

DEMOGRAPHIC AND HISTOPATHOLOGICAL CHARACTERISTICS OF COLORECTAL POLYPS: A DESCRIPTIVE STUDY BASED ON SAMPLES OBTAINED FROM SYMPTOMATIC PATIENTS

DEMOGRAFSKE IN HISTOPATOLOŠKE ZNAČILNOSTI KOLOREKTALNIH POLIPOV: DESKRIPTIVNA RAZISKAVA NA OSNOVI VZORCEV, PRIDOBLENIH OD SIMPTOMATSKIH PACIENTOV

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ABSTRACT

Keywords:

colorectal polyp, epidemiology, colonoscopy examination, Albania

Background. Colorectal polyps (CP) are common among individuals older than 50 years. Some polyp types can precede colorectal cancer (CRC). This study aimed at describing histopathological characteristics of colorectal polyps in relation to age and gender among symptomatic patients referred for a colonoscopy examination during 2011-2014 in Tirana, Albania.

Methods. Study population included 267 individuals aged ≥ 20 years and diagnosed with ≥ 1 polyp during a colonoscopy examination. A total of 346 polyps were identified, excised and measured, and underwent histopathological examination.

Results. Adenomas accounted for 79.8% of all polyps and tubular type was the most frequent one (74.4%). The majority of polyps (42.5%) were small (<1 cm), 38.7% of a medium size (1-2 cm) and 18.8% large (>2 cm). Adenomas were larger than non-adenomatous polyps ($p<0.01$)

There was no gender difference with regard to patient age ($p=0.22$) or polyp size ($p=0.84$). Adenomas were more frequent among men compared to women ($p=0.02$). Age was strongly related to polyp characteristics. The proportion of adenomas increased significantly with age ($p<0.01$). Within adenomas, the proportion of villous types - a precursor of colorectal cancer - increased remarkably with age ($p=0.01$). Older age was positively associated with potentially malignant adenomas (defined as adenomas > 1 cm and showing high-grade dysplasia) ($p<0.01$).

Conclusion. Adenomas accounted for the majority of polyps. Their morphology, size and malignant potential were related to patient age.

IZVLEČEK

Ključne besede:

kolorektalni polipi, epidemiologija, kolonoskopija, Albanija

Uvod. Kolorektalni polipi (CP) so pogost pojav pri posameznikih po 50 letu starosti. Nekatere vrste polipov se lahko razvijejo v kolorektalnega raka (CRC). Ta raziskava skuša opisati histopatološke značilnosti kolorektalnih polipov v povezavi s starostjo in spolom med simptomatskimi pacienti, ki so bili napoteni na kolonoskopsko preiskavo v obdobju od leta 2011 do 2014 v Tirani, Albanija.

Metode. Raziskava je vključevala 267 posameznikov, starih 20 ali več let, ki jim je bil med kolonoskopijo diagnosticiran najmanj en polip. Skupno je bilo identificiranih, odstranjenih, izmerjenih in podvrženih histopatološki preiskavi 346 polipov.

Rezultati. Adenomi so predstavljali 79,8% vseh polipov, med njimi pa je prevladoval tubulni tip (74,4%). Večina polipov (42,5%) je bilo majhnih (<1 cm), 38,7% je bilo srednje velikosti (1-2 cm), 18,8% pa je bilo velikih (>2 cm). Adenomi so bili večji kot ne-adenomatozni polipi ($p<0,01$).

Z vidika starosti pacientov ($p=0,22$) oziroma velikosti polipa ($p=0,84$) ni bilo bistvene razlike med spoloma. Adenomi so bili bolj pogosti pri moških kot pri ženskah ($p=0,02$). Starost je močno povezana z značilnostmi polipa. Delež adenomov se je s starostjo bistveno povečal ($p<0,01$). V smislu adenomov se je delež viloznih tipov - prekursorjev kolorektalnega raka - s starostjo izjemno povečal ($p=0,01$). Višja starost je potrjeno povezana s potencialno malignimi adenomi (opredeljeno kot adenomi >1 cm, ki izkazujejo visoko stopnjo displazije) ($p<0,01$).

Zaključek. Adenomi predstavljajo večino polipov. Njihova morfologija, velikost in potencial rakavosti je povezan s starostjo pacienta.

