Colon Adenomas and Polyps Developing Synchronously, Without Carcinoma

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Background: Prevention of colorectal carcinomas is based on early detection and removal of precancerous lesions. Our goal was to perform a comparison between clinicopathological features of adenomas/polyps developed in the presence and in the absence of a colon carcinoma.
Materials and methods: We studied a total of 117 colon adenomas and polyps selected from the material of the Pathology Department of the Emergency County Hospital of Tîrgu Mureş. We compared and correlated through statistic analysis the clinicopathological factors, gender, age of the patients, localization, histological type, grade of dysplasia.
Results: 24.6% of A/P develop synchronously with a carcinoma and affect especially women and patients between 50–60 and 70–80 years; these are mainly tubular adenomas, localized more frequently in the left colon. Adenomas and polyps developed without a carcinoma are more frequent in males, in patients between 60–70 years, and are mainly tubulovillous adenomas.
Conclusions: One out of 4 colon carcinomas are associated with one or more precancerous lesions.

Keywords: adenoma, polyp, carcinoma, colon

Introduction

Colorectal cancers are a major cause of morbidity and mortality. Precancerous lesions of the colon comprise hyperplastic polyps (HP), serrated adenomas (SA) and classical adenomas: tubular adenomas (TA), villous adenomas (VA), tubulovillous adenomas (TVA) [1].

HPs are more frequent in patients between 50–60 years of age, while adenomas affect especially people of 60–70 years. HP is localized mostly to the left colon and rectum [2].

The incidence of SA has been estimated to be between 1–2.4% [3], but certain studies report even 10% [4], while predominant localization is in the recto-sigmoid [2]. The risk of malignant transformation is estimated to be between 4.3–5.8% [3,4], reaching even 10% in case of lesions over 10 mm [2].

In Western countries classical adenomas affect 50% of the population over 50 years of age, and the incidence is rising with age. Some studies report a slight predominance of males, but the difference is not significant. 60% of the adenomas are in the recto-sigmoid colon, with a less than 1 cm diameter, and 30% are larger than 1.5 cm with a villous structure and dysplasia. As the number of adenomas rises, so rises in parallel the risk of dysplasia and carcinoma (CC) occurrence; the risk of malignant transformation is greatest with VA (29–70%).

The adenoma-carcinoma sequence refers to transformation of an adenoma with mild-moderate dysplasia into an adenoma with severe dysplasia ("carcinoma in situ"), and into invasive and metastatic carcinoma [5]. Later the serrated pathway has also been described [6]. The adenoma-carcinoma sequence is characteristic to classical adenomas, and the serrated mechanism has been described especially in HP and some SA [7,8].

Material and methods

In our study we established two groups of precancerous lesions: adenomas and polyps (A/P) developing synchronously (A/P+CC), and A/P developing without colon carcinomas (A/P-CC). We correlated the clinicopathological characteristics of these tumors in order to delineate their role in colorectal carcinogenesis.

We studied a total of 117 colon adenomas and polyps (A/P) selected from the material of the Pathology Department of the Emergency County Hospital of Tîrgu Mureş. The biopsies and resection tissue pieces were fixed in buffered, neutral pH, 4% formalin solution and embedded in paraffin. The 5 μm thick sections were stained with Hematoxylin-Eosin and examined under an optical microscope (Nikon Eclipse E600).

We established two groups of precancerous lesions: A/P developing without carcinoma (A/P-CC) and A/P developing synchronously with a colon carcinoma (A/P+CC). The clinicopathological factors in focus were gender, age of the patients, histological type, and grade of dysplasia. Using statistical tests we determined the correlations between the above mentioned factors. Statistical testing was performed using the GraphPad In Stat 3.06 statistic calculation software (GraphPad Software Inc., San Diego, USA).

Results

Out of 117 A/Ps 31 (26.5%) developed synchronously with a carcinoma. The majority of A/Ps develop in males; the male/female ratio is 1.54/1. A/P+CC are more frequent in females, while A/P-CC affect especially men; the male/female ratio is 0.93/1 and 1.86/1, respectively (Table I).

