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The association of metabolic syndrome with the characteristics of colorectal adenomas

Povezanost metaboličkog sindroma sa karakteristikama kolorektalnih adenoma

Dimitrije Damjanov*†, Željka Savić*†, Olgica Latinović Bošnjak*, Žarko Krnetić*, Vladimir Vračarić*, Nebojša Janjić*†, Božidar Dejanović*†

***University Clinical Center of Vojvodina, Clinic for Gastroenterology and Hepatology, Novi Sad, Serbia; †University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia**

Abstract

Background/Aim. Metabolic syndrome (MetS) is associated with an increased risk of developing colorectal cancer (CRC). However, data on its relationship with colorectal adenomas (CRA), the primary precancerous lesions, remain unclear and limited in certain regions. The aim of this study was to examine the characteristics and distribution of CRA in patients with and without MetS. **Methods.** A cross-sectional study was conducted, including 80 patients with CRA, of whom 40 had MetS (MetS group), and 40 did not meet the criteria for MetS (control group). Demographic data, risk factors for CRC (smoking, alcohol consumption, and family history of CRC), protective factors (use of acetylsalicylic acid and nonsteroidal anti-inflammatory drugs, physical activity), and polyp characteristics (size, number, localization, and degree of advancement) were collected and compared between the two groups. The diagnosis of CRA was established by histological examination of polyp specimens retrieved during colonoscopy. The diagnosis of MetS was made if three or more of the following criteria were present: increased waist circumference (≥ 94 cm for males, or ≥ 80 cm for females); hypertriglyceridemia (≥ 1.7 mmol/L); reduced high-density lipoprotein cholesterol levels (< 1.0 mmol/L for males, or < 1.3 mmol/L for females); arterial hypertension (systolic blood pressure ≥ 130 mmHg, and/or diastolic blood pressure ≥ 85 mmHg); fasting hyperglycaemia (≥ 5.6 mmol/L). **Results.** The average age of the patients was 61 years. Males and females were equally present in both groups, as were all the common risk factors for CRA. There were no differences between the groups regarding adenoma size, number of detected adenomas, localization of adenomas, and the degree of histological advancement of the adenoma. **Conclusion.** No significant association was found between the presence of MetS and the characteristics and distribution of CRA in our study. Further studies with larger samples and biomarker analyses are needed to better understand the potential role of MetS-related factors in colorectal carcinogenesis.

Key words:
adenoma; colon; colorectal neoplasms; metabolic syndrome; polyps; risk factors.

Apstrakt

Uvod/Cilj. Metabolički sindrom (MetS) je povezan sa povećanim rizikom od razvoja kolorektalnog karcinoma (KRK). Međutim, podaci o njegovoj povezanosti sa kolorektalnim adenomima (KRA), primarnim prekanceroznim lezijama, ostaju nedovoljno jasni i ograničeni u određenim regionima. Cilj rada bio je da se ispitaju karakteristike i raspodela KRA kod bolesnika sa i bez MetS-a. **Metode.** Sprovedena je studija preseka koja je obuhvatila 80 bolesnika obolelih od KRA, od kojih je 40 imalo MetS (MetS grupa), dok 40 nije ispunjavalo kriterijume za MetS (kontrolna grupa). Prikupljeni su i upoređeni između dve grupe demografski podaci, faktori rizika za KRK (pušenje, konzumacija alkohola, porodična anamneza KRK), zaštitni faktori (upotreba acetilsalicilne kiseline i nesteroidnih antiinflamacijskih lekova, fizička aktivnost), kao i karakteristike polipa (veličina, broj, lokalizacija i stepen uznapredovalosti). Dijagnoza KRA postavljana je histološkom analizom uzoraka polipa dobijenih tokom kolonoskopije. Dijagnoza MetS postavljena je ukoliko su bila prisutna tri ili više sledećih kriterijuma: povećan obim struka (≥ 94 cm kod muškaraca ili ≥ 80 cm kod žena); hipertrigliceridemija (≥ 1,7 mmol/L); nizak nivo *high-density lipoprotein*–HDL holesterola (< 1,0 mmol/L kod muškaraca ili < 1,3 mmol/L kod žena); arterijska hipertenzija (sistolni krvni pritisak ≥ 130 mmHg i/ili dijastolni krvni pritisak ≥ 85 mmHg); hiperglikemija natašte (≥ 5,6 mmol/L). **Rezultati.** Prosečna starost bolesnika bila je 61 godina. Muškarci i žene bili su podjednako zastupljeni u obe grupe, kao i svi uobičajeni faktori rizika za KRA. Nije bilo razlika između grupa u

