

The presence of more than two index adenomas is the strongest predictor of metachronous colon adenomas

Data from a Swiss polyp registry

Daniel Külling, Andreas D. Christ, Nidayi Karaaslan, Michael Fried, Peter Bauerfeind

Division of Gastroenterology, Department of Internal Medicine, University Hospital of Zurich, Switzerland

Summary

Question under study: To assess whether patient or adenoma characteristics at index colonoscopy could be predictors of metachronous adenomas and of advanced metachronous adenomas at first surveillance colonoscopy.

Methods: This retrospective study evaluated polypectomies of 372 adenomas in 214 patients who underwent a first follow-up colonoscopy after a median of 17 months. Logistic regression analysis was used to assess the association of baseline patient and adenoma characteristics with the development of any metachronous adenomas and of advanced adenomas (>1.0 cm, or villous component, or severe dysplasia, or early cancer).

Results: Eighty-one patients (38%) demonstrated 130 metachronous adenomas including 21 cases (10%) with advanced adenomas. The presence of more than 2 baseline adenomas was significantly associated with the finding of adenomas at

follow-up (odds ratio 2.44, 95% confidence interval 1.27–4.68, $p = 0.010$). Patient age (≥ 60 versus < 60) and size of largest adenoma (> 1.0 cm versus ≤ 1.0 cm) demonstrated borderline significance. However, neither gender, most advanced histology (tubulo-villous/villous versus tubular), nor most advanced dysplasia (severe/early cancer versus mild/moderate) at baseline colonoscopy were related with the development of metachronous adenomas. Furthermore, none of the analysed patient and polyp characteristics demonstrated an association with the development of advanced metachronous adenomas.

Conclusion: Patients with over 2 adenomas at baseline colonoscopy are at highest risk for the finding of adenomas at follow-up.

Key words: colon polyp; adenoma; colonoscopy; follow-up

Introduction

The hypothesized adenoma-carcinoma sequence has led to a widespread policy of colonoscopic polypectomy for the prevention of colorectal cancer [1]. Furthermore, colonoscopy is an integral part of the follow-up programme for patients having undergone polypectomy because of an adenomatous recurrence rate of 30–50% [2–7], which is higher than the incidence rate of adenomas [4]. Because of cost, potential complications and the inability of performing an unlimited number of examinations, efforts need to be made to identify groups of patients at higher risk for developing metachronous adenomas and, in particular,

those with a high malignant potential. Recent literature has adopted the term “advanced adenoma” to describe adenomas with a size > 1.0 cm, with tubulo-villous or villous histology, or with high-grade dysplasia or early carcinoma, features predicting an increased likelihood of malignant transformation [3, 8, 9].

We sought to reveal whether patient or adenoma characteristics at initial colonoscopy could be predictors of the development of any metachronous adenomas and of advanced metachronous adenomas at first follow-up colonoscopy.

Methods

Patients

Between the years 1986 and 2000, 1,681 colorectal polyps removed during 826 colonoscopies in 494 patients were documented in the Registry of Colorectal Polyps at the University Hospital of Zurich, Switzerland. This retrospective analysis was based on the data of the 214 patients with adenomas at index colonoscopy who underwent a first surveillance colonoscopy prior to the year 2000. From 1986 to 1996 all follow-up colonoscopies were scheduled to be performed after one year, regardless of polyp histology. After 1996, follow-up was usually carried out after 3 years, but after 6–12 months for malignant polyps. As the endoscopies were not part of a prospective study, follow-up timing may have differed by a few months from the above schedule in individual patients. Patients with gross colon cancer, inflammatory bowel disease, or familial polyposis and patients without adenoma at initial colonoscopy were excluded. Age at index colonoscopy and gender were recorded for each patient. The cut-off point for age groups was chosen at 60 years (≥ 60 versus < 60) in accordance with the published literature [3, 7].

