

Recurrence and Carcinogenetic Rates of Colorectal Polyps

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Rezumat

Recurența și carcinogeneza polipilor colorectali

Scop: de a determina rata de recurență a polipilor recto-colonici benigni într-un interval de 5 ani și de a compara rata de dezvoltare a leziunilor carcinomatoase intrapolipoide la subiecții polipectomizați față de subiecții nepolipectomizați.

Material și Metodă: un lot de 77 de pacienți diagnosticați cu leziuni polipoide recto-colonice în perioada 2014-2019 au fost supuși colonoscopiei la momentul inițierii studiului și apoi anual pe un interval de cinci ani.

Rezultate: Rata de recidivă a polipilor a crescut anual de la 5 la 12,5%; cea mai mare rată a fost observată în ultimii doi ani. Riscul cumulativ la cinci ani de leziuni neoplazice a fost de 73% la pacienții fără polipectomie și de 20% la cei cu rezecție endoscopică ($p < 0,05$).

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Comparând rata de recurență a leziunilor benigne (60%) la pacienții fără constatări neoplazice cu rata de recurență a adenoamelor la pacienții cu leziuni benigne (40%), s-a constatat un risc mai mare de recidivă în prima categorie și părea a fi influențat de istoricul personal al leziunilor adenomatoase preexistente.

Concluzie: s-a raportat un risc crescut de recidivă a polipilor colorectali pe parcursul a cinci ani; mai mult decât atât, rata de transformare malignă în primii trei ani a fost semnificativ mai mare în rândul pacienților cu polipi nerezecați sau incomplet rezecați comparativ cu cei la care rezecția a fost completă.

Cuvinte cheie: polipi colorectali, recidiva polipilor colorectali, cancer colorectal, teste imunohistochimice, colonoscopie

Abstract

Aim: to determine the recurrence rate of benign recto-colonic polyps in a 5-year interval, and compare the development rate of intrapolyoid carcinomatous lesions in polypectomized versus non-polypectomized subjects.

Material and Method: a group of 77 patients diagnosed with recto-colonic polypoid lesions during the period 2014-2019 underwent colonoscopy at the time of study initiation and then annually during a five-year interval.

Results: The recurrence rate of polyps increased annually from 5 to 12.5%; the highest rate was noted in the last two years. The five-year cumulative risk of neoplastic lesions was 73% in patients without polypectomy and 20% among those with endoscopic resection ($p < 0.05$). Comparing the recurrence rate of benign lesions (60%) in patients without neoplastic findings with the recurrence rate of adenomas in patients with benign lesions (40%), a higher risk of recurrence was found in the first category, and seemed to be influenced by the personal history of pre-existing adenomatous lesions.

Conclusion: an increased risk of colorectal polyps recurrence was reported during five year follow up; moreover, during the first three years an increased risk of malignant transformation was observed among cases in which endoscopic resection was not feasible when compared to those in which complete excision was feasible.

Key words: colorectal polyps, recurrence of colorectal polyps, colorectal cancer, immunohistochemical tests, colonoscopy

Background

Colorectal polyps are protrusion lesions that project from the mucosal surface to the colorectal lumen, with occurrence rates ranging from 1% to 43% (1). The recurrence of colorectal polyps is caused by various factors and leads to the carcinogenesis of colorectal cancer, which ranks third in incidence and second leading cause in terms of cancer-related deaths worldwide (2). Due to the high risk of

adenoma to carcinoma transformation resection is suggested for colorectal polyps (3). There is a consensus concerning the carcinogenic factors of colorectal polyps, but it is still unclear whether the factors that cause carcinogenesis are identical to those which cause recurrence. Therefore, it is necessary to elucidate the causative factors of polyp recurrence. It is postulated that the recurrent risk factors for colorectal polyps across some aspects with prophylaxis recommendations.

Colorectal polyps recur most frequently in male patients, aged >60 years, who are obese and have a long history of cigarette and alcohol preference; meanwhile, it has been demonstrated that long administration of non-steroidal anti-inflammatory drugs diminishes the risk of malignant transformation (4-7). As for genetic variation, a history of diseases and some polymorphisms are also recurrent factors (8). Proximal growth site along the colorectal wall, three or more polyps with large diameter (≥ 10 mm), and a great proportion of villous structure of polyps are present in populations at high risk of recurrence (9). Uncomplete polypectomy could delay follow-up surveillance and missed diagnosis would substantially increase the recurrence rate of colorectal polyps (10). Both the advanced colonoscopy technique and regular surveillance are recommended for patients (11). A diet that is low in fat and red meat and high in vitamin D, dry beans, fruits, and vegetables (contains flavonoids and fiber) may reduce colorectal adenoma recurrence (12,13,14).

Most colorectal cancer (CRC) arise from "classical" adenomatous polyps, through the traditional adenoma-carcinoma sequence, mostly via the well characterized chromosomal instability pathway (15,16,17). More recently, a distinct molecular pathway has been described: the serrated neoplasia pathway, accounting for approximately 30% of CRC. In this critical route to CRC, the adenoma-carcinoma sequence is accelerated, and sessile serrated lesions are the main precursor lesions (18). Colorectal malignant polyps (MP) are polyps with invasive cancer into the submucosa harboring a variable risk of lymph node involvement, which can be estimated through evaluation of morphological, endoscopic, and histologic features (19). MP are increasingly found along with the widespread use of colonoscopy. Careful endoscopic inspection of colorectal polyps is essential to distinguish between MP amenable for endoscopic resection and those requiring major oncological surgery (20). Endoscopists should be capable of performing an optical diagnosis using image enhancing techniques and should

have a profound knowledge about the endoscopic resection techniques best suited for each type of polyp. Pathological reports are then essential for further management of colorectal malignant polyps (21). The presence of high-risk features (positive margin, deep SMI (>1 mm), poorly differentiated carcinoma, lymphovascular invasion, tumor budding and piecemeal resection) indicates a need for surgery in most cases, although location, comorbidities and patient preference should be considered when making the final decision (22).

Starting from the data in the literature which appreciates an extremely varied recurrence rate of recto-colonic polyps, between 5% and 60%, variety explained largely by the type of population study – clinical trials, retrospective studies or prospective studies - we conducted a study over a period of five years (2014-2019) aiming to estimate and compare the recurrence rate of polyps and the development of colorectal cancer in polypectomized versus non-polypectomized subjects.

