What is the consequence of hyperplastic polyps ? Do adenomas and colorectal cancer develop in these patients ? A clinical study

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Abstract

Aim : **Do patients with hyperplastic polyps (HP) have an increased risk for developing adenomas and colorectal cancer (CRC) ? A study was done to detect the number of patients developing adenomas and CRC.**

Material and methods : **From 1990-1995 all patients with a HP diagnosed via endoscopy and significant follow-up were studied. The patients were separated in three groups ; Group 1 HP in patients with previous adenoma and/or CRC. Group 2 HP with a concurrent adenoma and/or CRC. Group 3 patients with only HP.**

Results : **Group 1 consisted of 20 patients, group 2 of 39 patients, and group 3 of 136 patients The follow-up was 12.5, 12.6, and 13.4 years respectively. In group 1 there was one patient with an adenoma in the index investigation. In group 2 adenomas were seen coinciding to hyperplastic polyp(s) in 29 patients, while in 11 cases there was a colorectal cancer. Obviously patients in group 3 only had hyperplastic polyps. In group 1 7 patients previously had an adenoma and 12 previously had colorectal cancer. Four patients in group 3 developed cancer : 13, 14, 15, and 15 years after the detection of a hyperplastic polyp. In group 2 only one patient developed cancer in the cecum 9 years after the index investigation. In the four patients of group 3 who developed cancer no one previously had a serrated adenoma at revision of the original histology. Twelve patients developed an adenoma.**

Conclusion : **Only five CRC's developed in patients with HP. Thus, at the best the risk for developing CRC in patients with HP is not very high and equals that of adenomas.** (Acta gastroenterol. belg., **2010**, 73, **441-444**).

Key words : hyperplastic polyps, colorectal cancer, adenomas, epidemiology, colonoscopy.

Introduction

The adenoma carcinoma sequence has been well accepted in the medical community. Follow-up endoscopy in patients with adenomas is recommended at regular intervals. It is the premise that this method will ultimately lead to a decrease in the prevalence of colorectal cancer. Besides adenomas, hyperplastic polyps in the colon and rectum are frequently diagnosed. The general believe is that hyperplastic polyps do not pose a risk factor for development of colorectal cancer. However, in recent years a new syndrome has been recognized in which multiple hyperplastic polyps are present in the colon and rectum. This syndrome poses an extra risk factor for development of colorectal cancer (1,2).

Lesions formerly classified as hyperplastic actually represent a heterogeneous group of polyps, some of which seem to have a significant risk for neoplastic transformation. These so-called serrated adenomas demonstrate characteristic molecular alterations not commonly seen in colorectal adenomas, and they probably progress to colorectal cancer by means of a new pathway : the serrated neoplasia pathway (2).

An ongoing debate in the literature discusses the necessity of follow-up endoscopy in patients with hyperplastic polyps (3). The significance of hyperplastic polyps in relation to the risk of colon cancer is unknown (4). It also is not yet clear whether patients with incidental hyperplastic polyps or serrated adenomas have an increased risk for developing colorectal cancer.

For this reason a study was done in patients with hyperplastic polyp(s) and significant follow-up in order to detect the percentage of patients developing adenomas and cancer.

Material and methods

From a time period of six years (1990-1995) all patients with the histological diagnosis of a hyperplastic polyp in the colon or rectum were retrieved from the files of the department of Pathology of the Zaans Medical Centre, the community hospital of the Zaanstreek region in the Netherlands. Obviously the diagnosis was made after colonoscopy with polypectomy or biopsy.

Patients with one or more hyperplastic polyps were included in the present study. From all patients a search was done for previous and following pathology reports in order to identify colorectal cancer, previous adenomas, and newly developed hyperplastic polyps, adenomas, or cancer during follow-up. In addition, the reports of the endoscopy department were searched for presence of the follow-up endoscopies in these patients.

Age at time of diagnosis of the hyperplastic polyp in the specified time period, gender, time of follow-up, and findings at follow-up were noted.

