Research Article

Prospective evaluation of the effectiveness of colonoscopic polyp resection

Abstract

Background: Colon cancer incidence is on the rise and despite having undergone a colonoscopy to screen and remove all visible polyps as a preventive measure, nearly 1 in 110 patients will develop colon cancer within 3 years. The three main possible explanations for this are missing polyps, incompletely removed polyps, or rapidly growing tumors.

Objective: To determine the proportion of colonic polyps ≤ 3 cm in size that show evidence of residual polyp tissue following colonoscopy and polypectomy.

Methods: Patients who presented for colonoscopy at a community center were invited to participate in this study. Those who had confirmed adenoma were invited to repeat the procedure in 2 to 6 months with biopsies at the resection site to check for the presence of residual polyp tissue. Exclusion criteria included the absence of adenoma in the resected lesion, contraindication to polypectomy or follow-up colonoscopy, refusal to participate in follow-up examination, and other conditions increasing colon cancer risk. If polyps between 5 mm and 30 mm were found, the endoscopist resected them using the hot snare polypectomy technique or endoscopic mucosal resection (EMR).

Results: Ninety-one patients completed the study protocol, with 105 lesions being studied. The second procedure was performed between 2 and 24 months. All analyzed lesions were adenoma, and three of them were associated with intramucosal adenocarcinoma. Others included 60 tubular lesions, 37 tubulovillous lesions, and 5 serrated lesions. Thirty-two lesions were flat and were removed by EMR; polypectomy was performed for 73 lesions. There was no residual tissue in the polypectomy group. The EMR group presented three cases of incomplete resection without adenocarcinomas.

Conclusion: Our study showed that flat lesions might be an important cause of incomplete resection. In addition, we documented the complete resection of pedunculated lesions in all studied patients. This study provides more evidence to validate the empirical perception in the medical field that assumes the complete resection of pedunculated polyps. Therefore, we suggest that patients who undergo snare removal of pedunculated polyps should follow the regular protocol for colon cancer screening, with colonoscopy every 5 to 10 years. Meanwhile, the surveillance scheme should be reviewed for patients who undergo removal of flat lesions smaller than 30 mm.

Keywords: colonoscopy, polyp, polypectomy, resection effectiveness

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Introduction

Approximately 135,000 new cases of colorectal cancer occur annually in the United States, and a third of these are expected to result in death.[1] Several lines of evidence suggest that colon cancers arise from colon polyps and that it takes more than ten years for a small polyp to undergo cancerization.[2–7] This forms the basis for the current practice of post-colonoscopic polypectomy every 5 to 10 years, so that all visible metachronous polyps are removed. Investigators in the National Polyp Study estimated that colon cancer incidence could reduce by as much as 90% through serial colonoscopy and polypectomy.[8]

Colonoscopic polypectomy is an effective way to reduce colon cancer mortality.[9] It has been shown that screening leads to short-term increases in colorectal cancer incidence as a result of increased detection of prevalent cases, followed by a reduction in incidence and mortality from the disease due to subsequent polypectomies.[10] According to a recent study, the expectation for most countries is to reduce colon cancer rates by 2035. Mortality is also expected to decrease, even though the absolute number of deaths from colorectal cancer is expected to increase due to aging and population growth.[10]

However, several large prospective studies using this strategy have failed to demonstrate such a dramatic reduction in colon cancer incidence.[11–14] The compilation of data from three of these studies showed no significant difference in colon cancer incidence among patients undergoing serial colonoscopy and age-matched population-based controls.[15] Thus, despite having undergone a colonoscopy leading to removal of all visible polyps, nearly 1 in 110 patients will develop colon cancer within the next 3 years.[16]

There may be several reasons why patients undergoing serial colonoscopy develop colon cancer: polyps were missed or incompletely removed, or patients developed rapidly growing tumors.[16,17]

Two studies provided indirect evidence to suggest that incomplete polyp removal plays a very important role in the subsequent development of an interval colon cancer [cancer that develops in the interval between two surveillance colonoscopy examinations]. In the first study, Robertson et al. found that in 7 of 19 (37 %) patients with interval cancers, tumors developed at the site of a previously removed polyp.[15] In another study, Pabby et al. attributed 4 of 13 (31%) interval colon cancers to incomplete polyp resection.[18] Incompletely removed polyps contain the same advanced genetic mutations as the larger

original polyp, and may, therefore, exhibit a rapid doubling time, resulting in a total of two of the three main reasons.