Material and Method

The aim of the study was to determine the recurrence rate of benign colorectal polyps during a 5 year interval and to compare the risk of malignant transformation in polypectomized versus non-polypectomized subjects, on a group of 77 patients endoscopically diagnosed with colorectal polypoid lesions during the period 2014-2019. All patients underwent colonoscopy at the time of entering the study and then annually during the five-year study period.

Written consent was obtained from all patients for clinical examination, endoscopy and polypectomy. The initial study group included 92 patients, however, complete follow up during the five year period was possible only in 77 cases.

To determine the diagnosis at the time of entry into the study, the subjects were endoscoped within the first 6 months from the start of the study. In the situation where the patients underwent several colonoscopies

before 2014, it was considered that the first endoscopic examination performed on the patient should also be the start of the prospective active follow-up. If the patients were diagnosed with concomitant benign and malignant colorectal lesions at the time of study initiation, we considered the malignant lesions as the dominant ones outranking the benign polyposis colorectal lesions.

The cases were classified into three diagnostic groups: patients without neoplastic lesions, patients with benign polypoid lesions who underwent polypectomy and patients with benign polypoid lesions who did not undergo endoscopic resection.

If colorectal carcinoma lesions appeared during the active follow-up period, the specific patient was excluded from the group; if benign polypoid lesions occurred during the active

follow-up period, the patient was reevaluated to estimate the rate of development of intrapolyoid neoplastic lesions.

At the time of the initiation of the study, in 2014, the group of 77 patients identified by colonoscopy was divided into three groups: patients with benign polypoid lesions who underwent complete endoscopic polypectomy, patients with benign polypoid lesions who did not undergo endoscopic polypectomy and patients without malignant or benign neoplastic endoscopic lesions. It should be mentioned the fact that patients in the second category were cases in which a polyp was seen during endoscopy and endoscopic polypectomy was attempted, but it was not possible as well as those cases in which a proper bowel preparation was not accomplished and therefore, polyps could not be properly identified (Fig. 1).

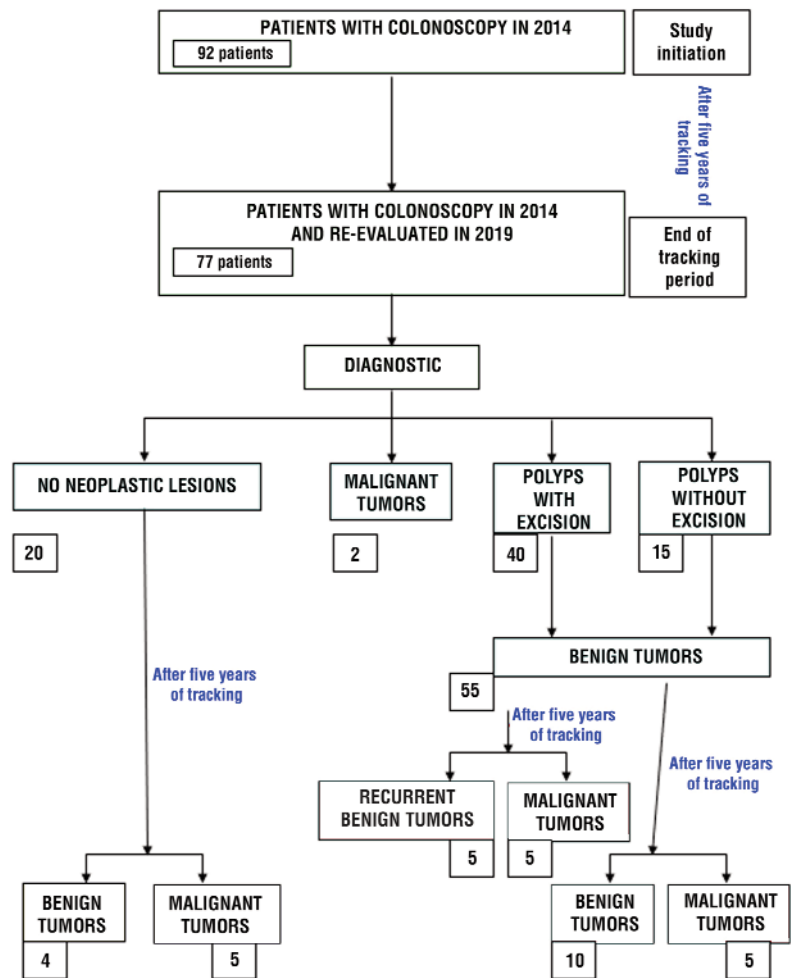


Figure 1. Flowchart of study participant selection

Two patients who were diagnosed with malignant lesions since the beginning of active follow-up and considering this, they were excluded from the study group.

In the case of patients without benign or malignant neoplastic endoscopic lesions, we evaluated the incidence of benign and/or malignant neoplasm annually and at an interval of 5 years.

In patients with endoscopically resected benign polypoid lesions at the time of the initial (diagnostic) colonoscopy, the recurrence rate of benign polyps and the incidence of malignant neoplastic transformation were monitored.

In cases with benign polypoid lesions in which polypectomy was not feasible at the initial moment due to technical difficulties or due to incomplete visualization of the incompletely prepared bowel, we evaluated only the incidence of malignant transformation. The final diagnosis of benign or malignant transformed polyps was established after performing immunohistochemical staining for p53 gene protein (p53) and for nuclear cell proliferation antigen (PCNA).

The statistical analysis of the batch was performed by the EpiInfo program and Statgraphics Plus 6.0. Quantitative variables were expressed as mean \pm standard deviation. Qualitative variables were compared by the χ^2 test or Fischer's Exact Test (2-tailed, p-level < 0.05).

Using this statistical analysis technique, it was aimed to verify the differences that appeared in patients with benign versus malignant colorectal lesions in terms of age, gender, malignant transformation of benign lesions (with or without polypectomy), incidence of colorectal adenomas in subjects without polypoid lesions at the time of inclusion in the study and the recurrence rate of rectocolonic polyps in patients with benign lesions diagnosed at the time of inclusion in the study.

Results

From the total group initiated in 2014, of 92 patients, only 77 patients had a complete

colonoscopy follow up for the next five years and were reevaluated in 2019 - the remaining 15 patients being noncompliant with this active endoscopic follow-up procedure.

Two subjects out of 77 patients remaining in the study, presented malignant neoplastic lesions, and were therefore excluded from the study group from the very beginning; 20 patients did not present adenomatous or carcinomatous colorectal polypoid lesions, while the majority of patients (55) presented benign polypoid lesions. From this last category of 55 patients with benign polypoid lesions, diagnosed at the time of initial colonoscopy, a number of 40 polyps were excised at the first endoscopic examination, while another 15 polyps were not resected due to technical reasons or due to incomplete bowel preparation (Fig. 1).