For the sake of the study the patients were separated in three groups : Group 1 consisted of all patients with a hyperplastic polyp in whom previously, after endoscopy,

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an adenoma and/or colorectal cancer was diagnosed. Group 2 consisted of patients in whom at time of the endoscopy not only a hyperplastic polyp was removed but also an adenoma and/or colorectal cancer were diagnosed. And finally, group 3 consisted of patients who underwent their first endoscopy and in whom only a hyperplastic polyp(s) were present.

The biopsy specimens of patients developing cancer or adenoma were re-evaluated in order to detect presence of serrated adenomas (an entity not known in the beginning of the nineties of the last century).

Statistical analysis was done with chi-square test for contingency tables and t-test. A value below 0.05 was considered statistically significant. Analysis was done on basis of intention to scope and follow-up principle.

Table 1. — **Patients who attended endoscopic follow-up at (semi)-regular basis**

	Number	follow-up present	follow-up absent
Group 1	20	8 (40%)	12 (60%)
Group 2	39	20 (51%)	19 (49%)
Group 3	136	44 (32%)	92 (68%)

P = ns.

Table 2. — **Findings at follow-up of the patients in the three different groups**

	Number	adenoma	hyperplastic polyp	cancer
Group 1	20	5 (25%)	3 (15%)	–
Group 2	39	11 (28%)	10 (26%)	1 (3%)
Group 3	136	12 (9%)	15 (11%)	4 (3%)

P = ns.

Results

In the specific time period 195 patients with hyperplastic polyp(s) were identified. The total number of endoscopies of colon and rectum in the years 1990 and 1991 was not known. In 1992, 1993, 1994, and 1995 this was 1013, 1092, 1044, and 1081 respectively.

Group 1 consisted of 20 patients (9 men, 11 women, mean age 60.9 years standard deviation 13.9, range 36-86). Group 2 consisted of 39 patients (22 men, 17 women, mean age 59.9 years SD 12.3, range 38-82), and finally group 3 comprised of 136 patients (70 men, 66 women, mean age 56.3 years, SD 14.4, range 23-82). There was no statistical difference between the three groups. Unfortunately, due to the retrospective character of the study, there was no data available on number and localisation of the polyps in all patients.

The mean follow-up time in the three groups of patients was 12.5, 12.6, and 13.4 years respectively (p = ns).

Fifty six patients died, no one in relation to colorectal cancer. There was no difference in numbers of patients that died in the three groups. Also there was no difference in follow-up time on the deceased patients.

In group 1 there was one patient with an adenoma in the index investigation. In group 2 adenomas were seen coincidental to hyperplastic polyp(s) in 29 patients, while in 11 cases there was a colorectal cancer. Obviously patients in group 3 only had hyperplastic polyps. In group 1, 7 patients previously had an adenoma and 12 previously had colorectal cancer.

Table 1 shows the patients that attended follow-up at regular basis, this is the follow-up program that was followed in the early nineties. The intensity of this follow-up has been subject of changes in the next years. Table 2 shows the findings at follow-up in patients in the three groups. Four patients in group 3 developed cancer : 13, 14, 15, and 15 years after the detection of a hyperplastic polyp. One in the sigmoid, one in the ascending colon, and two in the cecum. In group 2 only one patient developed cancer in the cecum 9 years after the index investigation. In the four patients of group 3 who developed cancer no one previously had a serrated adenoma at revision of the original histology. Twelve patients developed an adenoma. Of these six originally had a hyperplastic polyp, while in six other cases a serrated adenoma was present at histological revision.

Table 3 shows the histological characteristics of the polyps detected during follow-up. Patients in group 3 showed the highest number of tubular adenomas.

Discussion

Hyperplastic polyps are not thought to carry a malignant potential, they are usually considered to be an innocent finding. Best-practice guidelines indicate that these polyps do not require surveillance colonoscopy. Carr *et al*. assessed the prevalence of colorectal polyps of different types in an unselected population. Adenomas were found in 65% of patients, hyperplastic polyps in 30%, serrated adenomas in 4.6%, mixed hyperplastic adenomatous polyps in 0.4% (5).

