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Screening colonoscopy tests in acromegaly patients – authors' observations

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A – Study Design, **B** – Data Collection, **C** – Statistical Analysis, **D** – Data Interpretation, **E** – Manuscript Preparation, **F** – Literature Search, **G** – Funds Collection

Summary **Background.** The prevalence of adenomas which cause acromegaly is estimated at 50–70 mln people. They secrete excess of growth hormone and increase the risk of benign and malignant tumours. Intestinal tumours are considered the most common types of lesion. In order to diagnose them early, a colonoscopic examination should be performed every 2–3 years.
Objectives. The aim of the study was to estimate the frequency of the performed colonoscopies in acromegaly patients, and to assess their applicability in the detection of neoplastic lesions of the colon.
Material and methods. The study involved 69 patients with acromegaly (26 M, 43 F), aged 26–83 years (mean 58.9 ± 11.0). The authors analyzed medical records and the results of additional tests.
Results. Colonoscopy was performed in 30 patients (43.5% of cases), was well tolerated and without serious complications. 70% of colonoscopies revealed polyps of the colon and 6.7% revealed colon carcinoma. In 9 patients (30% of conducted studies) colonoscopy examination showed no pathological changes. Only in 4 cases the test was performed more than once.
Conclusions. Current recommendations regarding colonoscopic examinations in all acromegaly patients are implemented in less than half of the cases. Recommendations relating to colonoscopy being repeated every 2–3 years are followed occasionally. Colonoscopy is a diagnostic test of great significance. In 70% of cases it enables the detection and removal of pathological lesions of the colon. As a low-invasive, safe and well-tolerated examination it should be performed in all patients. GPs should make acromegaly patients aware of the importance of colonoscopy and refer them for periodic follow-up examinations.
Key words: acromegaly, colonoscopy, colon neoplasm.

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Background

Acromegaly is a rare chronic disease whose prevalence is estimated at 50–70 million people, and which is most often caused by a benign, slowly growing pituitary adenoma excessively secreting growth hormone (GH), which in turn leads to the increased synthesis of growth factors (mainly the insulin-like growth factor-1, IGF-1). Excess of IGF-1 causes gradual, very characteristic changes in a patient's appearance, as well as organ and metabolic complications and benign and malignant tumours [1–3]. The vast symptomatology of acromegaly is associated with diagnostic errors, and may delay proper diagnosis and thus negatively affect the length and quality of life of patients [1, 4]. The most significant consequences of acromegaly include cancerous diseases, most often such as colorectal cancers. IGF-1 stimulates the proliferation of colorectal epithelial cells and the development of polyps, which may degenerate into cancers [1–5]. Therefore, in accordance with the current guidelines [2], these patients should be under the specialist oncological care and undergo colonoscopy examination every 2–3 years.

Objectives

The aim of the study was to estimate the frequency of colonoscopies performed in acromegaly patients in relation to the relevant guidelines in Poland, and to evaluate the prevalence of benign and malignant colorectal neoplasms in these patients.

Materials and methods

The study involved 69 patients (26 men, i.e. 37.7% of the study group, and 43 women, i.e. 62.3% of the study group) treated for active acromegaly at the Department of Endocrinology of Medical University and Endocrinology Hospital Outpatient Clinic in Lublin in the years 2000–2015.

The patients' ages ranged from 26 to 83 years (mean 58.9 ± 11.0). Active acromegaly was confirmed based on lack of inhibition of GH secretion in the oral glucose tolerance test with 75 g of glucose, increased level of IGF-1 concentration and the presence of pituitary adenoma in magnetic resonance (MR) examination. Medical documentation was analyzed concerning endoscopic examinations of the digestive tract, and the results of histopathological examinations of the visualized and removed pathological lesions in the large intestine.

The obtained results were statistically analyzed using STATISTICA v. 10.0 software (StatSoft, Poland). Values of the analyzed parameters measured in a nominal scale were characterized using count and percentage, while in a ratio scale using mean value and standard deviation. Variables with normal distribution (patients' age) and skew distribu-

tion (disease duration, time between acromegaly diagnosis and colonoscopy examination) were evaluated using the Shapiro–Wilk test. The U Mann–Whitney test was used to compare two independent groups. The ch-square test was used to evaluate differences and dependencies between analyzed measurable parameters. A 5% inference error was assumed, as well as the related significance level of $p < 0.05$ indicating the presence of statistically significant differences or dependencies.