The majority of A/Ps (87.1%) affect patients between 50–80 years, 11.9% develop between 20–50 years, and 0.8% over 80 years. The mean age in women and men displays no significant statistical difference (p=0.81).

A/P+CCs are diagnosed later than A/P-CCs (Table I). A/P+CC occur more frequently in two age groups (51–60 years and 71–80 years), while A/P-CC appear between

Table I. Gender, mean age and localization of the lesions

	A/P-CC	A/P+CC	A/P
Gender			
Females	30 (34.8%)	16 (51.5%)	46 (39.3%)
Males	56 (69.1%)	15 (48.3%)	71 (60.6%)
Mean age (years)	61.9±2.3	65.9±3.8	63±1.9
Localization			
Right colon	10 (19.2%)	8 (25.8%)	18 (78%)
Left colon	42 (80.7%)	23 (74.2%)	65 (22%)

A/P – adenomas/polyps, A/P-CC – adenomas/polyps developed in absence of a carcinoma, A/P+CC – adenomas/polyps developed in presence of a carcinoma

61–70 years of age; the age shows statistically significant correlation with the presence or absence of associated malignant lesions (p=0.036) (Figure 1).

A/Ps were located mainly in the left colon (Table I). A/Ps of the right colon affect more frequently males (M:F = 2:1), as opposed to those of the left colon (M:F = 1.24:1). A/P-CCs develop more frequently in the left colon (LC:RC = 4.2), as opposed to A/P+CCs (LC:RC = 2.8) (Table 1).

In our patient population the most frequent histological types were TA (46.15%) and TVA (41.02%), followed by VA (5.15%), SA (5.12%), and HP (2.56%). The histological type of A/Ps does not correlate with gender of the patients (p=0.54). HPs and SAs affect mainly patients between 20–50 years (66.6%), and are more rare after the age of 50 years (33.3%); classical adenomas are more frequent in patients over 51 years of age (89.7%) (Figure 2). All SAs and VAs, and the majority of TAs and TVAs (78%) were localized to the left colon.

A/P-CCs are more frequently TVAs (50%) and TAs (33.7%), the rest being HPs and SAs. The majority of A/P+CCs (80.6%) are TAs, and only 16.1% TVAs (Figure 3, 4). Statistically there is a significant correlation between the histological type and the presence or absence of CC associated to A/P (p <0.0001).

49.57% of A/Ps show no dysplasia. Out of those with dysplasia, the most frequent A/Ps were the ones with moderate dysplasia (23.07%). Dysplasia was absent in all HPs.

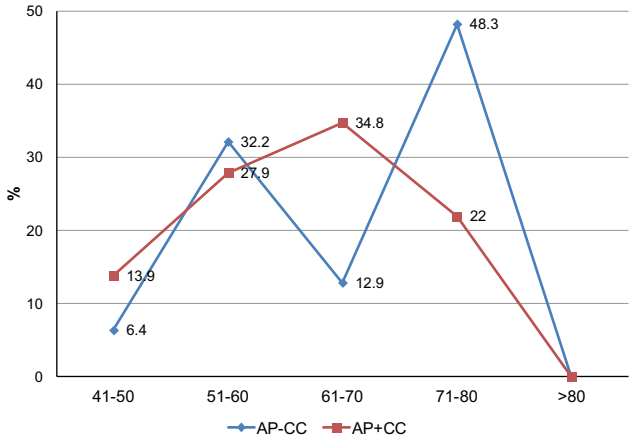

Fig. 1. Percent distribution into age groups of adenomas/polyps (A/P) developing synchronously (A/P+CC), and in absence (A/P-CC) of a carcinoma

It was demonstrated in 31.48% of TAs, in 66.6% of VAs, in 66.6% of TVAs and in 100% of SAs. Also, we noted a significant statistical correlation between the histological type and the grade of the dysplasia (p <0.0001). The grade of the dysplasia is not correlated with gender and age of the patients, and localization of the tumor; still, the number of cases without dysplasia is rising with age (Figure 5).