Correspondence to: Dimitrije Damjanov, University of Novi Sad, Faculty of Medicine, Hajduk Veljkova 3, 21 137 Novi Sad, Serbia. E-mail: dimitrije.damjanov@mf.uns.ac.rs

pogledu veličine adenoma, broja otkrivenih adenoma, lokalizacije adenoma i stepena histološke uznapredovalosti adenoma. **Zaključak.** Nije utvrđena značajna povezanost prisustva MetS sa karakteristikama i distribucijom KRA u našoj studiji. Neophodne su dalje studije sa većim uzorcima i analizom biomarkera kako bi se bolje razumela moguća uloga faktora povezanih sa MetS u kolorektalnoj karcinogenezi.

Ključne reči:
adenom; crevo, debelo; kolorektalne neoplazme; metabolički sindrom; polipi; faktori rizika.

Introduction

Colorectal cancer (CRC) is among the most preventable malignant diseases [1]. A key element in the carcinogenesis of most CRC cases is the polyp, a benign precancerous lesion [2]. The adenoma-carcinoma sequence is the most common pathway for the transformation of colorectal polyps into cancer [3]. The gradual progression of polyps into CRC over several years in the general population offers a valuable opportunity for early detection and removal [4, 5].

It is particularly important to identify risk factors for the development of colorectal adenomas (CRA), as this can aid in screening, risk modification, and prevention of CRC [6]. Risk factors for developing colorectal tumors include a family history of CRC or colorectal polyps, smoking, alcohol consumption, physical inactivity, and obesity [7, 8]. Additionally, research indicates that metabolic syndrome (MetS) is also a risk factor for CRC [9, 10]. The link between MetS and CRC is primarily attributed to insulin resistance and the role of insulin-like growth factor-1 [11, 12].

While some studies have demonstrated that MetS and its components are associated with the presence, multiplicity, and advancement of CRA [11–13], others have not confirmed these findings [14, 15]. Furthermore, most available data originate from East Asian and Western populations, whereas literature from Southeast Europe remains scarce. A prior regional study confirmed MetS as a predictor for CRA but found no associations with CRA characteristics [16].

The aim of our study was to examine differences in the characteristics and distribution of CRA between patients with and without MetS. Establishing such associations could potentially influence CRC screening strategies and post-polypectomy surveillance recommendations in clinical practice, particularly in populations with a high prevalence of MetS.

Methods

This cross-sectional study was conducted at the Department of Gastrointestinal Endoscopy of the University Clinical Center of Vojvodina, Novi Sad, Serbia. Individuals who underwent total colonoscopy and were diagnosed with CRA between February and July 2023 were invited to participate in an informative interview. Only individuals who voluntarily provided informed consent after an informational interview were enrolled in the study.

The study was approved by the Ethics Committee of the University Clinical Center of Vojvodina (No. 00-188, from October 27, 2022).

The study included 80 patients, divided into two groups. The first group included 40 consecutive patients aged 40 to 75 years with CRA who were diagnosed with MetS, i.e., the MetS group. The second group, i.e., the control group, consisted of 40 consecutive patients within the same age range who had CRA but did not meet the diagnostic criteria for MetS. Exclusion criteria included pregnancy, inadequate bowel preparation, CRC, inflammatory bowel disease, prior colon resection, insulin therapy, and the presence of hyperplastic polyps.

Colonoscopy was performed by gastroenterohepatologists and nurses with extensive experience in endoscopy. Data were extracted from medical records and included the following parameters: polyp size (measured using the diameter of open biopsy forceps), polyp morphology, number of polyps, and polyp distribution. Adenomas were classified as advanced if they met any of the following criteria: size ≥ 10 mm, presence of high-grade dysplasia, or presence of a villous component [17].

Anamnestic data for each participant from both the study and control groups were collected using a pre-designed questionnaire. Participants were interviewed and provided information on the following: age, gender, smoking status, alcohol consumption, family history of CRC, use of acetylsalicylic acid (ASA) and nonsteroidal anti-inflammatory drugs (NSAIDs), physical activity levels, elevated blood pressure (BP), diabetes mellitus, low high-density lipoprotein cholesterol (HDL-C), elevated triglycerides (TG), and medications used.

Venous blood samples of the participants were collected in the morning following a 12-hr fasting period. Glucose, TG, and HDL-C levels were measured using standard methods on an automated biochemical analyzer. Waist circumference was measured according to the World Health Organization guidelines [18], and BP was recorded using the Korotkoff method.