Hyperplastic polyps can be heterogeneous. Recent literature suggests that some of these polyps may be morphologically and genetically distinct and lead to microsatellite unstable colorectal cancers. There is now evidence for an alternative pathway of colorectal carcinogenesis implicating hyperplastic polyps and serrated adenomas (2,3). Most are innocuous, but subsets may have malignant potential (6,7). Risk factors for neoplastic progression include multiple, large, and proximally located polyps. Aberrant methylation resulting in the silencing of cancer genes may be an important underlying mechanism, particularly in pathways progressing to tumors with DNA microsatellite instability. Lesions intermediate between hyperplastic polyp and cancer include admixed polyps and serrated adenomas (8). Serrated adenomas are histologically defined by the presence of both hyperplastic and adenomatous features.

Table 3. — **Histological characteristics of adenomas detected at follow-up endoscopy**

	group 1	group 2	group 3
Tubular adenoma	2 (40%)	7 (63%)	11 (91%)
Tubulovillous adenoma	3 (60%)	4 (37%)	1 (9%)
Villous adenoma	–	–	–
Mild dysplasia	5	8	7
Moderate dysplasia	–	3	3
Severe dysplasia	–	–	2

Glaser *et al*. defined the relationship between serrated adenomas and the future development of adenomatous polyps. A total of 17,226 colonoscopic biopsies and polypectomies were identified. Of these, 80 patients (0.5%) with serrated adenomas were found. Of all patients with serrated adenomas, 7 (9%) had concomitant CRC. Serrated adenomas are rare, but a significant association between serrated adenomas and the subsequent development of adenomatous polyps was found (9).

There are papers in the literature reporting on an increased risk of proximal cancer in patients with distal hyperplastic polyps. However, in a large study in over 2300 patients the presence of distal located hyperplastic polyps was not found to be a risk factor for proximal cancer.

The discovery of hyperplastic polyps on screening sigmoidoscopy should not prompt colonoscopy (10,11).

A new syndrome has been recognized, the hyperplastic polyposis syndrome. This syndrome is characterized by the presence of multiple hyperplastic polyps in the colon. Seven out of 13 patients (54 percent) with hyperplastic polyposis were diagnosed with colorectal cancer. Four had cancer on initial diagnosis of hyperplastic polyposis and in three the developed cancer despite frequent colonoscopic surveillance. Five of seven colorectal cancers were located in the right colon (12). In a study from New Zealand 24 patients with this syndrome were described. All were of European ancestry. All patients had small polyps (< 5 mm) however 15 (63%) had at least one polyp > or = 10 mm, the largest being 45 mm. There were 21 CRCs in 14 patients with a mean age at diagnosis of 61 years. The majority of tumors occurred in the proximal colon (13).

However, in the present study only four (2.9%) out of 136 patients with hyperplastic polyp(s) developed cancer. At revision of histology no one has a serrated adenoma. However, in the group of patients who developed an adenoma, 50% appeared to have a serrated adenoma in the index endoscopy. No patient fulfilled the definition of the hyperplastic polyposis syndrome. This number of patients developing cancer is very low. Hence, the presence of a low number of these polyps hardly can be called a risk factor. The vast majority of hyperplastic polyps are small, left-sided, and inconsequential in nature. However, hyperplastic polyps that are large, right-sided, mixed, and found in association with a family history of carcinoma may represent an "atypical" group, and their clinical significance is uncertain. It is believed that these atypical lesions should not be lumped together with the common variety of diminutive hyperplastic polyps (14). It has been suggested that transformation from serrated polyps to invasive cancers can be rapid and occurs when the lesions are small. One case was described of a sessile serrated adenoma showing rapid transformation into a submucosal invasive carcinoma in a short period of 8 months (15).

The present study reflects normal daily practice. It was done in a community hospital that does not have a specific interest in colorectal diseases. It is no referral center for adenomas and colorectal cancer. A very long follow-up was noted. Most published studies in the literature originate in tertiary referral clinics with a specific interest in these diseases. Hence, mostly biased populations are studied. The results are clear, only four colorectal cancers develop in patients in whom hyperplastic polyp(s) was diagnosed. This is not different from the one cancer in patients belonging to group 2. Patients in group 2 had a higher risk of developing cancer because they had adenomas as well. Thus, at the best the risk for developing colorectal cancer in patients with hyperplastic polyps is not very high. Obviously, all patients still alive and not in follow-up did not develop colorectal cancer. Development of adenomas of course is not sure because adenomas can be present without any clinical sign.

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