Compared to women, men in the studied group had a significantly higher rate in benign lesions (46% vs 33%, $p < 0.001$); however, in malign lesions no significant difference could be observed (5.7% versus 5.2%, $p > 0.05$). The comparative study between the age of patients and the prevalence of colorectal adenomatous and carcinomatous lesions highlighted the increase in lesional prevalence with advancing age (Fig. 2).

The results of the endoscopic screening performed in the period 2014-2019 in patients who did not present neoplastic lesions at the beginning of the study, are represented

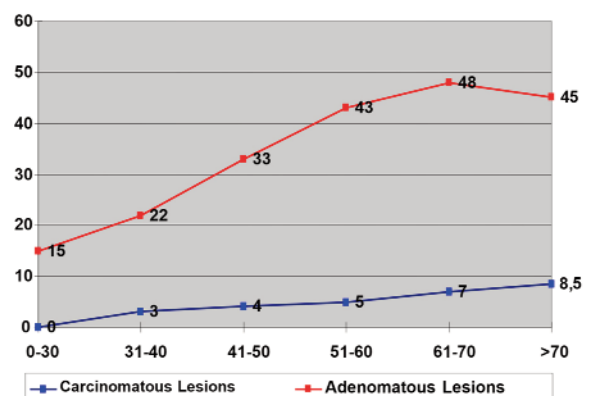


Figure 2. Age and prevalence of adenomatous lesions and colorectal carcinomas in the studied group

Table 1. Lesion diagnosis at 5 years of patients without neoplastic findings at the start of the study

| Endoscopic diagnosis | First year | | Second year | | Third year | | Fourth year | | Fifth year | |
|---|------------|-----|-------------|----|------------|----|-------------|----|------------|----|
| | No. | % | No. | % | No. | % | No. | % | No. | % |
| No neoplastic lesions at baseline | 20 | 100 | 19 | 95 | 14 | 70 | 13 | 65 | 11 | 55 |
| They developed benign lesions from those without lesions at baseline | 0 | 0 | 1 | 5 | 4 | 28 | 3 | 15 | 4 | 20 |
| They developed malignant lesions from those without lesions at baseline | 0 | 0 | 0 | 0 | 2 | 10 | 4 | 20 | 5 | 25 |

graphically in *Table 1* and *Fig. 3*.

From the total of 20 patients who did not present neoplastic lesions (adenomatous or colorectal carcinomatous) at the start of the study, the incidence rate of benign lesions varied between 5% and 20%, with a cumulative five-year rate of 60%. In the same group of subjects, the incidence rate of malignant lesions varied between 0 and 25%, with a five-year cumulative rate of 55%. The peak of the incidence of malignant lesions developed in patients without neoplastic determinations at the beginning of the study, was constituted in the last year of the study compared to the peak of the incidence of benign lesions, which was reached in the third and in the fifth year of active endoscopic surveillance.

The validate the strict adenomatous character (*Fig. 4*) and the polypous carcinomatous character (*Figs. 5, 6*) in this group of subjects it was performed the immunohistochemical method of p53 and PCNA dosage.

Table 2 shows the results of the subjects diagnosed with recto-colonic adenomas at the time of study initiation. This group consisting of 55 subjects, was divided into two subgroups, depending on the type of endoscopic instru-

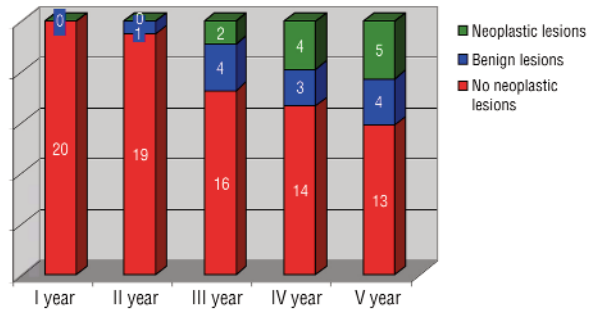


Figure 3. The lesional diagnosis at 5 years of patients without neoplastic findings at the start of the study

mentation performed during the first diagnostic colonoscopy. Thus, in the group of subjects who underwent endoscopic polypectomy, we investigated the recurrence rate of adenomas and the incidence rate of carcinomas; in subjects who did not undergo endoscopic resection, we only followed the incidence rate of malignant lesions. The recurrence rate of polyps increased annually from 5 to 12.5%; the highest rate was noted in the last two years. In order to follow the effect of polypectomy on the risk of malignant determinations, we compared the incidence rate of malignant

Table 2. Lesion diagnosis after five years of patients with endoscopic polyps (resected versus non-resected)

| Patients with benign lesions | First year | | Second year | | Third year | | Fourth year | | Fifth year | |
|---------------------------------|------------|-----|-------------|-----|------------|-----|-------------|------|------------|------|
| | No. | % | No. | % | No. | % | No. | % | No. | % |
| Colonoscopy with polypectomy | 40 | 100 | 40 | 100 | 40 | 100 | 40 | 100 | 40 | 100 |
| Recurrent benign lesions: | 0 | 0 | 2 | 5 | 4 | 10 | 5 | 12.5 | 5 | 12.5 |
| Colonoscopy with polypectomy | 40 | 100 | 40 | 100 | 40 | 100 | 40 | 100 | 40 | 100 |
| Malignant lesions: | 0 | 0 | 0 | 0 | 2 | 5 | 1 | 2.5 | 5 | 12.5 |
| Colonoscopy without polypectomy | 15 | 100 | 15 | 100 | 15 | 100 | 15 | 100 | 15 | 100 |
| Malignant lesions: | 0 | 0 | 0 | 0 | 3 | 20 | 3 | 20.0 | 5 | 33.3 |