Polyp definitions

On the basis of the National Polyp Study cohort [10], adenomas were classified as small (≤ 5 mm), medium (6–10

mm), or large (> 10 mm), and the total number of adenomas at colonoscopy was grouped as > 2 versus ≤ 2 . Adenomas were classified as tubular, tubulo-villous, or villous with mild, moderate or severe dysplasia according to the World Health Organization recommendations [11]. Adenomas with sizes over 1.0 cm, with tubulo-villous or villous histology, or with high-grade dysplasia or early cancer (carcinoma cells infiltrating the submucosa without involvement of the muscularis propria) were defined as advanced adenomas [3, 8, 9].

Analysis

If more than one adenoma was found at initial or follow-up colonoscopy, only the most advanced degree of each polyp characteristic (size, histology, dysplasia) was taken into account for evaluation. Logistic regression analysis was performed to test the association of each baseline characteristic with the development of any metachronous adenoma or of advanced metachronous adenoma. The associations were expressed using odds ratios (OR) with their 95% confidence intervals (CI). Chi-square tests with Yates' correction for continuity were used to assess the significance of the association of a baseline characteristic with the outcome. A p-value of less than 0.05 was considered significant.

Results

There were 135 male (63%) and 79 female patients (37%) with a median age of 61 years (interquartile range 54–67, full range 25–83). The median time period between index colonoscopy and follow-up colonoscopy was 17 months (interquartile range 12–24, full range 10–39).

Polyp characteristics at baseline and at follow-up (table 1)

At initial colonoscopy, 372 adenomas were found in the 214 patients. The largest adenomas demonstrated a size > 1.0 cm in 76 cases (36%). The most advanced degree of polyp histology included 98 tubulo-villous (46%) and 10 villous adenomas (5%) with 32 cases (15%) showing severe dysplasia and 5 early cancer (2%). A total of 125 patients (58%) demonstrated one or more advanced adenomas.

At follow-up colonoscopy, 130 adenomas were found in 81 patients (38%), whereas 133 individuals demonstrated no further adenomas. Among the 81 patients with metachronous adenomas, 7 (9%) demonstrated a large size > 1.0 cm, and the most advanced histology included 16 tubulo-villous (20%) and 3 villous adenomas (4%) with 4 severe dysplasias (5%). There was no adenoma with early cancer at follow-up. Twenty-six percent of the patients with metachronous adenomas demonstrated advanced adenomas resulting in a 10% rate of metachronous advanced adenomas, compared to the 214 patients with adenomas at initial colonoscopy.

Association of baseline characteristics with outcome (figures 1 and 2)

By logistic regression analysis, the presence of more than 2 baseline adenomas was significantly associated with the finding of adenomas at follow-up (OR 2.44, 95% CI 1.27–4.68, $p = 0.010$) (fig. 1).

Table 1

Polyp characteristics at baseline and follow-up colonoscopy. Data are expressed as number of patients (percentage).

Characteristic	Baseline	Follow-up
Patients with adenoma	214 (100%)	81 (100%)
Number of adenomas per patient	125 (58%)	57 (70%)
1	54 (25%)	13 (16%)
2	18 (8%)	4 (5%)
3	17 (8%)	7 (9%)
≥ 4		
Size of largest adenomas (cm)	53 (25%)	45 (56%)
≤ 0.5	85 (40%)	29 (36%)
0.5–1.0	76 (36%)	7 (9%)
> 1.0		
Histology of worst adenomas	106 (50%)	62 (77%)
Tubular	98 (46%)	16 (20%)
Tubulo-villous	10 (5%)	3 (4%)
Villous		
Dysplasia of worst adenomas	106 (50%)	53 (65%)
Mild	71 (33%)	24 (29%)
Moderate	32 (15%)	4 (5%)
Severe	5 (2%)	0 (0%)
Early cancer		
Patients with advanced adenomas	125 (58%)	21 (26%)

Figure 1

Association of baseline characteristics with the development of any metachronous adenomas. OR: odds ratio; CI: confidence interval; vs.: versus.