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1 BACKGROUND

Colorectal cancer (CRC) poses a great burden on population health. It represents the 4th and 3rd most common type of cancer among men and women, respectively (1). The estimated lifetime risk of developing the disease is 5% (2). Its incidence is increasing in the majority of countries, including South-Eastern European countries (3). Such increase is influenced (among other things) by the adoption of a Western-type diet and lifestyle (4). Costs related to CRC care account for 12% of cancer costs, making it the 2nd most expensive cancer to treat. CRC represents the 2nd cause of cancer-related deaths among men aged from 40 to 79 and women older than 80 years (2).

Colorectal polyps are very common among middle-aged individuals, with a prevalence being as high as up to 30%. The epithelial type (either adenomatous or hyperplastic) represents the most common form of colorectal polyps, followed by non-epithelial (inflammatory and juvenile) polyps (5). Some polyp types, especially adenomas, are considered to be precursors of CRC (6, 7). Despite the evidence on the beneficial role of screening in reducing the burden of CRC (8), in Albania no screening programs or prevention measures have been implemented due to limited financial and human resources. No studies have explored the burden of CRC and its precursors in general population either. Therefore, available information on CRC incidence and mortality in Albania is based on calculated extrapolations using the data from neighboring countries and not taking into account genetic, cultural, environmental, social and racial differences across the countries (9). In such conditions, a less expensive alternative is to analyze polyp characteristics among symptomatic individuals in order to identify the burden of precancerous types among them.

The aim of this study was to explore for the first time in Albania, the morphologic and histopathological characteristics of colorectal polyps, and describe their distribution with regard to age and gender, using samples from 267 consecutive patients referred to the gastroenterologist for a colonoscopy examination.

2 SUBJECTS AND METHODS

2.1 Study Population

During 2011-2014, 1100 the patients aged ≥ 20 years were referred by a family doctor or gastroenterologist to undergo a colonoscopy examination in relation to their symptoms (hematochezia, melena, positive fecal occult blood, abdominal pain, constipation or chronic diarrhea). A total of 67 patients (69.8% men) were excluded due to the presence of CRC and another 766 patients (48.9% men) were excluded due to the negative findings (lack

of polyps) during the examination. The study population comprised 267 individuals (64.8% men) with at least one diagnosed and resected polyp. The patients with colorectal cancer were the oldest (mean age 62.7 years) and those with negative findings were the youngest (mean age 49.9 years).

2.2 Endoscopy Procedure

Colonoscopy examinations were performed by two doctors. Any time a polyp was identified, a polypectomy procedure followed. In case of suspected malignancy, a cold forceps biopsy was obtained. The procedure was performed with Narrow band Imaging (NBI, EVIS EXERA II CV-180 Olympus™), high definition endoscopes and without the use of chromo-endoscopy during the identification procedure. Opened biopsy forceps of 7 mm and opened polypectomy snare with known diameter were used for measuring the polyps before piecemeal resection. Cold forceps and cold snare have been the polypectomy methods of choice for smaller polyps, and hot snare has been the method of choice for larger polyps.

2.3 Histopathological Examination

All specimens were histologically examined by a pathologist and, when in doubt (26 cases), a second, experienced pathologist was called to help reaching a decision. First, we measured the height and diameter of each specimen. After that, we put them in formalin solution. Once fixed, the specimen was sectioned in such a way that the relationship of the stalk to the head of the polyp was clear. To avoid missing a small focus of carcinoma, the entire specimen was submitted for histologic evaluation. The sections were stained with hematoxylin eosin (HE). All slides were examined under a light microscope (4X, 10X and 40X dry objectives).

2.4 Classification of Polyps

The 2010 World Health Organization (WHO) criteria were applied to assess the grade of dysplasia and architecture of the polyps (10). Adenomatous polyps were divided into low-grade or high-grade dysplasia. Depending on the presence and volume of villous tissue, adenomatous polyps were further classified as tubular, tubulovillous or villous.

The presence of hypercellular stroma, large mucin-filled cysts, the lack of smooth muscle core and flattened epithelium were used as criteria to diagnose a juvenile polyp. Finally, the presence of various degrees of inflammatory infiltrate, ulceration, edema and granulation tissue were the criteria on the basis of which the diagnosis of an inflammatory polyp was made.