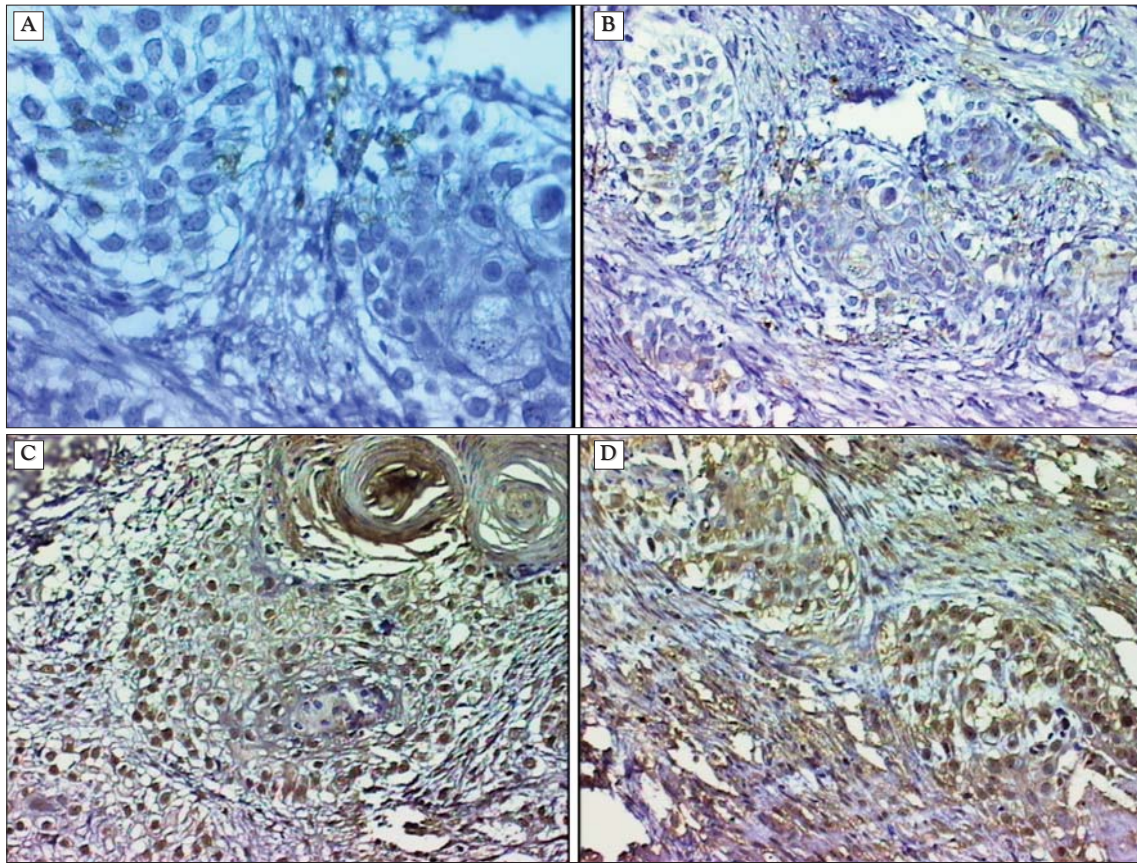


Figure 4 (A,B,C,D). Histological fragments with strictly adenomatous areas of villous polyps from the group of subjects who did not present neoplastic lesions at the beginning of the study

lesions in the two groups of subject, those with and without polypectomy.

The result was as expected: the five-year cumulative risk of neoplastic lesions was

higher in patients without polypectomy (73%) compared to the group of patients with endoscopic resection (20%), ($p < 0.05$).

In the category of patients who did not

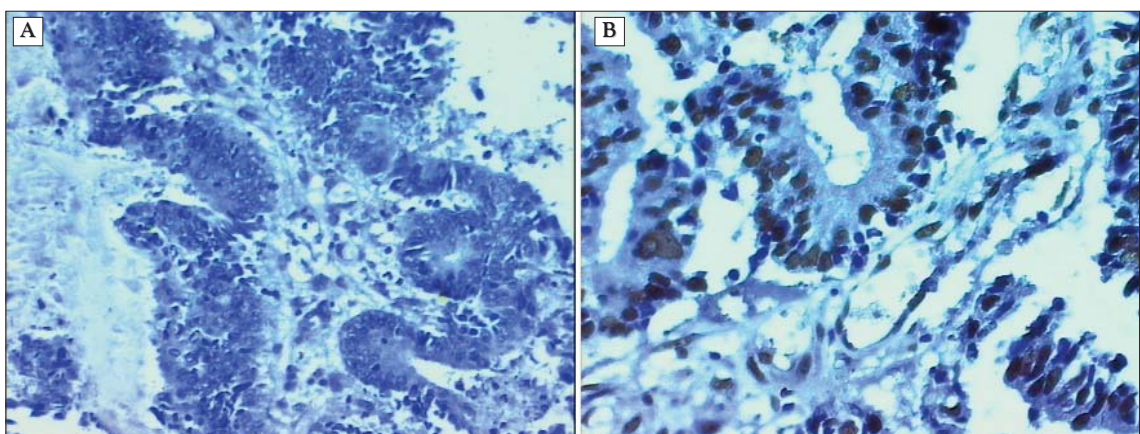


Figure 5 (A,B). Histological fragments with carcinomatous areas of villous polyps from the group of subjects who did not present neoplastic lesions at the beginning of the study. **(A)** Negative immunohistochemical reaction for p53; **(B)** Positive immunohistochemical reaction for PCNA.