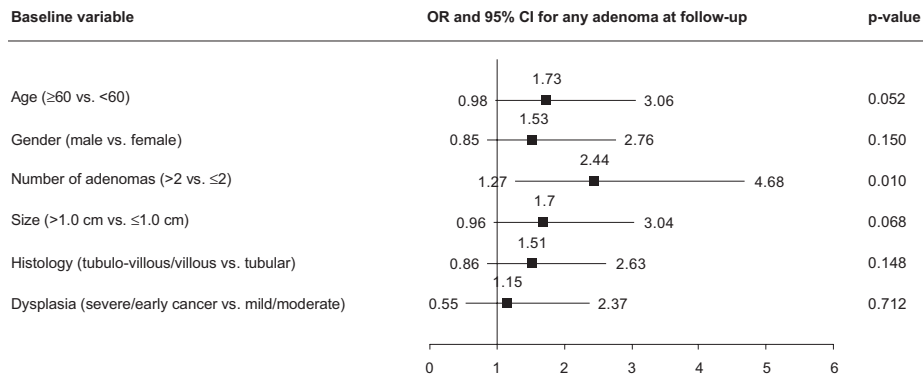
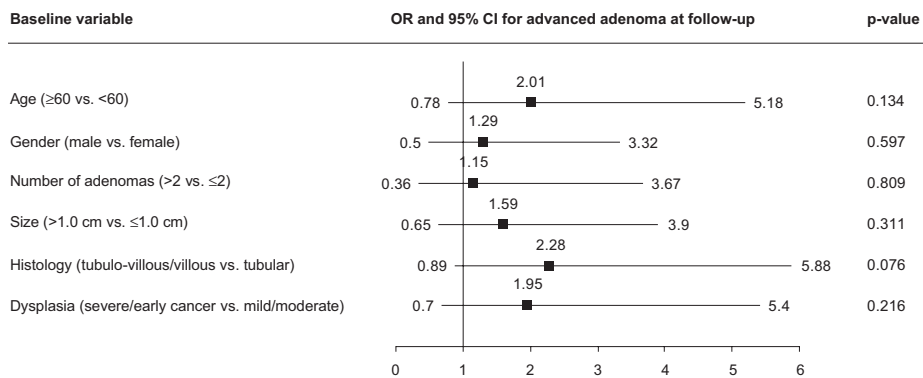


Figure 2

Association of baseline characteristics with the development of advanced metachronous adenomas. OR: odds ratio; CI: confidence interval; vs.: versus.



Fifty-four percent of patients with over 2 adenomas at initial colonoscopy developed metachronous adenomas. Patient age ≥60 years (OR 1.73, 95% CI 0.98–3.06, p = 0.052) and adenoma size >1.0 cm (OR 1.70, 95% CI 0.96–3.04, p = 0.068) were close to statistical significance for predicting metachronous adenomas. However, neither patient gender, highest degree of histology (tubulo-

villous/villous versus tubular), nor most advanced dysplasia (severe/early cancer versus mild/moderate) at baseline colonoscopy were associated with the development of metachronous adenomas. Furthermore, none of the analysed patient or polyp characteristics demonstrated an association with the development of advanced metachronous adenomas (fig. 2).

Discussion

Our analysis indicates that the presence of more than 2 adenomas at baseline colonoscopy is the strongest predictor of metachronous adenomas after a median of 17 months after endoscopic polypectomy. Fifty-four percent of patients with over 2 index adenomas demonstrated metachronous adenomas at follow-up. For comparison sake the overall adenoma recurrence rate was 38%, which confirms the published literature [2–7].

The association of metachronous adenomas with the number of index adenomas is the only finding common with previous studies on post-polypectomy follow-up [2–4, 6, 7, 12, 13]. The presence of multiple adenomas may indicate an anomalous diffuse proliferative state representing a fertile field for metachronous adenoma growth [14], while one or two single adenomas may indicate only isolated alterations of the colonic mucosa. In the latter case, endoscopic polypectomy

could have a curative significance since the focus of altered proliferation is removed.