Discussions

Our study followed the main clinicopathological factors of colon A/Ps, focusing on whether these lesions developed synchronously or in absence of colon carcinoma.

In our patient population A/Ps developed especially in men and in patients over 50 years of age, in the left colon. National and international bibliographic data confirms our observations related to gender, age of the patients and localization of A/Ps [9–16].

There are studies stating a higher mean age: 64.6–73 years [12,14,17], or lower mean age: 46.3–50 years [13] of A/P patients as compared to our results Khan et al. [18] noted that men with A/P have a higher mean age than

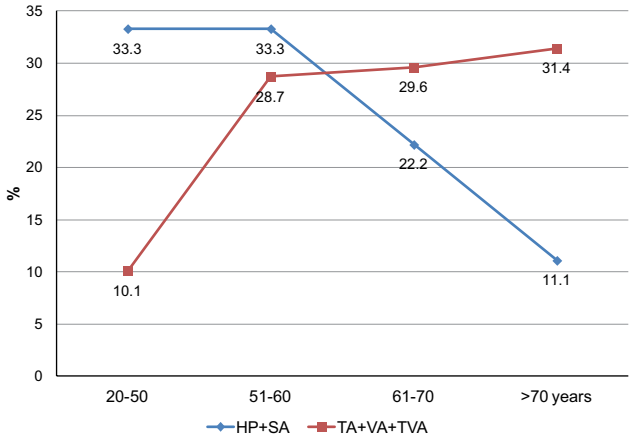

Fig. 2. The ratio between histological type of adenomas/polyps and age of the patients

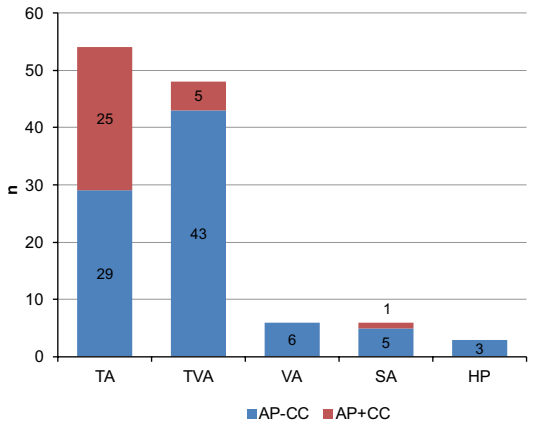

Fig. 3. Histological type of adenomas/polyps (A/P) developing synchronously (A/P+CC) and in absence (A/P-CC) of a carcinoma