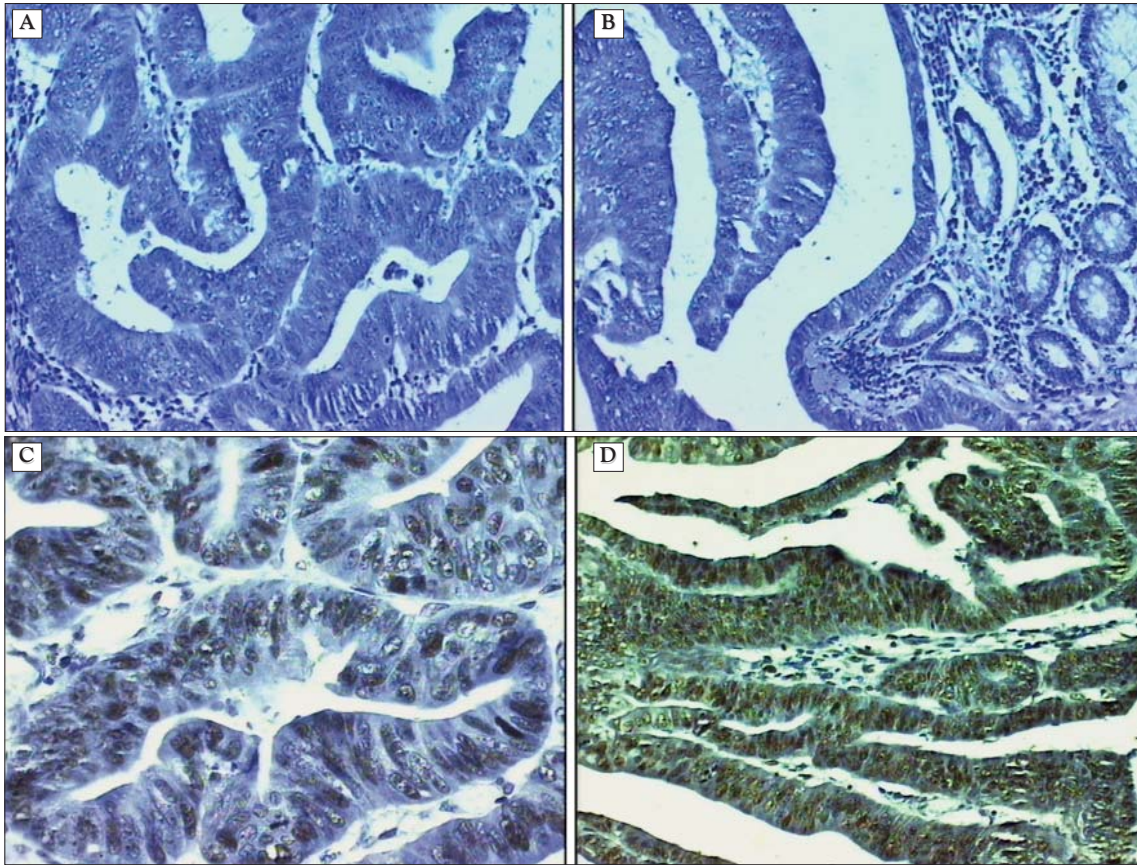


Figure 6 (A,B,C,D). Histological fragments with carcinomatous areas of villous polyps from the group of subjects who did not present neoplastic lesions at the beginning of the study. **(A)** Immunohistochemical reaction negative for p53; **(B)** Immunohistochemical reaction denytive for p53; **(C)** Immunohistochemical reaction positive for PCNA; **(D)** Immunohistochemical reaction positive for PCNA.

undergo the polypectomy procedure, the presence of malignant neoplastic lesions was highlighted by immunohistochemical measure-

ments of p53 and PCNA (*Figs. 7, 8*); in the category of patients with resection of polyps at the time of their inclusion in the group,

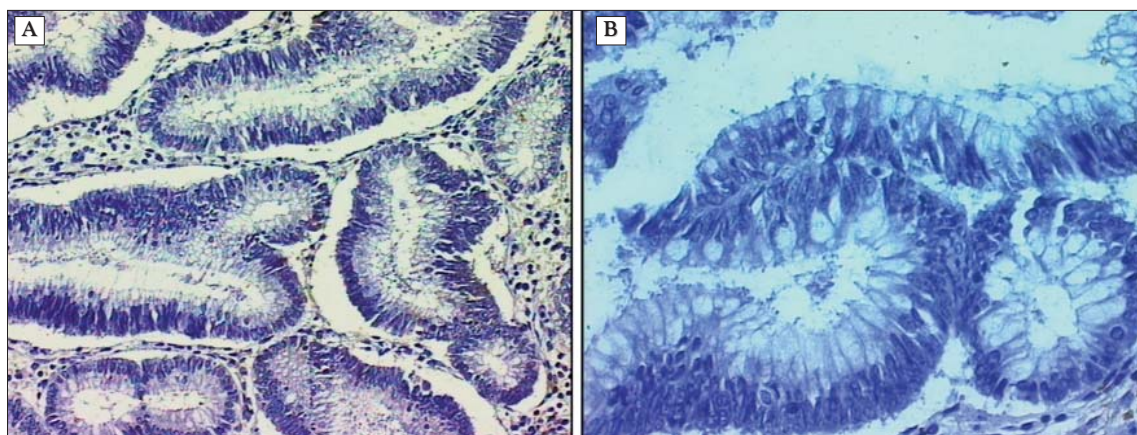


Figure 7 (A,B). Histological fragments with carcinomatous areas of polyps from the group of subjects who had polyposis lesions at the beginning of the study, without polypectomy. **(A)** Immunohistochemical reaction negative for p53; **(B)** Immunohistochemical reaction denytive for p53.

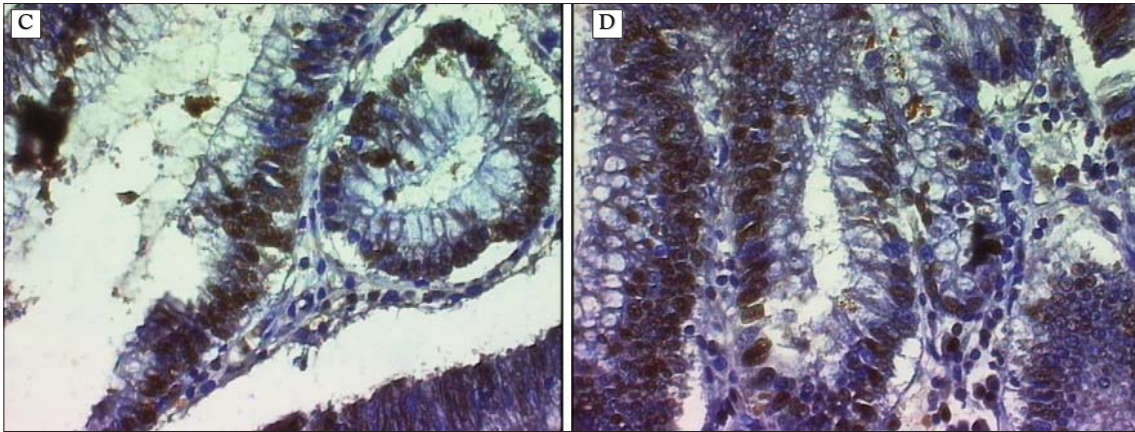


Figure 7 (C,D). Histological fragments with carcinomatous areas of polyps from the group of subjects who had polyposis lesions at the beginning of the study, without polypectomy. (C) Immunohistochemical reaction positive for PCNA; (D) Immunohistochemical reaction positive for PCNA.

immunohistochemical dosing of p53 and PCNA confirmed the presence of malignant lesions (Figs. 9, 10).