2.5 Statistical Analysis

Continuous variables are presented as mean and standard deviation (SD), while categorical variables are presented as numbers and proportions. Independent sample t-tests were used for comparisons of continuous, normally distributed variables. Categorical variables were compared using the chi square test. Two-sided tests with a 0.05 significance level were used. All statistical analyses were performed using STATA 13 (Stata Corp LP, 4905 Lakeway Drive, College Station, Texas, USA).

3 RESULTS

A total of 267 patients, aged ≥ 20 years, with at least one resected polyp during the colonoscopy examination, were included in the study. The minimum number of polyps per person was one (in 211 patients) and the maximum five (in 2 patients). This yielded a total of 346 polyps (the unit of analyses).

Adenomas accounted for 79.8% of all cases. The majority of polyps (42.5%) were small (<1 cm); 38.7% were of medium size (1-2 cm) and the rest (18.8%) large (>2 cm) (Table 1).

Table 1. Characteristics of the study participants.

Characteristics of the study population	All n=346	Men n=229	Women n=117	P value*
Age (years), mean (SD)	54.1 (13.3)	54.8 (13.1)	52.8 (13.6)	0.22
Polyp type, n (%)				0.02
Non-adenomatous	70 (20.2)	38 (16.6)	32 (27.1)	
Adenomatous	276 (79.8)	191 (83.4)	85 (72.9)	
Polyp size (cm), n (%)				0.84
<1	147 (42.5)	95 (41.5)	52 (44.4)	
1-2	134 (38.7)	91 (39.7)	43 (36.8)	
>2	65 (18.8)	43 (18.8)	22 (18.8)	

*Obtained from chi square tests (for categorical variables) or two-sample t-test (continuous variables) comparing men and women

Hyperplastic and tubular types accounted for the majority (71.4% and 74.4%) of non-adenomatous and adenomatous polyps respectively (Table 2).

Table 2. Distribution of non-adenomatous and adenomatous polyps by gender.

Polyp types	Total	Men	Women	P value
Non-adenomatous polyps, n (%)	70	38	32	0.92
Hyperplastic	50 (71.4)	28 (73.6)	22 (68.8)	
Inflammatory	14 (20.0)	7 (18.5)	7 (21.8)	
Juvenile	6 (8.6)	3 (7.9)	3 (9.4)	
Adenomatous polyps, n (%)	276	191	85	<0.01
Tubular	205 (74.4)	151 (79.1)	54 (46.6)	
Tubulovillous	59 (21.3)	31 (13.5)	28 (23.7)	
Villous	12 (4.3)	9 (3.9)	3 (2.5)	

3.1 Gender-specific Analyses

There were no statistically significant gender difference with regard to age ($p=0.22$) and polyp size ($p=0.84$). Adenomatous polyps were more frequent among men compared to women ($p=0.02$) (Table 1). When analyzed separately, we did not observe gender differences in the distribution of non-adenomatous polyps ($p=0.92$), while adenomas were distributed differently between men and women ($p<0.01$). The tubular type accounted for 79.1% of all adenomas among men and only for 46.6% of them among women (Table 2).

3.2 Polyp Size

Overall, non-adenomatous polyps were smaller than adenomas ($p<0.01$). Small polyps (< 1 cm) comprised the absolute majority (82.8%) of non-adenomatous polyps, while the distribution of adenomas with regard to size was more proportional. Middle-sized polyps (1-2 cm) accounted for 44.5% of cases, followed by small (32.3%) and large (> 2 cm) ones (23.2%) (Table 3).

Table 3. Distribution of polyps by size.

Polyp types	Polyp Size		
	< 1 cm	1-2 cm	> 2 cm
Non-adenomatous polyps, n (%)	58 (82.8)	11 (15.7)	1 (1.5)
Hyperplastic	47 (94.0)	3 (6.0)	-
Inflammatory	11 (78.6)	3 (21.4)	-
Juvenile	-	5 (83.3)	1 (16.7)
Adenomatous polyps, n (%)	89 (32.3)	123 (44.5)	64 (23.2)
Tubular	82 (40.0)	99 (43.3)	24 (11.7)
Tubulovillous	7 (11.9)	19 (32.2)	33 (55.9)
Villous	-	5 (41.7)	7 (58.3)

We did not observe any gender differences with regard to size when analyses were conducted separately among non-adenomatous polyps ($p=0.52$) and adenomas ($p=0.71$) (Figure 1).

