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Diabetes association of polyps and colon cancer

Authors' Contribution:
A–Study Design
B–Data Collection
C–Statistical Analysis
D–Data Interpretation
E–Manuscript Preparation
F–Literature Search
G–Funds Collection

Tomasz Miłek[ABCDEF], Karol Forysiński[B], Piotr Myrcha[D], Piotr Ciostek[D]

I Chair and Clinic of General, Vascular and Oncological Surgery at II Faculty of Medicine of the Medical University of Warsaw

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ABSTRACT:

Aim: The aim of the study was to retrospectively assess the relationship between the occurrence of polyps and colon cancer in patients with type 2 diabetes.

Methods: In 2014–2015, 976 colonoscopies were performed in patients. We compared the number of polyps with high-grade dysplasia and colorectal cancers in patients with and without diabetes. In addition, in the diabetic group we documented the relationship between HbA1C and the occurrence of polyps with high-grade dysplasia, and colon cancer. The data were statistically analyzed.

Results: 1. Patients with diabetes show a higher incidence of polyps with high-grade dysplasia/carcinoma – 32/91 (35.16%) in comparison to patients without diabetes – 136/885 (15.37%), P < 0.001; 2. Patients with diabetes show a higher incience of polyps with cancer – 9/91 (9.89%) as compared to patients without diabetes – 18/885 (2.03%), P < 0.001. 3) Colorectal cancer occurred significantly more often in uncontrolled diabetes (P = 0.022).

Conclusion: The conducted study shows a significant association between type 2 diabetes and the incidence of colorectal adenomas. These findings may lead to a conclusion that diabetic patients are at a higher risk of developing colorectal cancer, thus are in higher need for controlled colonoscopy. Therefore, it may be worth considering a scheme for screening patients in the above-mentioned group with colonoscopy.

KEYWORDS: colorectal cancer, colorectal polyps, diabetes mellitus

INTRODUCTION

Colon cancer is the second most common cause of mortality due to malignant neoplasms in Poland in both genders. Every year 16 000 new cases of colon cancer are diagnosed. Since 1980 the number of cases among men has increased nearly 4 times and about 3 times in women. Most colon cancers arise from developing polyps. Indirect evidence from the National Colorectal Research indicates that not many polyps develop into advanced cancer in a short period of time in patients without risk factors, and that colonoscopy with polypectomy can reduce the incidence of colorectal cancer (CRC) [1]. All current screening methods focus primarily on early detection and removal of adenomas of the colon. As a result, it is important to identify risk factors of colorectal adenomas to develop a more effective screening strategy in order to prevent CRC. Type 2 diabetes and colorectal cancer are the most common diseases in the world. In both diseases an increase in the number of new cases is predicted every year. As compared with the rest of the European Union, Poland has the highest mortality rate of colorectal cancer in both genders; the mortality rate in 2013 was 25% in men and 13% in women. Colon cancer is closely associated with type 2 DM. Diabetes increases the risk of colorectal cancer by 40–60% (2–5). This relationship could be associated with the use of Metformin. Metformin is a biguanide that inhibits glycogen breakdown and of gluconeogenesis and increased glucose uptake in muscle tissue. Unlike other hypoglycemic drugs, metformin does not cause hypoglycemia. Therefore, it is often used in the initial stage of treatment [6]. Metformin is also responsible for the activation of AMP-activated protein kinase (AMPK). Recent studies suggest that AMPK is activated by a low dose of metformin and inhibits the formation of irregular crypt foci (ACF), which are a specific marker of CRC [7, 8].

MATERIAL AND METHODS

In 2009–2011 colonoscopy was performed in 976 patients with type 1 and type 2 diabetes. Each patient gave written consent to colonoscopy treatment and collection of samples for histopathological examination. We compared a number of polyps with high-grade dysplasia and colorectal cancers. In addition, in the diabetic group we documented the relationship between HbA1C and the occurrence of polyps with high-grade dysplasia and colon cancer. Adenomas were confirmed by histopathological preparations taken during endoscopic biopsy.

Patients were compared by age, gender, location of polyps, hypoglycaemic medication, histopathological level of differentiation and the level of glycosylated hemoglobin [HbA1c]. Polyps discovered during colonoscopy were divided on the basis of the histopathological diagnosis, namely, characterized by low-grade dysplasia, high-grade dysplasia and adenocarcinomas.

RESULTS

Categorical variables were presented as percentages. For their analysis, the chi-square test with the corresponding amendments was applied depending on the number of cases in the subgroups. Differences significant for the statistics were with P < 0.05. The whole statistical analysis was performed using Statistica 12.5.