Comparing the recurrence rate of benign lesions (60%) in patients without neoplastic findings at the start of the study, with the

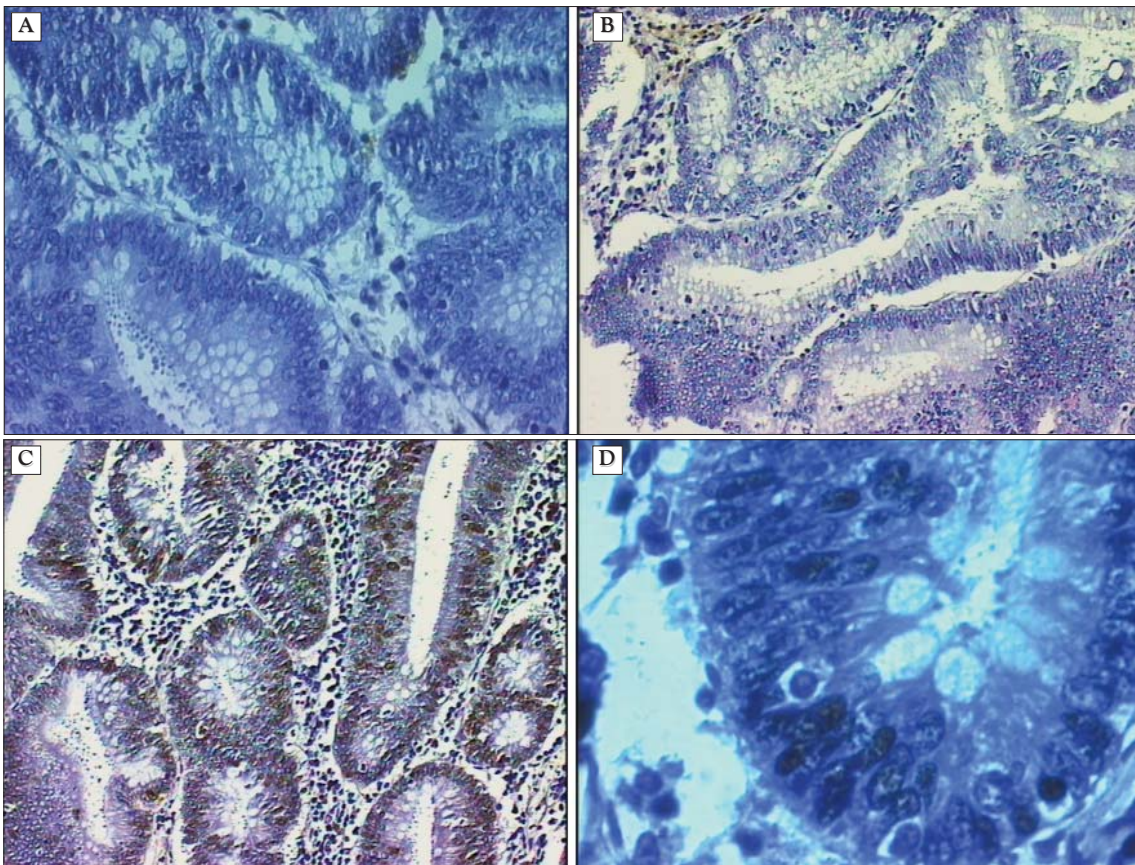


Figure 8 (A,B,C,D). Histological fragments with carcinomatous areas of polyps from the group of subjects who had polyposis lesions at the beginning of the study, without polypectomy. (A) Immunohistochemical reaction negative for p53; (B) Immunohistochemical reaction negative for p53; (C) Immunohistochemical reaction positive for PCNA; (D) Immunohistochemical reaction positive for PCNA.

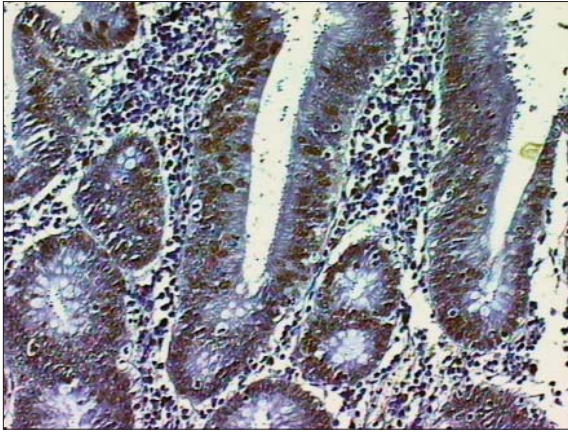


Figure 8 (E). Histological fragments with carcinomatous areas of polyps from the group of subjects who had polyposis lesions at the beginning of the study, without polypectomy
(E) Positive immunohistochemical reaction for PCNA

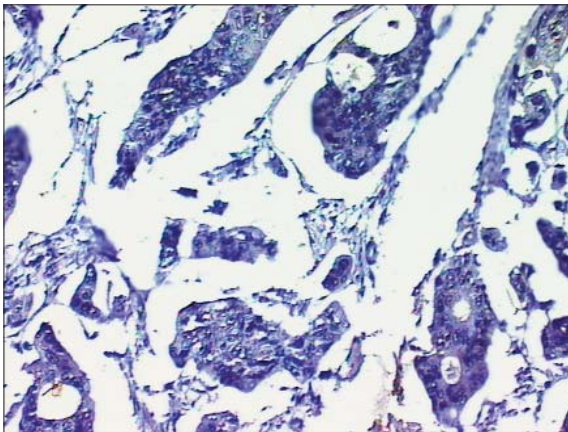


Figure 9 (A). Histological fragments with carcinomatous areas of recurrent polyps from the group of subjects who underwent resection at the beginning of the study
(A) Negative immunohistochemical reaction for p53

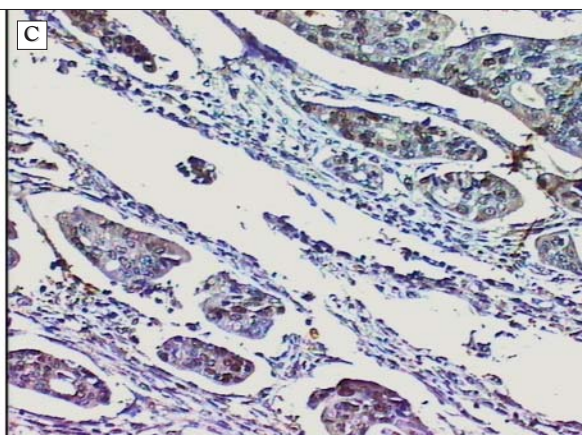
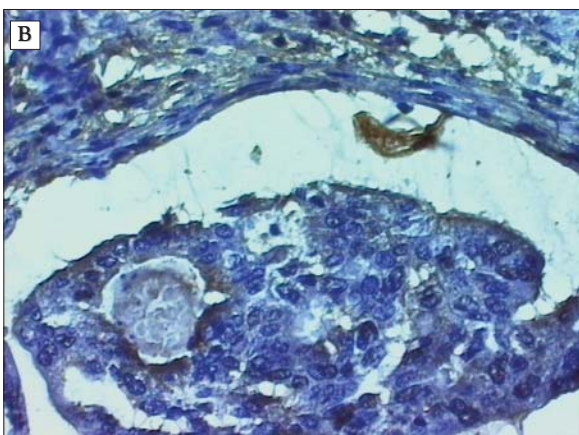