Furthermore, morphology and size play important roles in the totality of polyp removal. According to this, the "SMSA" score system determines the complexity of a polyp based on four relevant factors: size, morphology, site, and access.[19]

Most experts agree that removal of large sessile polyps is often incomplete following a single attempt at colonoscopic polypectomy and recommend the repetition of colonoscopy within 6 months to ensure complete resection.[20] Data for small and medium-sized polyps constituting the vast majority of polyps encountered in clinical practice come from an abstract by Ellis et al. They showed that the presence of residual polyp tissue could be demonstrated in up to 22% of patients following colonoscopic polypectomy.[21–23] Despite limited and contrary data, it has been widely assumed that colonoscopic polypectomy is effective in completely removing small and medium-sized polyps.

There is a common mentality regarding the pedunculated morphology, assuming that they are, in general, completely removed. In addition, the "SMSA" score system for determining the complexity of a polyp attributes a high level of 3 points (3 in 3) to flat lesions, whereas pedunculated polyps receive 1 point.[19] However, few studies have analyzed the removal of pedunculated polyps. Moreover, a majority of studies in the field are restricted to the academic environment.

Thus, we aimed to determine the proportion of colonic polyps ≤3 cm in size considering morphology that shows evidence of residual polyp tissue following colonoscopic polypectomy.

Methods

This study is a real-life analysis; hence, it expresses the phenomenon outside the academic environment. Our procedures consisted of inviting patients presenting for colonoscopy at a community center to participate in this study. The endoscopic procedures were conducted by experienced endoscopists with equivalent technical skills. Bowel preparation was ensured with mannitol solution before the procedure. If patients presented with a polyp during colonoscopy, those who agreed to participate and signed the informed consent were marked with a permanent marker (tattoo) adjacent to the polypectomy site. Patients with confirmed adenoma were invited to repeat the procedure in 2 to 6 months with biopsies at the resection site to check for the presence of residual polyp tissue. This study was approved by the Ethical Committee of the Federal University MS and was performed at a single center in Brazil, by one of two experienced gastrointestinal endoscopists (more than 10 years of practice).

The inclusion criteria included a history of colon cancer screening by colonoscopy, agreement to participate in the study, and provision of written consent. Exclusion criteria were the absence of adenoma in the resected lesion, contraindication to polypectomy or follow-up colonoscopy, refusal to participate in follow-up examination, and other conditions that increase colon cancer risk (such as familial adenomatous polyposis or inflammatory bowel disease). Colonoscopy was performed guided by standard clinical practice using a 180 Olympus scope. If polyps between 5 mm and 30 mm were found, the endoscopist resected them using the hot snare polypectomy technique or endoscopic mucosal resection (EMR). If many polyps were found, only two of them were included in our analyses.

Pedunculated lesions were extracted by polypectomy, performed with conventional snare and electrocautery (usually coagulation). Flat lesions were removed by EMR, performed using saline plus methylene blue submucosal injection followed by a blend current with the snare. Furthermore, a resection of the lesion en bloc was performed in all adenomas submitted to EMR. However, if any limitations were met with the total resection of the lesion, it was completed with an endoscopic piecemeal mucosal resection of the residual polyp. Polypectomy was performed during the removal of the device following practical routine. The technical choices for resections were performed following the well-established polypectomy routines according to the European Guidelines. The polyp diameter was measured by recording the dimensions of the snare catheter.

The lesions were retrieved and sent for histological examination. The resection sites were marked with a carbon-based permanent marker. Two sub-mucosal injections of 0.5 mL of a sterile carbon black suspension for tattooing tissue during the colonoscopic procedures were made on either side of the polypectomy site. If more than two polyps were found, the endoscopist would choose the first two that met the size criteria.

Patients who presented with adenomas were invited to undergo sigmoidoscopy or colonoscopy to review and biopsy the polypectomy scar. Although the protocol requested a follow-up examination after 6 months, patients who returned up to 24 months after the initial procedure were also retained in the study. Thus, those who did not undergo a follow-up examination within 24 months were excluded.