Results

Colonoscopy was performed in 30 patients, i.e. 43.5% of the total group, comprising 19 women (44.2% of the study group) and 11 men (42.3% of the study group). The patients' age at endoscopic examination was 41–74 years (mean 60.5 ± 9.4). The examination was performed after various periods from the date of acromegaly diagnosis: in 11 patients shortly after the diagnosis (up to 6 months), and in 19 patients in the period of 1–18 years after the diagnosis (median 3.5 years; min. 1 month, max. 18 years). Of the 16 persons diagnosed with acromegaly within the past 4 years (2012–2015) 11 patients (68.8%) underwent colonoscopy. In the group of the remaining 53 patients diagnosed earlier, the examination was performed in 19 persons (35.8%), and in 9 of them (17%) also in the past 4 years. No statistically significant differences were found in relation to the patients' age and gender, or disease duration and the time passed since the diagnosis and referral for colonoscopy.

Colorectal polyps were found in 70% of the performed examinations (in 21 patients, i.e. in 30.4% of the acromegaly population), including colorectal cancer in 2 women, i.e. in 6.7% of the patients who underwent the examination. Polyps were found more frequently in men (9 cases, i.e. 81.8% of the studied group) than in women (12 cases, i.e. 63.2% of the studied group). However, this difference was of no statistical significance. Colonic diverticula or no pathological lesions were found in 9 patients, i.e. 13% of the study group (30% of the performed examinations). Patients' characteristics and the results of colonoscopic examination performed once are presented in Table 1.

Statistical analysis showed no significant dependencies between gender and age of the study group and the pathological lesions found in the intestine. However, a statistically significant increase of colorectal polyp incidence with disease duration was confirmed ($p < 0.001$). Only in 4 cases the examination was repeated: in 3 W – two times and in 1 W – three times (Table 2).

Table 1. Characteristics of acromegaly patients who underwent one colonoscopic examination

No.	Gender	Age	Year of acromegaly diagnosis	Year of colonoscopy performance	Age on colonoscopic examination	Indications for examination	Examination result
1	W	65	1996	2012	62	anemia	colonic diverticula
2	W	59	1997	2010	54	anemia	sigmoid colon polyp
3	W	55	2015	shortly after diagnosis	55	screening test	no changes
4	W	79	2006	2010	74	screening test	no changes
5	W	66	2009	shortly after diagnosis	60	screening test	sigmoid colon polyps
6	W	67	2014	shortly after diagnosis	66	screening test	descending colon polyp, sigmoid colon diverticula
7	W	62	2014	shortly after diagnosis	61	screening test	sigmoid colon and rectum polyposis, sigmoid colon diverticulosis
8	W	59	2000	2014	58	screening test	ascending colon polyp
9	W	66	2008	2009	60	screening test	transverse colon polyps
10	W	55	1998	2015	55	screening test	sigmoid colon diverticula
11	W	43	2013	shortly after diagnosis	41	screening test	diverticula of descending colon and sigmoid colon
12	W	69	1997	2009	63	screening test	caecum polyps, rectosigmoid junction cancer
13	W	62	2008	2014	61	screening test	sigmoid colon polyps
14	W	47	2000	2014	46	screening test	no changes
15	W	72	2001	2013	70	screening test	colon polyps and diverticula
16	M	69	1987	2005	59	screening test	no changes
17	M	46	1997	2014	45	screening test	rectal polyps
18	M	68	2012	2014	67	screening test	colon polyps
19	M	55	2006	2010	50	screening test	colon polyp
20	M	45	2015	one month after diagnosis	45	screening test	no changes
21	M	59	2014	2014	59	screening test	sigmoid colon and rectum polyposis
22	M	44	2015	shortly after diagnosis	44	screening test	colon polyps

Table 1. Characteristics of acromegaly patients who underwent one colonoscopic examination

No.	Gender	Age	Year of acromegaly diagnosis	Year of colonoscopy performance	Age on colonoscopic examination	Indications for examination	Examination result
23	M	63	2013	shortly after diagnosis	65	screening test	sigmoid colon and rectum polyps, colon and sigmoid colon diverticulosis
24	M	66	2005	2010	61	screening test	rectal polyps
25	M	50	2014	shortly after diagnosis	49	screening test	rectal polyps
26	M	55	2013	shortly after diagnosis	53	screening test	sigmoid colon and rectum polyps

Table 2. Characteristics of acromegaly patients who underwent repeated colonoscopic examination

No.	Gender	Age	Number of performed colonoscopies	Years since acromegaly diagnosis	Age on colonoscopic examination	Indications for examination	Examination result
1	W	69	1	9	67	chronic anemia	colonic diverticula
			2	11	69	chronic anemia	colonic diverticula
2	W	61	1	3	58	abdominal pain, occult blood in stool	colorectal polyps
			2	4	59	follow-up examination	colorectal polyps
3	W	71	1	shortly after diagnosis	62	screening test	polyposis and diverticulosis
			2	1	63	follow-up examination	polyposis and diverticulosis
4	W	70	1	9	63	screening test	colorectal polyps
			2	13	67	follow-up examination	colorectal polyps
			3	16	70	abdominal pain, pencil thin stools, anemia	ascending colon cancer

In 18 patients, despite the polyps found during the first colonoscopy, the examination was not repeated. Endoscopic examination was well tolerated with no significant complications. In 39 patients aged 26–83 years (mean 58 ± 12) colonoscopic examination had not been performed, despite the time from 2 months to 29 years (median: 10.5 years) passed since acromegaly diagnosis. The patients who underwent colonoscopy, as well as those who did not, showed no statistically significant differences with regard to age, gender or disease duration.