In contrast, Rex et al. [15] found in back-to-back colonoscopies that patients with multiple adenomas were more likely to demonstrate further adenomas at a second examination than patients with none or single adenomas detected at the first examination. The authors concluded that the impact of multiple adenomas on the risk of missing an adenoma at colonoscopy may be the major factor underlying the assumed predictive value of multiple adenomas for recurrent adenomas. Our retrospective study is not able to differentiate whether the adenomas found at follow-up colonoscopy were true recurrent polyps or pre-existing polyps that had been missed at initial colonoscopy. Probably the adenomas found at follow-up colonoscopies represent a mixed collection of recurrent and persistent polyps; the latter form

being more likely with larger polyp size and a shorter time interval since the initial colonoscopy.

Apart from the number of adenomas, some studies demonstrated patient age [2], male gender [7], and polyp size [2, 12] had a predictive value of metachronous adenomas. Age and size may have reached statistical significance in our analysis, too, had the patient sample size been larger. Interestingly, not a single study found the villous histology or the grade of dysplasia to be predictive of the outcome at follow-up colonoscopy. This indicates, that the histo-pathologic examination of the removed polyps is of minor importance for the risk assessment of metachronous adenomas.

Confirming the published literature [3], 10% of our patients demonstrated metachronous adenomas with a size >1 cm, and/or villous components and/or severe dysplasia, defined as advanced adenomas [3, 8, 9]. In accordance with a recent analysis of the Polyp Prevention Study Group [6], no patient or polyp characteristic at baseline colonoscopy was predictive of advanced adenomas at follow-up in our study. In contrast, a small analysis from Greece found that advanced metachronous adenomas were detected only in patients aged 60 years or over [3]. In the American National Polyp Study [2], the number of adenomas at enrollment was a significant factor for adenomas with advanced pathological features at follow-up. Adenoma size and number were predictors of metachronous advanced adenomas in a recent study that, however, excluded patients without adenoma at follow-up colonoscopy [9].

These negative or inconsistent results indicate that there are no conclusive baseline patient or polyp characteristics allowing the identification of patients who may develop adenomas with an advanced growth pattern, and who would consequently be at a higher risk for developing malignant neoplasms. The lack of predictive parameters of the development of advanced colon adenomas may be explained in some cases by the presence of advanced mini-de-novo colorectal neoplasms. These do not follow the adenoma-carcinoma hypothesis and have been shown to exist in the European population also [16, 17].

In conclusion, due to the retrospective design the results of this study are not powerful enough to prompt changes in everyday management of such patients by neglecting the size and histology of removed polyps. However, a high number of adenomas may be considered the strongest predictor of more adenomas at follow-up. Whether the adenomas found at surveillance endoscopy are true new or just previously missed polyps is without immediate clinical significance for the patient.

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Correspondence:

*PD Dr. med. Daniel Külling
GastroZentrum Hirslanden
Seefeldstrasse 214
CH-8008 Zürich
E-Mail: kulling@gmx.ch*

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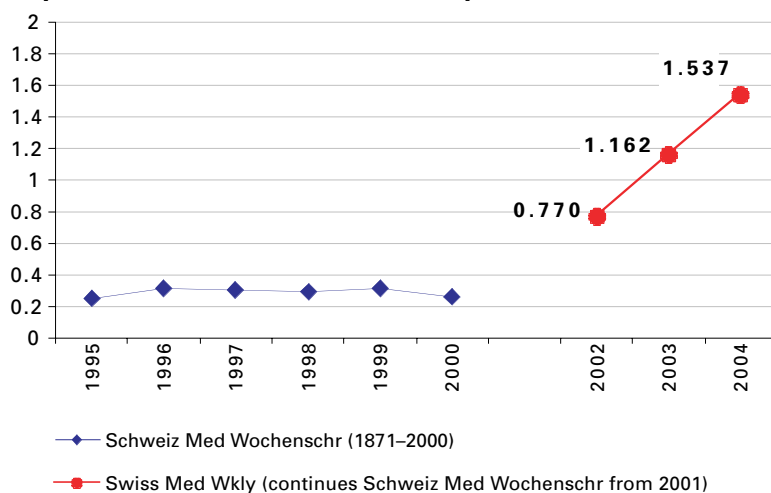
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