Participants were diagnosed with MetS if they fulfilled three or more of the following criteria: increased waist circumference (≥ 94 cm for males or ≥ 80 cm for females); elevated TG or use of TG-lowering medications (≥ 1.7 mmol/L); reduced HDL-C levels or use of HDL-C-raising medications (< 1.0 mmol/L for males or < 1.3 mmol/L for females); elevated BP or use of antihypertensives (systolic BP ≥ 130 mmHg and/or diastolic BP ≥ 85 mmHg); fasting hyperglycemia or use of antihyperglycemic medications (≥ 5.6 mmol/L) [19].

Statistical analysis

Data were entered and analyzed using IBM SPSS statistical software, version 22.0. Descriptive statistical methods were applied to summarize the sample, including

measures of central tendency (mean), dispersion (standard deviation), and distribution range (minimum and maximum values). To address the research objectives and hypotheses, the Chi-square test was employed as a non-parametric method for comparing nominal-level data. In addition, the relationships between the variables of interest were evaluated using Pearson's linear correlation coefficient (a parametric method) and Spearman's rank correlation coefficient (a non-parametric method). The value of $p < 0.05$ was considered statistically significant.

Results

Demographic characteristics

The study included 80 patients with CRA. The sample was gender-balanced, with 40 males and 40 females. The average age of the patients was 60.76 years (standard deviation: 7.85). The distribution of MetS prevalence according to gender and age is provided (Table 1). The results of the independent samples test conducted to examine age differences between patients with MetS and those without MetS indicated a statistically significant difference, with older age observed in the group of patients with MetS.

Risk factors and protective factors for colorectal adenomas

Risk and protective factors for CRA in patients with MetS and in the control group were analyzed. When comparing patients with MetS to the control group, the results show that a statistically significant difference between these two groups exists only in the use of ASA, with more frequent use observed in patients with MetS (Table 2).

Table 1

Demographic data in the MetS and control groups

Parameters	Group		Test	*df*	*p*
	MetS	control			
Gender					
male	21 (52.5)	19 (47.5)	$\chi^2 = 0.20$	1	> 0.05
female	19 (47.5)	21 (52.5)			
Age, years	63.12 ± 6.70	58.40 ± 8.28	$t = 2.805$	78	**< 0.05**

MetS – metabolic syndrome.
All values are given as numbers (percentages) or mean ± standard deviation.
Bold value indicates statistical significance, $p < 0.05$.

Table 2

Risk and protective factors for CRA in the MetS and control groups

Parameters	Group		χ^2	*df*	*p*
	MetS	control			
Risk factors					
smoking status					
smokers	14 (35.0)	16 (40.0)			
ex-smokers	13 (32.5)	9 (22.5)			
non-smokers	13 (32.5)	15 (37.5)	1.003	2	> 0.05
Alcohol consumption					
yes	2 (5.0)	5 (12.5)			
no	38 (95.0)	35 (87.5)	1.409	1	> 0.05
Family history of CRC					
yes	8 (20.0)	13 (32.5)			
no	32 (80.0)	27 (67.5)	1.614	1	> 0.05
Protective factors					
ASA and/or NSAID use					
yes	12 (30.0)	4 (10.0)			
no	28 (70.0)	36 (90.0)	5.000	1	**< 0.05**
Physical activity					
yes	34 (85.0)	37 (92.5)			
no	6 (15.0)	3 (7.5)	1.127	1	> 0.05

CRA – colorectal adenomas; MetS – metabolic syndrome; CRC – colorectal cancer; ASA – acetylsalicylic acid; NSAID – nonsteroidal anti-inflammatory drug.
All values are given as numbers (percentages).
Bold value indicates statistical significance, $p < 0.05$.

Polyp characteristics in the total sample

The size of the polyp was ≥ 10 mm in the majority of cases. Sessile and pedunculated CRA were represented in relatively similar numbers. The majority of CRA were found in the distal colon, while fewer cases were observed in the proximal colon or in both parts of the colon. In most cases, only one CRA was present, while two or more adenomas were observed in a significantly smaller number of cases. In 57 cases, CRA were classified as advanced (Table 3).

Polyp size

There were no statistically significant differences in polyp size based on gender (χ^2 = 3.170, p > 0.05) or age (r = -0.006, p > 0.05). None of the risk or protective factors showed a statistically significant correlation with the size of CRA (smoking: r = 0.095, p > 0.05; alcohol: r = -0.030, p > 0 .05; family history: r = 0.045, p > 0.05; ASA: r = -0.112, p > 0.05; physical activity: r = -0.027, p > 0.05). No statistically significant differences in the size of CRA were observed between patients with MetS and the control group (Table 4).