The mean age was about 65 years, the minimum and the maximum age were 20 and 93 years respectively.

As much as 52.46% were women, while 47.54% were men, as summarized in Tab. I.

Tab. I. Age of patients participating in the research.

CLASS	GENDER			
	NUMBER	TOTAL	PERCENT	TOTAL %
Women	512	512	52,45902	52,4590
Men	464	976	47,54098	100,0000

Tab. II. Patient class – suffering from type 2 diabetes and non-diabetics.

CLASS	GROUP			
	NUMBER	TOTAL	PERCENT	TOTAL %
Diabetic	91	91	9,32377	9,3238
Non-diabetic	885	976	90,67623	100,0000

Tab. III. The frequency and location of polyps in diabetics and non-diabetics.

CLASS	POLYP LOCATION				
	GROUP	NUMBER	TOTAL	PERCENT	TOTAL %
Right side of the colon	Diabetic	30	30	32,96703	32,9670
Left side of the colon	Diabetic	51	81	56,04396	89,0110
Both sides of the colon	Diabetic	10	91	10,98901	100,0000
????????????	Diabetic	0	91	0,00000	100,0000
Right side of the colon	Non-diabetic	322	322	36,38418	36,3842
Left side of the colon	Non-diabetic	486	808	54,91525	91,2994
Both sides of the colon	Non-diabetic	77	885	8,70056	100,0000

Tab. IV. Frequency of dysplasia and carcinomas in patients with type 2 diabetes and non-diabetic patients.

CLASS	CANCER VS. DYSPLASIA				
	GROUP	NUMBER	TOTAL	PERCENT	TOTAL %
Dysplasia	Diabetic	82	82	90,10989	90,1099
Cancer	Diabetic	9	91	9,89011	100,0000
Dysplasia	Non-diabetic	867	867	97,96610	97,9661
Cancer	Non-diabetic	18	885	2,03390	100,0000

Tab. V. Frequency of small and large dysplasia in patients with type 2 diabetes and non-diabetics.

LOW-GRADE DYSPLASIA VS. HIGHHGRADE DYSPLASIA/CANCER					
CLASS	GROUP	NUMBER	TOTAL	PERCENT	TOTAL %
Low-grade dysplasia	Diabetic	59	59	64,83516	64,8352
High-grade dysplasia/ cancer	Diabetic	32	91	35,16484	100,0000
Low-grade dysplasia	Non-diabetic	749	749	84,63277	84,6328
High-grade dysplasia/ cancer	Non-diabetic	136	885	15,36723	100,0000

Patients were compared in two groups. One of them consisted of patients with type 2 diabetes (9.32%), while the second group included non-diabetic patients (90,67%) (Tab. II.).

In the course of the study we were able to document the presence and location of polyps in patients with type 2 diabetes. As a result, we found that in both groups the polyps were often located on the left side of the colon (around 56% of patients with diabetes and 54% of non-diabetic patients) (Tab. III.).

Given the incidence of cancer and dysplasia in the two groups of patients, it was found that cancer affects as many as 9.89% of patients with type 2 diabetes, and only 2% of patients without diabetes. In turn, dysplasias occur in 90.10% of patients with diabetes while up to 97.96% of patients did not have this health problem (Tab. IV.).

Low-grade dysplasia was found less frequently in patients with diabetes, i.e. in 64.83% of the cases, compared to non-diabetics were it was found in 84.63%. On the other hand, high-grade dysplasia was more common in diabetic patients (35.16%) than in non-diabetics (15.36%) (Tab. V.).

According to the above results, we were able to check the treatment patients received for type 2 diabetes. It was found that most of the patients used insulin therapy, and the treatment used least frequently was insulin therapy combined with metformin (Tab. VI.).

Analyzing the incidence of cancers vs. dysplasia, it was found that cancer occurs significantly more often in uncontrolled diabetes ($P = 0.022$) (Tab. VII.). This follows from the calculations of OR 5.72 (95% CI: 1.32–24.87), which in practice means that there is a significantly greater chance (6 times) of developing cancer in patients with uncontrolled diabetes than in patients with controlled diabetes.

DISCUSSION

Numerous studies show that types I and II diabetes are closely correlated with an increased incidence of cancer affecting the following organs: colon, breast, endometrium, kidneys, liver, and other malignant neoplasms [14]. A number of meta-analyses indicated an increased risk of colon cancer in patients with type II diabetes [15]. A retrospective study conducted on a large patient population by Limburg et al. [17] demonstrated correlations between diabetes and the risk of CRC – the Standardized Incidence Ratio was 1.39. A similar relationship was presented in the Nurse's Health Study by Hu et al. [18].