Discussion

The proliferative and anti-apoptotic activities of GH and IGF-1, associated with an increased risk of neoplasia in the course of acromegaly are commonly known phenomena. The incidence of mild and malignant neoplasms increases with acromegaly duration, and malignant neoplasms account for a third of causes of death [6, 7]. Among neoplastic lesions the most common ones are polyps and colorectal cancers [8, 9]. According to the relevant literature, the risk of colon polyps in the course of acromegaly is 3.2 times greater than in the general population, irrespective of age or gender [10]. Polyps, in turn, may contribute to the development of colorectal cancers. Therefore, regular colonoscopy screening tests are recommended to detect and remove polyps and eventually lower mortality related to colorectal cancers in this group of patients [8, 9, 11, 12].

In the studied acromegaly population only less than a half of patients (43.5%) underwent colonoscopy examination, which in 70% of cases revealed mild or malignant cancerous lesions. The patients who were diagnosed after 2012 underwent colonoscopy more frequently (68.6%) in comparison to the patients diagnosed before this date (35.8%), which may be associated with greater awareness of acromegaly-related complications, as well as the greater availability of such examinations in recent times. Of the patients who had suffered from acromegaly for a long time 17% underwent endoscopic examination of the large intestine only in the last 4 years, which also appears to confirm the above thesis.

The patients who underwent endoscopy, as well as those who did not, showed no statistically significant differences with regard to age, gender or disease duration in comparison with the sub-group, who did not have this examination, and therefore it might be concluded that these are not significant factors conditioning colonoscopy performance.

In our sampled material colorectal polyps were found in 30.4% of patients, similarly to the results indicated by other authors: Koksal et al. – 30.3% [10], Dworakowska et al. – 35% [12], lower than in Kurimoto et al. – 40.2% [8], and greater than indicated by Bałdys-Waligórska et al. in a group of 101 acromegaly patients – 13% [13] or in the group of 235 patients studied by Terzolo et al. – 23.4% [14]. Colorectal polyps were found more frequently in our sampled materials than reported by Koksal et al. (12.3%) [10] or Terzolo

et al. (14.6%) [14] in the general population. Contrary to the findings of other authors, who observed a similar incidence of mild colorectal lesions in both genders [10, 15], in our study they were more numerous in men, similarly to the general population [10, 16, 17]. However, this difference was of no statistical significance.

In our study the incidence of colorectal cancer was greater (6.7%) in comparison to Bałdys-Waligórska's et al. group – 2% [13] or Terzlo et al. – 4.3% [14], and significantly more frequent than in the control group consisting of 233 persons, studied by Terzlo et al. – 0.9% [14], but less frequent than in Kurimoto's et al. – 10.3% [8].

Repeated colonoscopic screening tests in acromegaly patients confirm the high risk of new polyps development in the large intestine, particularly in patients who were found to have polyps during the first examination [12, 14], and in persons with an uncontrolled disease and a high concentration of IGF-1 [12]. In such cases the authors recommend tests be repeated every 5 years, and in the group at lower risk every 10 years [12].

Polish guidelines regarding diagnostic-therapeutic measures recommend a colonoscopy test in all acromegaly patients every 2–3 years [2].

Of our patients, only in 4 cases was the examination was performed more than once: in 3 women – two times, and in 1 woman – three times, and only in 2 patients the first colonoscopy was performed as a screening test, and in 2 other women it was indicated due to additional symptoms, i.e. chronic anemia in one case, and abdominal pain and occult blood in stool in the other case. Other colonoscopies were performed in relation to the revealed pathological lesions in the large intestine during the previous examination (Table 2).

The fact that 39 patients (56.5%) of the studied population, despite the long time after acromegaly diagnosis, did not undergone colonoscopy indicate the ignorance and fear of this test. It is supposed that due to the same reason 18 patients with diagnosed polyps did not undergo the follow-up test. The authors believe that in such cases GPs' role as information providers is of crucial importance.

The limitation of our study is the relatively low number of patients, which is related to the low prevalence of acromegaly in the general population. Despite this, our observations, similarly to the findings of the previously cited authors [8, 9, 11, 12], confirm the importance of screening colonoscopy tests in all acromegaly patients, in accordance with the relevant Polish guidelines [2]. The fact that acromegaly presence significantly increases the incidence of colorectal polyps should impel the early referral of patients for colonoscopic examinations.