Polyp morphology

There were no statistically significant differences in polyp morphology based on gender (χ^2 = 2.464, p > 0.05) or age (r = -0.067, p > 0.05). None of the risk or protective factors showed a statistically significant correlation with the

Table 3

Polyp characteristics in the total sample

Characteristics	n (%)
Polyp size	
≤ 5 mm	3 (3.8)
6–9 mm	24 (30.0)
≥ 10 mm	53 (66.3)
Polyp morphology	
sessile	37 (46.3)
pedunculated	43 (53.8)
Number of polyps	
1	60 (75.0)
2	18 (22.5)
≥ 3	2 (2.5)
Distribution of polyps	
proximal colon	11 (13.8)
distal colon	61 (76.3)
proximal and distal	8 (10.0)
Advanced adenoma	
yes	57 (71.3)
no	23 (28.7)

n – number.

Table 4

Polyp characteristics in the MetS and control groups

Characteristics	Group		χ^2	*df*	*p*
	MetS	control			
Polyp size					
≤ 5 mm	0 (0.0)	3 (7.5)			
6–9 mm	14 (35.0)	10 (25.0)			> 0.05
≥ 10 mm	26 (65.0)	27 (67.5)	3.686	2	
Polyp morphology					
sessile	19 (47.5)	18 (45.0)			> 0.05
pedunculated	21 (52.5)	22 (55.0)	0.050	1	
Number of polyps					
1	31 (77.5)	29 (72.5)			
2	8 (20.0)	10 (25.0)			> 0.05
≥ 3	1 (2.5)	1 (2.5)	0.289	2	
Distribution of polyps					
proximal	7 (17.5)	4 (10.0)			
distal	31 (77.5)	30 (75.0)			> 0.05
proximal and distal	2 (5.0)	6 (15.0)	2.835	2	
Advanced adenoma					
yes	27 (67.5)	30 (75.0)			> 0.05
no	13 (32.5)	10 (25.0)	0.549	1	

MetS – metabolic syndrome.
All values are given as numbers (percentages).

morphology of CRA (smoking: $r = 0.030$, $p > 0.05$; alcohol: $r = -0.068$, $p > 0.05$; family history: $r = 0.098$, $p > 0.05$; ASA: $r = -0.038$, $p > 0.05$; physical activity: $r = -0.013$, $p > 0.05$). No statistically significant differences in the morphology of CRA were observed between patients with MetS and the control group (Table 4).

Polyp number

There were no statistically significant differences in polyp number based on gender ($\chi^2 = 5.067$, $p > 0.05$) or age ($r = -0.010$, $p > 0.05$). None of the risk or protective factors showed a statistically significant correlation with the number of CRA (smoking: $r = 0.065$, $p > 0.05$; alcohol: $r = 0.159$, $p > 0.05$; family history: $r = 0.152$, $p > 0.05$; ASA: $r = -0.204$, $p > 0.05$; physical activity: $r = 0.185$, $p > 0.05$). No statistically significant differences in the number of CRA were observed between patients with MetS and the control group (Table 4).

Polyp distribution

There were no statistically significant differences in polyp localization based on gender ($\chi^2 = 3.621$, $p > 0.05$) or age ($r = -0.065$, $p > 0.05$). None of the risk or protective factors showed a statistically significant correlation with the localization of CRA (smoking: $r = -0.052$, $p > 0.05$; alcohol: $r = 0.024$, $p > 0.05$; family history: $r = -0.071$, $p > 0.05$; ASA: $r = 0.039$, $p > 0.05$; physical activity: $r = 0.217$, $p > 0.05$). No statistically significant differences in the localization of CRA were observed between patients with MetS and the control group (Table 4).

Polyp advancement

There were no statistically significant differences in polyp advancement based on gender ($\chi^2 = 1.526$, $p > 0.05$) or age ($r = 0.002$, $p > 0.05$). None of the risk or protective factors showed a statistically significant correlation with the advancement of CRA (smoking: $r = 0.154$, $p > 0.05$; alcohol: $r = -0.097$, $p > 0.05$; family history: $r = 0.128$, $p > 0.05$; ASA: $r = -0.166$, $p > 0.05$; physical activity: $r = 0.039$, $p > 0.05$). No statistically significant differences in the frequency of advanced CRA were observed between patients with MetS and the control group (Table 4).