Figure 9 (A,B). Histological fragments with carcinomatous areas of recurrent polyps from the group of subjects who underwent resection at the beginning of the study.
(B) Immunohistochemical reaction positive for PCNA; (C) Immunohistochemical reaction positive for PCNA.

recurrence rate of adenomas in patients with benign lesions existing since the beginning of the study (40%), it is found that the risk of recurrence is higher in the first category of subjects; the data obtained from the study demonstrates that the risk of recurrence of polyps is less influenced by the personal history of pre-existing adenomatous lesion (*Table 1* and *Table 2*).

Discussions

The p53 gene (protein 53 KD) is responsible for malignant conversion in colorectal carcinogenesis. Normally, the p53 protein blocks aberrant cell proliferation and induces apoptosis in these DNA-damaged cells, the intimate mechanism of the event being cell cycle arrest in the G1/S phase, with DNA separation before genome replication. Under normal conditions, the p53 gene has a role as a "guardian of the genome", that is, monitoring the integrity of DNA during cell division. The protein product of the normal alleles (Wilde type) of the p53 gene negatively regulates cell growth and proliferation, blocking cells in the G1 phase of the cell cycle. The loss and/or alteration of the p53 protein, as a result of gene rearrangements, can cause the deregulation of cell growth, through replication errors and genetic accumulations. If DNA is damaged, p53 blocks

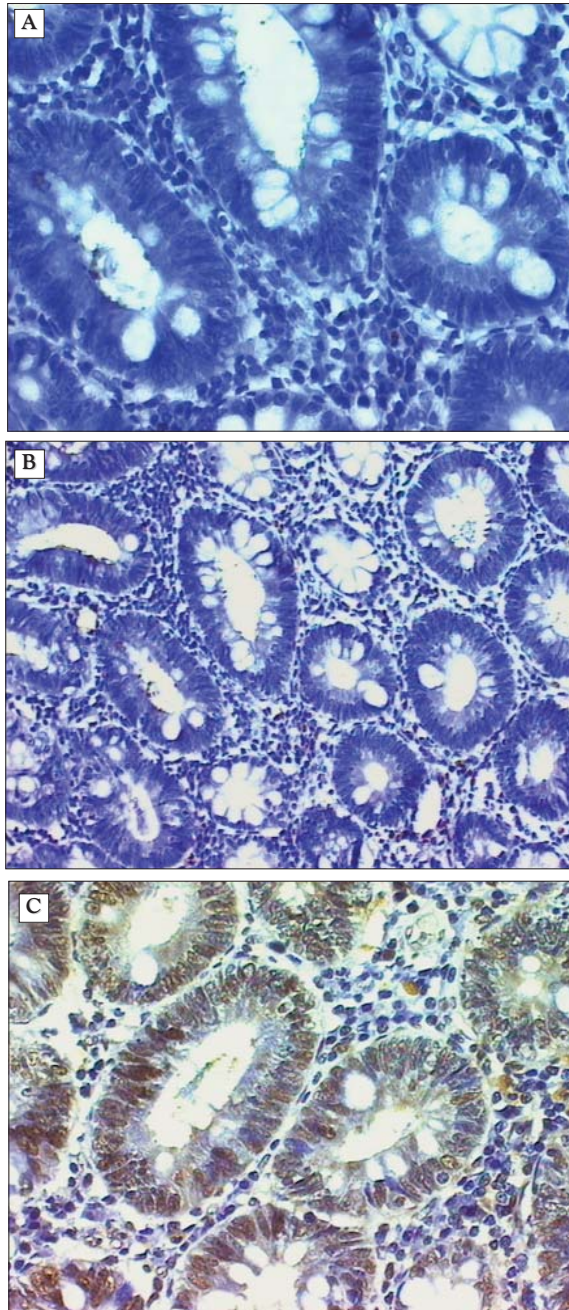


Figure 10. Histological fragments with carcinomatous areas of recurrent polyps from the group of subjects who underwent resection at the beginning of the study.
 (A) Immunohistochemical reaction negative for p53;
 (B) Immunohistochemical reaction negative for p53;
 (C) Positive immunohistochemical reaction for PCNA.

replication, favoring the activity of genome repair systems. When DNA repair fails, p53 induces cell self-destruction through apoptosis. In cells where p53 is inactivated, replication does not stop, resulting in genetic instability.

This instability is expressed during cell division, favoring a rapid selection of aneuploid clones or rearranged cells. p53 mutations are rarely detected in colorectal adenomas, indicating the late involvement of the p53 gene in the carcinogenetic process. p53 overexpression in colorectal adenomas is found in polyps with high dysplasia, with negative implications on prognosis. p53 constitutes an outpost in the molecular diagnosis of colorectal neoplasm (immunohistochemical detection of nuclear/cytosolic accumulated p53 oncoprotein, p53 antibodies) and hereditary predisposition to cancer (molecular screening to identify Li-Fraumeni syndrome), a potential indicator of poor prognosis (p53 anomalies are associated with tumors in advanced stages, with a low degree of differentiation and aggressive histological characteristics) and a potential therapeutic strategy (development of drugs that mimic the tumor-suppressive function of p53 or immunotherapeutic interventions). p53 overexpression in colorectal adenomas is found in polyps with high dysplasia, with negative implications on prognosis. p53 constitutes an outpost in the molecular diagnosis of colorectal neoplasm (immunohistochemical detection of nuclear/cytosolic accumulated p53 oncoprotein, p53 antibodies) and hereditary predisposition to cancer (molecular screening to identify Li-Fraumeni syndrome), a potential indicator of poor prognosis (p53 anomalies are associated with tumors in advanced stages, with a low degree of differentiation and aggressive histological characteristics) and a potential therapeutic strategy (development of drugs that mimic the tumor-suppressive function of p53 or immunotherapeutic interventions).

tumors in advanced stages, with a low degree of differentiation and aggressive histological characteristics) and a potential therapeutic strategy (development of drugs that mimic the tumor-suppressive function of p53 or immunotherapeutic interventions).