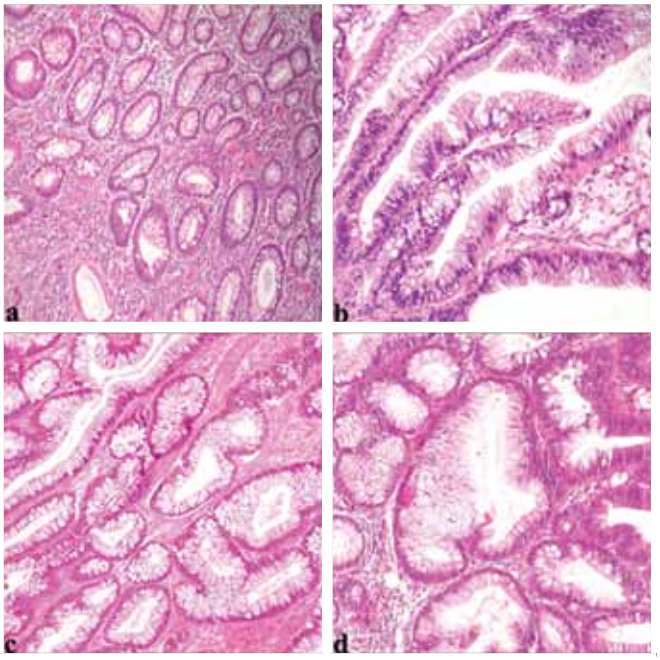

Fig. 4. (a) Non dysplastic hyperplastic polyp developed in absence of a carcinoma, HE, 10×; (b) villous adenoma with low dysplasia developed in absence of a carcinoma, HE, 20×; (c) tubulovillous adenoma with low dysplasia developing synchronously with a carcinoma, HE 10×; (d) serrated adenoma with moderate dysplasia developed in absence of a carcinoma, HE, 20×.

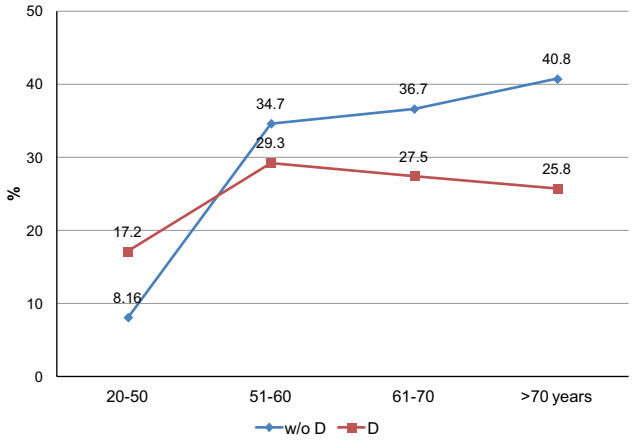

Fig. 5. The ratio between presence (D) and absence of dysplasia (w/o D) in adenomas/polyps and age of the patients

women, and Hoffmeister et al. [19] states that the mean age was approximately equal between sexes.

In our study A/Ps developed in the right colon were more frequent in men. Instead, McCashland et al. [20], Nouraie et al. [21] and Forsberg et al. [22] emphasized that they are more frequent in women. Recent studies highlight the increase with age of the incidence of right colon adenomas [15,23].

Our results concerning incidence of SA, VA, and TA are confirmed by literature data [10,13,16,21]. We noted that HPs and SAs affect mainly patients younger than 50 years, and classical adenomas are more frequent in patients over 51 years of age; these results are partially confirmed by literature data [2]. All histological types were localized more frequently to the left colon; this observation has been confirmed by other authors as well [5]. Data concerning localization of SAs are contradictory: according to Freeman et al. [24] most of the SAs develop in the right colon, and according to Chandra et al. [3] in the left colon.

In our patient population the ration between A/Ps with and without dysplasia was approximately 1:1, while this was higher in a study by Mahadeva et al. [25]. Dysplasia was more frequent in A/Ps with villous component, and in SAs; this observation has been confirmed as well by many authors [2,5]. In our study A/Ps without dysplasia were more frequent in elderly patients, as opposed to Kurome et al. [26] who state that A/Ps with severe dysplasia develop especially in elderly patients.

The incidence of A/P+CCs in a study by Cheung et al. [27] was approximately 32%. In 75% of synchronous colorectal carcinomas was present also an associated adenoma [28]. Otherwise, there are no literature data concerning these tumor groups. In our patient population A/P+CCs developed especially in women, affecting mainly patients between 51–60 years and 71–80 years, with a higher mean age than A/P-CCs, which are more frequent in males and patients between 61–70 years of age. The majority of A/P+CCs were TAs, and A/P-CCs were mostly TVAs. A/P-CCs are located more frequently to the left colon. In a study by Gruia et al [28] synchronous carcinomas and adenomas developed in elderly patients are more frequent in right colon.

Conclusions

As a conclusion we note that 1 out of 4 colorectal carcinomas are associated with one or more polyps. Adenomas and polyps without carcinomas display dysplasia and villous components, suggesting an increased risk for malignant transformation.

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