Discussion

Malignant diseases represent a significant health problem for the population of Vojvodina. Tumors are the leading cause of morbidity and the second most frequent cause of death in this region (23.1% of cases) [20]. Globally, CRC is the third most frequently diagnosed malignant disease, and the second most common cause of malignancy-related mortality [21]. A similar situation is observed in Serbia [22]. The majority of CRC cases (60–65%) are sporadic, while 35–40% can be linked to hereditary predisposition for CRC [23].

Observing the population of patients with CRA in our region, based on our study results, if a significant difference in the characteristics and distribution of CRA between the MetS and control groups were to be established, the colonoscopy screening program, as well as the follow-up of patients after polypectomy, could be adapted according to the presence of MetS in individuals. This could influence morbidity and mortality associated with CRC. The central question of our research was: "Does the presence of MetS affect the size, number, localization, and histological characteristics of CRA?"

Age is one of the most dominant risk factors for CRA. With aging, the frequency, number, size, and degree of dysplasia of CRA increase [7, 24–27]. In our study, patients with MetS were statistically significantly older than patients who did not meet the criteria for MetS. This finding is expected, given that the prevalence of MetS increases with age [28]. The age of the patients did not statistically significantly correlate with the size, number, distribution, or degree of advancement of CRA, which contrasts with data reported in the literature. These discrepancies may be due to the limited sample size or population-specific differences.

Men have a 50% higher risk of having polyps larger than 10 mm and advanced polyps compared to women [29, 30]. Interestingly, the polyp detection rate is 5% higher in men than in women [31]. Contrary to the data from the literature, our study did not reveal statistically significant differences between men and women in terms of CRA size, localization, and number, nor in the prevalence of advanced polyps. This again may reflect sample size limitations or possible gender differences in health-seeking behavior and screening uptake.

The results of a 2021 meta-analysis showed that patients with MetS have a 1.39 times higher risk of having CRA compared to patients without MetS [32]. An important MetS-related factor responsible for the development of CRA is visceral obesity, given that visceral adipose tissue is hormonally active [33, 34]. In our study, no statistically significant difference was found in the distribution, number, size, or prevalence of advanced CRA in patients with MetS compared to those without MetS. This finding contrasts with previous research indicating that MetS significantly correlates with the presence of CRA at multiple locations [35], multiple CRA [36], larger CRA [37], and advanced CRA [13]. In a study by Trabulo et al. [14], participants with MetS had multiple CRA more frequently, but no differences were found in the size, distribution, or prevalence of advanced CRA compared to participants without MetS. Similarly, in a study by Milano et al. [15], MetS was significantly associated with the presence of colorectal polyps, but there were no differences in their size or number between participants with MetS and those without MetS. The discrepancy between our findings and those of other studies may be attributed to several factors. First, our sample size was relatively small. Second, the definition and measurement of MetS components, as well as the criteria for adenoma classification, vary across studies, complicating direct comparisons. Third, lifestyle and genetic factors specific to

our region could modulate the effect of MetS on colorectal neoplasia risk differently than in other populations.

When analyzing risk and protective factors for CRC in relation to MetS, our study found that patients with MetS were significantly more likely to use ASA and other NSAIDs. This is expected, as MetS patients often have cardiovascular or cerebrovascular diseases for which antiplatelet therapy is commonly indicated. However, none of the other commonly assessed risk or protective factors, including smoking, alcohol, physical activity, or family history of CRC, showed a statistically significant association with MetS in our cohort. Furthermore, none of these factors were associated with CRA characteristics such as size, morphology, number, distribution, or advancement.

These findings suggest that although MetS is an important systemic condition with established links to colorectal neoplasia, its influence on the phenotypic expression of CRA may vary depending on genetic, environmental, and lifestyle factors within specific populations. Given the inconsistency in the current literature, future studies in our region should aim for larger sample sizes and incorporate measurements of visceral fat and circulating adipokines such as adiponectin, leptin, and estrogen, which may play key roles in CRA pathogenesis [12, 33, 34].

The limitations of our study include a relatively small sample size and the use of a cross-sectional design.

Conclusion

Our study did not reveal a statistically significant difference in the sizes, number, distribution, and frequency of advanced colorectal adenomas between patients with and those without metabolic syndrome. The results of this research highlight the need for further research in our setting with larger sample sizes, incorporating the assessment of serum adipokine levels and evaluation of visceral obesity, in order to improve risk control for the development of colorectal adenomas and cancer.

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