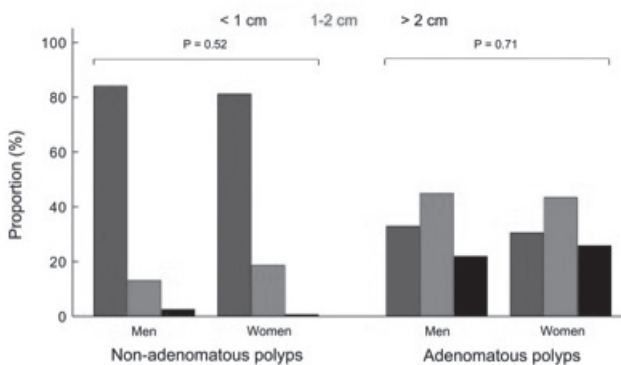


Figure 1. Gender differences pertaining to polyp size.

3.3 Influence of Age on Polyp Characteristics

A linear relationship was observed between patient age and type of polyp. Adenomas were more frequent than non-adenomatous polyps among all age groups, but this difference tended to increase with age ($p<0.01$) (Figure 2).

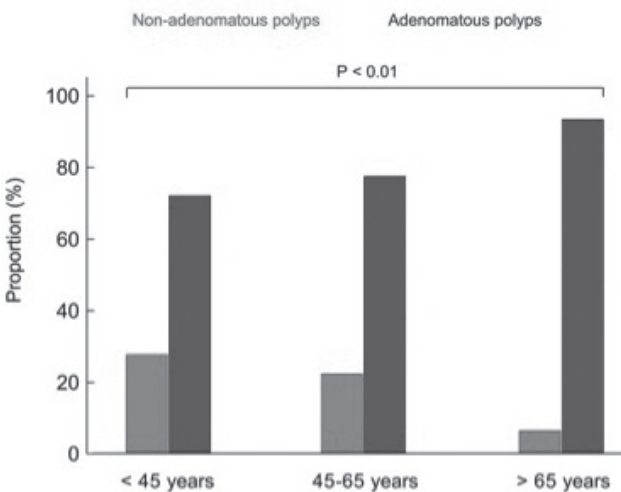


Figure 2. The distribution of polyps by age.

Age was also associated with subtype distribution among adenomas; tubular subtype accounted for 89.2% of all adenomas among patients < 45 years, but this proportion dropped with increasing age to 74.8% among patients 45-65 years and further to 59.7% among those > 65 years. On the contrary, the proportion of villous subtype - the most important CRC precursor - increased from 1.5% among patients < 45 years to 13.9% among those older than 65 years ($p=0.01$) (Figure 3).

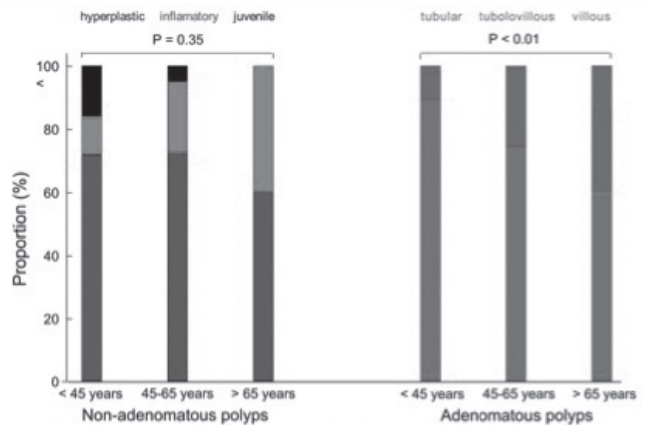


Figure 3. Age differences in the distribution of polyps.

Lastly, we explored the association between grade of dysplasia and patient age, and observed that older patients showed more often adenomas with high-grade dysplasia compared to their younger counterparts ($p=0.008$). However, high-grade dysplasia was not uncommon among young and middle-aged patients, and accounted, respectively, for 29.2% and 43.2% of all adenomas in these groups (Table 4).