Conclusions

The current guidelines regarding colonoscopic examination to be performed in all acromegaly patients are carried out in less than a half of cases. The guidelines advocating colonoscopic examination to be performed every 2–3 years are followed occasionally. In acromegaly patients colonoscopy is treated as a diagnostic test of great significance, since in as many as 70% of cases it confirms the presence of pathological lesions in the large intestine and simultaneously allows for their removal or sampling for histopathological examination. As a low-invasive, safe and well-tolerated examination it should be performed in all patients. Primary Health Care specialists should make acromegaly patients aware of the importance of colonoscopy, and refer them for this examination shortly after the diagnosis, and afterwards for periodic follow-up examinations.

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References

1. Bolanowski M, Kałużny M, Jawiarczyk A. Akromegalia – możliwe trudności diagnostyczne w praktyce lekarza rodzinnego. *Fam Med Prim Care Rev* 2010; 12(2): 317–319.
2. Bolanowski M, Ruchała M, Zgliczyński W, et al. Acromegaly – a novel view of the patient. Polish propos al of diagnostics and therapeutic procedure in the light of recent reports. *Endokrynol Pol* 2014; 65(4): 326–331.
3. Zieleniewski W, Michalak R. Akromegalia – niedoceniony problem zdrowotny w praktyce lekarza rodzinnego. *Fam Med Prim Care Rev* 2011; 13(2): 273–275.
4. Kałużny M, Bolanowski M. Acromegaly – a possible cause of diagnostic errors in family doctor's practice. *Fam Med Prim Care Rev* 2009; 11(2): 173–178.
5. Dutta P, Bhansali A, Vaiphei K, et al. Colonic neoplasia in acromegaly: increased proliferation or decreased apoptosis? *Pituitary* 2012; 15(2): 166–173, doi: 10.1007/s11102-011-03009.
6. Colao A, Ferone D, Marzullo P, et al. Systemic complications of acromegaly: epidemiology, pathogenesis, and management. *Endocr Rev* 2004; 25(1): 102–152.
7. Jenkins PJ, Besser M. Clinical perspective: acromegaly and cancer: a problem. *J Clin Endocrinol Metab* 2001; 86(7): 2935–2941.
8. Kurimoto M, Fukuda I, Hizuka N, et al. The prevalence of benign and malignant tumors in patients with acromegaly at a single institute. *Endocr J* 2008; 55(1): 67–71.
9. Rokkas T, Pistiolas D, Sechopoulos P, et al. Risk of colorectal neoplasm in patients with acromegaly: a meta-analysis. *World J Gastroenterol* 2008; 14(22): 3484–3489.
10. Koksal AR, Ergun M, Boga S, et al. Increased prevalence of colorectal polyp in acromegaly patients: a case-control study. *Diagn Ther Endosc* 2014; 2014: 152049, doi: 10.1155/2014/152049.
11. Lois K, Bukowczan J, Perros P, et al. The role of colonoscopic screening in acromegaly revisited: review of current literature and practice guidelines. *Pituitary* 2015; 18(4): 568–574, doi: 10.1007/s11102-014-0586-5.
12. Dworakowska D, Gueorguiev M, Kelly P, et al. Repeated colonoscopic screening of patients with acromegaly: 15-year experience identifies those at risk of new colonic neoplasia and allows for effective screening guidelines. *Eur J Endocrinol* 2010; 163(1): 21–28, doi: 10.1530/EJE-09-1080.
13. Bałdys-Waligórska A, Krzentowska A, Gołkowski F, et al. The prevalence of benign and malignant neoplasms in acromegalic patients. *Endokrynol Pol* 2010; 61(1): 29–34.
14. Terzolo M, Reimondo G, Gasperi M, et al. Colonoscopic screening and follow-up in patients with acromegaly: a multicenter study in Italy. *J Clin Endocrinol Metab* 2005; 90(1): 84–90.
15. Bolfi F, Miot HA, Resende M, et al. Frequency of various types of neoplasia in a group of acromegalic patients. *Arq Bras Endocrinol Metabol* 2013; 57(8): 612–616.

16. Yanik S, Akkoca AN, Özdemir ZT, et al. Evaluation of results of lower gastrointestinal endoscopic biopsy. *Int J Clin Exp Med* 2014; 7(12): 5820–5825.
17. Coleman HG, Loughrey MB, Murray LJ, et al. Colorectal cancer risk following adenoma removal: a large prospective population-based cohort study. *Cancer Epidemiol Biomarkers Prev* 2015; 24(9): 1373–1380, doi: 10.1158/1055-9965.

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