At the time of follow-up colonoscopy, the endoscopist located the polypectomy site, defined as the scar or the colonic mucosa between the two mucosal marks made by a carbon-based permanent marker. Patients in whom the marks were not visualized were excluded from the study. The polypectomy site was biopsied during the follow-up examination 6 months after polyp resection. Biopsies were targeted towards visible mucosal alterations at the polypectomy site.

The same experienced pathologist performed all analyses. A complete polypectomy was defined as the absence of residual adenomatous tissue from the biopsy of the polypectomy site. Incomplete polypectomy was defined as the presence of residual polyp tissue by histology at the polypectomy site. The statistical significance of the results was analyzed by calculating frequencies and using traditional parametric tests as well as non-parametric tests. The difference was considered statistically significant with $p < 0.05$ by Fisher's exact probability test.

Results

From January 2010 to December 2012, there were 5967 colonoscopies, among which 1491 were screening tests. Two hundred patients agreed to participate in this study, and 91 completed the study protocol, with 105 lesions being studied.

The average age was 56 years, with 58 female patients. The second procedure was performed 11 months later on average (2–24 months). All analyzed lesions were adenoma, and three of them had associated intramucosal adenocarcinoma. The others included 60 tubular lesions, 37 tubulovillous lesions, and 5 serrated lesions.

Thirty-two lesions were flat and were removed by EMR; polypectomy was performed for 73 lesions. Table 3 shows the characteristics of lesions removed by polypectomy or EMR. The

pedunculated polyp size ranged from 5 mm to 28 mm, and the flat lesion size ranged from 5 mm to 20 mm. There was no residual tissue in the polypectomy group. The EMR group presented three cases of incomplete resection without associated adenocarcinoma. Regarding histology, patient, polyp, and colonoscopy characteristics did not differ between the complete and incomplete resection groups. There were no serious complications, bleeding, perforation, or extended hospital stay.

Discussion

Recent literature points to colonoscopic polypectomy as an effective method to reduce colon cancer mortality.[9,24–28] However, some patients develop colon cancer interval. Interval cancer is well described in the literature,[29–31] and its three main causes are missed polyps (considered the most important), fast-growing tumors, and incomplete polypectomy.[32] This study aimed to determine the proportion of incomplete resection, mainly addressing the pedunculated type, since it is assumed that pedunculated polyps are completely removed. Endoscopic resection was evaluated from the perspective of a day-to-day practice in the university environment. As far as we searched in integral text archives in medical journals, this is the first study whose analysis is based on the "real" world or community center, outside the population selections of university centers, with a non-academic population sample. Thus, we seek to avoid the so-called diagnostic bias, whose effect falls on the results leading to inaccurate conclusions.[33] Very reliable data on complete and incomplete polypectomy were presented since they are based on tissue biopsy analysis.

The results showed the absence of residual tissue after resection of pedunculated polyps in all patients and 90% of complete resection of flat lesions (RSM) (p=0.026). Incomplete resection adenomatous lesions presented a larger average size than complete flat resection lesions submitted to the same technique (2% larger). It is important to highlight that the evidence in the literature suggests that incomplete resection increases with size[11,18,21] and colon location, although the difference in size presented in this study was not significantly different, but brings greater consistency to the frequency of this event.

The higher concentration of adenomas in the ascending colon in our sample and those submitted to EMR revealed excellent technical skills of endoscopists in this study because this location is not easy to visualize (score 2 of 2 in the SMSA score). In addition, the results obtained by EMR are added to the difficulties inherent to the site and morphology. Some of these presented incomplete resection in contrast to the group whose technique was polypectomy. Despite the different methods of resection, our findings agreed with other studies[21,22] indicating that localization is an important factor in polyp resection. Lesions located in the proximal region of the colon (ascending colon) increases the risk for incomplete resection. Polyps located in colonic folds or nearby, as well as flexures, may also have impaired visibility.[21]

