation and bleeding. The conclusion is that the choice between EMR and ESD should be based on the characteristics of the polyp, the experience of the operator, and the availability of resources. EMR is suitable for most polyps of 10 to 20 mm, but ESD may be preferable for larger polyps or polyps with more complex characteristics<sup>19</sup>.

When addressing the surgical technique of polypectomy, in the study conducted by Giri et al.<sup>22</sup> in 2022, the use of thread variations during the cold loop procedure was compared. The intervention was the use of a thin/dedicated wire loop (0.3 mm) for cold loop polypectomy compared to the use of a thick/traditional thread loop (0.47 mm) for FAP. The analysis showed that both types of hairs (thin and thick) are effective for the removal of colorectal polyps. However, the choice of wire type can influence the ease and efficiency of the procedure. Handles with thin threads can offer greater flexibility and maneuverability, which can make it easier to remove polyps in difficult places. On the other hand, thick wires can provide a feeling of greater control during the procedure. Differences in endoscopists' experience and equipment quality can also influence outcomes, as can polyp characteristics. The conclusion was that the choice between thin and thick hairs should be based on the endoscopist's experience and the characteristics of the polyp<sup>22</sup>.

Colonoscopy quality indicators also demonstrate that screening and surveillance colonoscopies provide a benefit in terms of reducing mortality and incidence of CRC. However, the procedure itself can result in adverse events. The vast majority of adverse events are minor, while serious complications include death, perforation, severe bleeding,

hospitalization, cardiovascular events, and severe abdominal pain. The American Society for Gastrointestinal Endoscopy (ASGE) recommends that perforation rates should not exceed 1/500 for all colonoscopies and post-procedure bleeding should remain below 1%<sup>27</sup>. It can be highlighted that adequate bowel preparation and cecal intubation are imperative to allow complete mucosal inspection and are therefore indispensable for the quality of the examination<sup>28</sup>.

Compared to the studies selected for review, recent literature reaffirms the importance of incorporating up-to-date surveillance guidelines into practice. The use of classification systems, such as NICE (Narrow-Band Imaging – International Colorectal Endoscopic), continues to be the current basis for characterization of polyps during examination and correct classification<sup>29</sup>. Future directions for improvement may include the incorporation of new machines, with the use of artificial intelligence and computer vision algorithms that analyze images in real time to identify anomalies that may be indicative of polyps or cancer, which has great potential to improve the efficiency and effectiveness of screening colonoscopy<sup>30</sup>. However, integrating AI systems into existing clinical workflows can be challenging and requires adjustments to current practices and technology infrastructure<sup>31</sup>.

The studies analyzed suggest that, despite the availability of several screening strategies, colonoscopy stands out as the gold standard approach for the early detection and treatment of polyps, directly impacting the reduction of the risk associated with CRC. Thus, an effective implementation of CRC screening programs for early lesion screening is necessary.

## **CONCLUSION**

The integrative review performed on endoscopic polypectomy of precursor lesions as a strategy for preventing CRC reveals the importance and efficacy of this procedure in reducing the incidence and mortality from the disease. The data analyzed demonstrate that the removal of polyps during colonoscopy, which is both a diagnostic and a treatment tool, plays a crucial role in preventing progression to CRC. Despite the emergence of new technologies and techniques, colonoscopy remains the gold standard and irreplaceable test for diagnosis associated with treatment and biopsy.

Therefore, the integration and application of this procedure in screening programs for CRC is essential to improve public health outcomes, avoiding late diagnosis. The promotion

of effective screening practices and the implementation of appropriate protocols for endoscopic polypectomy are recommended to optimize the prevention of Colorectal Cancer and thus promote the health and well-being of the population.

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