After 18 years of monitoring the Standardized Incidence Ratio was 1.43 in all the patients with diabetes reported at baseline. An early meta-analysis developed by Yuhar et al. [19] demonstrated that diabetes was an independent risk factor of CRC and was associated with an increased risk of CRC both in men and in women even after comprising cigarette smoking, obesity and physical activity with a relative risk at the level of 1.37. A prospective study by Schoen et al. [20] revealed a relationship between an increased insulin level and IGF-1 and the occurrence of colon adenomas, and also advanced adenomas in 458 asymptomatic patients who had undergone FSS.

Elwing et al. [21] compared 100 diabetic women with 500 non-diabetic women. Both groups underwent colonoscopy which revealed that diabetic women had a higher ratio of adenomas (37% vs. 24%, OR = 1.82) and advanced adenomas (14% vs. 6 %, OR = 2.38). Elwing et al. [21] conducted a retrospective clinical follow-up study on patients with and without adenoma and reported that diabetes, exposure to insulin and the use of thiazolidinedione were as-

sociated with a higher risk of adenoma formation. A recent study by Kanadiya et al. [22] included a retrospective analysis of 405 diabetic patients and 3038 nondiabetic individuals who had undergone their first colonoscopy. He reported that the risk associated with an increased occurrence of adenoma (OR = 1.35) and ADR was higher in diabetic patients (29.3%) compared to non-diabetic ones (23.9%). In type II diabetes the increase of IGF-1 factor which is due to hyperinsulinemia that is not provoked by peripheral insulin resistance, is responsible for the intensification of epithelial cell dysplasia and induces CRC proliferation [16].

The most common cause of CRC development is the presence of adenomatous colon polyps which undergo numerous gene mutations. In spite of a relationship between diabetes and colon adenomas [23, 24] and the fact that the use of metformin in type II diabetes reduced the risk of CRC [25], none of the available studies demonstrated a decreased incidence of colon polyps and colon adenomas in groups of patients treated with metformin. Diabetic patients may have disorders of digestive tract motor activity and problems with normal defecation due to autonomic neuropathy. This may lead to a decreased detectability of both adenomas and CRC in diabetic patients, because the preparation of the intestine is of key significance for high quality of colonoscopic screening.

Decreased detectability and excision of highly dysplastic polyps due to insufficient preparation may lead to an insidious CRC development in such patients. Moreover, reduced detectability of adenomas and CRC may result in underestimating the risk of their occurrence in individuals with diabetes. The present analysis shows a significant relationship regarding the development of adenomatous colon polyps in patients with type II diabetes. These conclusions should result in further research to develop a standardized regimen of performing periodic endoscopic examinations in patients with type II diabetes.

Tab. VI. Types of diabetes treatment used in patients with type 2 diabetes.

	TREATMENT THERAPY			
CLASS	NUMBER	TOTAL	PERCENT	TOTAL %
Insulin	44	44	4,50820	4,5082
Metformin	33	77	3,38115	7,8893
Insulin + metformin	14	91	1,43443	9,3238

Tab. VII. Analysis of the risk of cancer and dysplasia in patients with type 2 diabetes.

	SUMMARY TABLE: OBSERVED FREQUENCY		
HISTOPATHOLOGY (0/1)	HBA1C: 1 > 6,4; 2 < 6,41	HBA1C: 1 > 6,4; 2 < 6,42	TOTAL ROW
Dysplasia	22	60	82
% column	78,57%	95,24%	
% row	26,83%	73,17%	
Cancer	6	3	9
% column	21,43%	4,76%	
% row	66,67%	33,33%	
Total	28	63	91
	Statistics: Histopathology (0/1) (2) x Hba1C: 1 > 6.4, 2 < 6.4(2)		
statistics	p		
Double-sided Fisher test	p = 0,022		

CONCLUSIONS

The conducted study shows a significant association between type 2 diabetes and the incidence of colorectal adenomas. These findings may lead to the conclusion that diabetic patients are at a higher risk of developing colorectal cancer, thus requiring more need for controlled colonoscopy. Therefore, it may be worth considering a scheme for patients in the above mentioned group including screening with colonoscopy [10–12].

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Corresponding author: Dr Tomasz Miłek; Medical University of Warsaw, Kondratowicza Street 8, 03-242 Warsaw, Poland; Phone +48 604 422 345; E-mail: tomasz_milek@wp.pl

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