PCNA (proliferating cell nuclear antigen) - also known as cyclin - is an intranuclear polypeptide found in normal and tumor cells, identified as an auxiliary protein of DNA polymerase delta, in relations with DNA replication sites. There is a good correlation between the level of PCNA synthesis and the degree of cell proliferation. PCNA levels increase in the nucleus during G1 phase and decrease in G2 and M phases. There is a good correlation between the percentage of cells marked with antiPCNA antibodies, the mitotic activity and the histological grade of the tumor (Figs. 4, 5, 6, 7, 8, 9, 10).

Studies are cited in the literature in which the recurrence rate of benign colorectal polyps varies greatly. In the National Polyp Study (23) a prospective clinical trial estimated that the cumulative recurrence rate of adenomatous polyps was 41.7% when the subjects were examined colonoscopically at one year and at three years and 32%, respectively, when the colonoscopic examination it was performed only after three years of monitoring the patients. The results of the personal study carried out between 2014-2019 showed a recurrence rate of 40%, bringing up that for the period of the first three years, the recurrence rate was 15%. Although the results of the own study are close to those quoted in the literature, it must be emphasized that the population and conditions of the study were very different. Another important conclusion drawn from the National Polyp Study is that the recurrence rate is proportional to the number of polyps, their size, villous architecture and the degree of dysplasia, but also with age and family history of colorectal cancer.

When it comes to colorectal cancer surveillance, the follow up interval is usually guided by number, histology and size of resected polyps as well as of the presence of other risk factors for developing metachronous lesions (24,25). An

interesting study conducted on this issue included 122899 subjects submitted to colonoscopy; after a median follow up period of 10 years the authors reported 491 cases of colorectal cancers developed on subjects with previous adenomas - in 51 cases, with serrated polyps - in 24 cases and respectively in 42 cases with no previous lesion at colonoscopy. The risk of colorectal cancer development was higher among cases with advanced adenomas or with large serrated polyps; meanwhile, no significant differences were reported between cases with small adenomas or small serrated polyps and cases with normal colonoscopy at baseline (26). Individuals with advanced adenomas (≥ 10 mm, high-grade dysplasia, or tubulovillous or villous histology) and large (≥ 10 mm) serrated polyps had a significantly higher risk of colorectal cancer as compared with those without adenomas (RR 4.1 and 3.3, respectively). There was no significant difference in the risk of colorectal cancer between individuals with nonadvanced adenomas or small serrated polyps and those without adenomas at baseline. Another prospective study conducted on this issue included 15935 subjects submitted to colonoscopy; among these cases there were 2882 patients with advanced adenomas and 5068 non advanced adenomas. After a median follow up period of 13 years the incidence of colorectal cancer in subjects with advanced adenomas, non advanced adenomas and normal colonoscopy was 20, 9.1 and 7.5/10.000 person years. Meanwhile, the risk of colorectal cancer related death was significantly higher among cases with adenomas when compared to those with normal baseline colonoscopy. Although villosity is also considered to be predictive for metachronous colon cancer development, this fact failed to be demonstrated in other studies (27).

However, the most important risk factor for metachronous colorectal cancer development is related to the number of polyps, a direct correlation being observed (28). Therefore, a pooled analysis of four prospective studies came to demonstrate that subjects with more than four adenomas at baseline have a 24%

Table 3. Recommendations for post-colonoscopy adenoma follow-up (33)

| Baseline colonoscopy finding | Recommended interval for surveillance colonoscopy | Strength of recommendation | Quality of evidence |
|---|---|----------------------------|---------------------|
| Normal | 10 years | Strong | High |
| 1 to 2 tubular adenomas <10 mm | 7 to 10 years | Strong | Moderate |
| 3 to 4 tubular adenomas <10 mm | 3 to 5 years | Weak | Very low |
| 5 to 10 tubular adenomas <10 mm | 3 years | Strong | Moderate |
| Adenoma \geq 10 mm | 3 years | Strong | High |
| Adenoma with tubulovillous or villous histology | 3 years | Strong | Moderate |
| Adenoma with high-grade dysplasia | 3 years | Strong | Moderate |
| >10 adenomas on single examination | 1 year | Weak | Very low |
| Piecemeal resection of adenoma \geq 20 mm | 6 months | Strong | Moderate |

higher risk of developing colon cancer in future (29).

Moreover, the same study came to demonstrate that larger than 10 mm adenomas have a significantly higher risk of developing colorectal cancer (29).

The study conducted in the period 2014-2019 on a group of 77 patients with rectocolonic polyps highlighted the increase in lesion prevalence with advancing age, which corresponds to data from the literature. Since the main maneuver for actively monitoring the risk of recurrence and carcinomatous transformation of the subjects in the studied group was represented by colonoscopy, it was not possible to evaluate a series of risk factors for recurrence and carcinomatous transformation, as well as the histological type or the degree of dysplasia. Another important conclusion of the presented study is the demonstration of the increased risk of malignant transformation of colorectal adenomatous polyps polyposis present in patients without endoscopic resection, compared to subjects with polypectomized adenomatous lesions. The presented study highlights the increased risk of recurrence of colorectal polyps in a period of five years, a risk similar to that reported by studies in the literature, despite the important design differences. The high rate of recurrence and carcinomatous transformation of colorectal polyps necessitates an active prophylactic intervention. This active intervention may consist of including colonoscopy in the screening of patients who are at high risk of developing colorectal cancer and, possibly, in

the use of chemoprevention; these are potent and pertinent measures in the prevention of mortality and morbidity associated with colorectal cancer. The US recommendations for post colonoscopy follow up in subjects with normal colonoscopy or adenomas are summarized in *Table 3*. However, we should underline the fact that these recommendations do not apply to cases with hereditary colon cancer syndromes or with personal history of inflammatory bowel diseases or colon cancer (33).

Conclusions

According to our results, an increased risk of recurrence of colorectal polyps during a five year period is to be expected, demonstrating that for the period of the first three years an increased risk of malignant transformation of colorectal adenomatous polyps is expected in patients without endoscopic resection, compared to subjects with polypectomized adenomatous lesions. The high rate of recurrence and carcinomatous transformation of colorectal polyps needs an active prophylactic intervention that may consist of including colonoscopy in the screening of patients who are at high risk of developing colorectal cancer.

Author's Contributions

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Conflicts of Interests

There are no interest conflicts of interest.

Disclosure

The authors declare that they have no competing interests.

Ethical Statement

The study was conducted after receiving the Ethics committee approval no 23/2024.

Data Availability

The data generated in the present study may be requested from the corresponding author

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