As for morphology, flat lesions may be more difficult to distinguish from healthy mucosa, making them a challenge for complete resection.[22] All incomplete resections revealed a flat morphology. Polyps with advanced histology such as serrated adenoma, high dysplasia, or cancer, were not verified with incomplete resection in our samples, and all adenocarcinomas and serrated adenoma lesions were completely removed. Otherwise, the lesions with incomplete resection were tubular (2/3) and tubulovillous (1/3). These results are contrary to those of other studies.[22] Despite the previous recommendation

of block removal, the choice of technique may be limited by the characteristics of the target lesion. Variations in size and location near colonic folds may require resection into fragments, called endoscopic piecemeal mucosal resection. However, many studies claim that this fragmented resection is a very important risk factor for incomplete resection, while block removal is related to complete removal.[24–26] The results of our study follow this assumption, showing that 2/3 of incomplete resection was removed by the fragmented technique.

With regard to EMR, this study presented results similar to others, since the mean incomplete resection was 10 %.[27] Jung et al. published an elegant study, analyzing cold snare polypectomy for diminutive polyps, using EMR to remove all visible tissue.[28] It was 92% successful in obtaining complete polyp resection.

Pohl et al. performed biopsies on the margins after resection had been performed.[26] The overall result showed 10% incomplete resections. As biopsies and polypectomy were performed using the same procedure, there was no evidence that residual tissue could cause recurrence, and it is important to mention that the thermal lesion used in the margins of the lesion may continue to act on the days following resection, as an inflammatory process, thereby destroying the residual tissue in some cases.

It is known that residual adenomatous tissue presents rapid regeneration and growth, and residual tumor cells acquire attributes of greater malignancy, resulting in local recurrence of lesions.[25,28] The present study differs from having followed with biopsy and analysis of the scar tissue of patients after 6 months of the procedure on average. In such a way, we increased the chance of detecting a hypothetical tumor growing in the previously resected lesion. Pohl et al. calculated that 70%–80% of interval cancers could be related to lost lesions.[32] Similar to others, our study showed that 5% to 10% of resection of flat lesions are incomplete. This is possible to infer that rapid neoplastic growth would be the cause of interval cancer in less than 10 to 15%.

Through this study, we showed that flat lesions can be an important cause for incomplete resection, similar to previous findings. In addition, we documented the complete resection of pedunculated lesions in all participants.

Pedunculated lesions do not require special follow-up. However, to date, no studies have been conducted in a scenario external to academic environments. The present study is the first to show that snare polypectomy is effective for treating pedunculated lesions. Hence, we can admit that patients undergoing removal of pedunculated polyps can follow the regular protocol for colon cancer screening, with colonoscopy every 5 to 10 years. However, the flat lesion should follow a different surveillance scheme based on present findings to ensure complete tissue removal.[18]

This study was conducted in a single center with a small sample size, and it was not a blind one (all these factors causing biases should be considered). Moreover, the type of equipment used may consist of a limiting factor, since equipment such as a wide-angle endoscope improves visualization and detection rate of adenomas, preventing lost polyps and incomplete resection, and providing margins of the lesions.[34–35]

Despite its limitations, this study confidently suggests that RM should be the focus of the investigation of new techniques, improvement of their quality, and the possibility of association[21] for better management of flat lesions.

Possible advancements in this area can reduce colorectal cancer costs and burden of the health system. We conclude that patients with flat lesions (even if less than 30 mm), should undergo a second examination for incomplete resection verification and suggest changes in the surveillance regimen, thereby shortening the scheduled surveillance interval. On the contrary, the protocol with colonoscopy every 5 or 10 years for pedunculated lesions treated with snare polypectomy is advised to be considered. We were also able to provide strong evidence that, in the non-academic population sample, that is, community pedunculated polyps are less likely to undergo incomplete resection, confirming this belief on the part of professionals in the field. Finally, considering the nature of the techniques with their indications and limitations, as well as the morphology of polyps and their implications, we raised two main points: the constant training of endoscopists instead of just reducing the interval of the tests (aiming to reduce the risk factors related to the procedure), and treatment with argon fulguration at the edges of the lesion. Both recommendations may increase the complete resection rates and minimize future complications.

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Authors' contribution

Paez L: writing of text and supervision.

Cury M: survey execution, writing of the text, data collection.

Sawhney M: supervision of text.

Elias G: survey execution.

Borges AC: statistical analysis.

Nakao F: supervision of text.

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