Table 4. Distribution of polyps by size.

Grade of dysplasia	Age group			P value
	< 45 years	45-65 years	> 65 years	
Low-grade dysplasia	46 (70.8)	79 (56.8)	32 (44.4)	0.008
High-grade dysplasia	19 (29.2)	60 (43.2)	40 (55.6)	
< 1 cm	-	4 (2.9)	-	
≥ 1 cm	19 (29.2)	56 (40.3)	40 (55.6)	

4 DISCUSSION

This study showed that adenomas accounted for 79.8% of all polyps and they were more frequent among elderly and male patients. Within adenomas, the proportion of villous type - a direct precursor of CRC - increased remarkably with age. Further, adenomas found in older patients had in ~56% of cases high-grade dysplasia and were > 1 cm large (both indicators of a high malignant potential) (11). A direct comparison of our findings with previous studies is challenging due to differences with regard to study period and population (in terms of age, gender and ethnicity). In addition, it has been shown that the prevalence of adenomas based on autopsy studies is higher than that reported from studies based on endoscopy findings (12).

A study conducted in Denmark during 1986-1987 reported that adenomas accounted for the majority (60%) of the 305 examined polyps (13). A more recent analysis conducted in Western Australia reported that adenomas accounted for 70% of all polyps (14). In a study conducted in Canada in 2002, Khan et al. (15) reported that adenomas accounted for 83% of all polyps, followed by hyperplastic (12.3%) and inflammatory (2.8%) types. Among studies conducted outside Europe and North America, Tony et al. (16) reported that among 124 patients diagnosed with a polyp, 79.5% were adenomas, 10% juvenile, 9% hyperplastic and 1.5% inflammatory. The most recent published study (to our knowledge) was conducted in Iran in 2010 (17). Of the 856 polyps examined, 85% were adenomas. Of those, 56% were tubular, 17% villous and 27% tubulovillous. Findings from our study are in line with these previously conducted analyses.

4.1 Public Health Implications

To date, there is a general consensus on the beneficial role of screening average-risk individuals in their 50s every 10 years. Different suggested approaches (opportunistic or programmatic screening) help preventing CRC by removing polyps with high malignant potential (3) or detect CRC at an early stage, improving its prognosis. To illustrate, the 5-year survival is 90% if CRC is diagnosed early (while still localized) and only 10% in advanced stages when distant metastases develop (18).

We showed that the proportion of patients with high-grade dysplasia and size > 1 cm accounted for ~ 56% of patients older than 65 years. However, such adenomas with high malignant potential were not exclusively observed among older adults. They accounted for nearly 1/3 of adenomas observed among younger (< 45 years) and 40.3% of those observed among middle-aged (45-65 years) patients. Further, adenomas with a villous component (either tubulovillous or villous) accounted for ~ 10% of adenomas among patients < 45 years and 1/4 of those among patients 45-65 years. These results show clearly a potentially beneficial role of conducting screening programs among individuals in their fourth to fifth decade of life in order to identify polyps with high malignant potential and reduce the burden of CRC in Albanian population.

4.2 Strengths and Limitations

Our study is the first national study and one of the few recent analyses worldwide (16, 17) exploring histopathological characteristics of colorectal polyps and their distribution. However, it carries certain limitations, among which it is worth mentioning that the study population comprises consecutive symptomatic patients and not a representative national sample. Moreover, additional information on the disease stage would

provide additional valid evidence. Further, we do not know the type and distribution of such polyps among the severe cases that died before undergoing colonoscopy examination.

5 CONCLUSIONS

This study provides evidence that precancerous lesions are very frequent among symptomatic patients undergoing a colonoscopy examination. Although such lesions are more frequent among elderly people, a relatively high proportion of adenomas with malignant potential were found among younger individuals. These findings support the need for prevention strategies and screening programs in order to reduce the risk of future CRC in the Albanian population.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

FUNDING

None.

ETHICAL APPROVAL

The information used in this study was collected at the examination clinic and variables allowing direct identification of participants removed prior to data analyses. The study was conducted in accordance with the code of Ethics of the World Medical Association (Declaration of Helsinki).

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