Clinical Characteristics And Associated Factors Of Colonic Polyps In Acromegaly

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Research Article

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Abstract

Purpose: This study investigates the clinical characteristics and the associated factors of colonic polyps in patients with acromegaly.

Methods: We retrospectively reviewed clinical characteristics and colonoscopy findings of 86 acromegalic patients who received treatment between August 2015 and July 2020 at Xinqiao Hospital. We analyzed colonoscopy findings and correlation with growth hormone (GH)-secreting pituitary adenoma (GHPA) volume and hormonal/metabolic levels.

Results: Our analysis revealed that the prevalence of colonic polyps in acromegalic patients was 40.7% and increased significantly with advanced age, especially ≥ 50 years. Multiple polyps (62.8%) and colonic polyps in the left colon (54.2%) were detected more frequently. Compared to acromegalic patients without polyps, patients with polyps displayed higher IGF-1 $\times$ ULN levels ($P=0.03$). IGF-1 levels and GHPA volumes in patients with polyps showed increasing trends, although there were no significant differences. Meanwhile, patients with polyps in the right colon showed higher GH levels and GH nadir (GHnadir) levels in the oral glucose tolerance test (OGTT) than those with polyps in the whole colon ($P=0.023$ and $P=0.037$, respectively). GH levels were higher in patients with polyps diameter ≤ 5 mm than those with polyps diameter >5 mm ($P=0.031$). In addition, the univariate and multivariate logistic regression analysis exhibited GHPA volumes (OR: 1.09, 95% CI: 1.01–1.20; $P=0.039$) and IGF-1 $\times$ ULN Q2 levels (OR: 6.51, 95% CI: 1.20–44.60; $P=0.038$) were independent factors for predicting the risk of colonic polyp occurrence in acromegalic patients. A nomogram was created to evaluate the risk of colonic polyps in acromegalic patients.

Conclusion: The acromegalic patients are a high prevalence population of colonic polyps. Colonic polyps in acromegaly were multiple and frequently detected in the sigmoid colon and rectum. GHPA volumes and IGF-1 $\times$ ULN levels may be predictors of colonic polyp occurrence.

Introduction

Acromegaly is a chronic endocrine and metabolic disease, accompanied by excessive secretion of GH and insulin-like growth factor-1 (IGF-1) by growth hormone (GH)-secreting pituitary adenoma (GHPA) [1, 2]. The increased mortality rate in acromegaly results from cardiovascular and cerebrovascular diseases, respiratory complications, and neoplastic complications such as colorectal cancer [3, 4].

Colonic polyps and diverticula are typical digestive complications in acromegaly. The significantly increased risk of colonic polyps in patients with acromegaly compared with the general population is well recognized [5]. The prevalence of colonic polyps in acromegalic patients reported a wider range from 7 to 76% [6–9], while there is still a lack of epidemiological data in China. Most colorectal cancer derives from an “adenomatous polyp-carcinoma sequence,” and the process generally takes 10–15 years [10]. However, according to the current findings, colorectal cancer occurrence remains controversial in acromegaly. A nationwide survey in Italy reported an overall standardized incidence ratio (SIR) for colorectal cancer of 1.67 (95% CI: 1.07–2.58) [11, 12]. At the same time, population-based studies did not identify any significant risk of colorectal cancer [13]. In acromegalic patients, a better understanding of digestive diseases, especially colonic polyp developments, is critical for early diagnosis and clinical intervention of colorectal cancer.

To gain insights into the clinical characteristics and the associated factors of colonic polyps in acromegaly. In this retrospective study, we collected the clinical data of 86 acromegalic patients who underwent a colonoscopy at diagnosis in our center. We analyzed the prevalence, number, size, and site distribution of colonic polyps and other clinical indicators. Furthermore, we identified the associated risk factors of colonic polyps in patients with acromegaly.

Materials And Methods

Patients

We retrospectively collected data of acromegalic patients followed at the Second Affiliated Army Medical University (Xinqiao Hospital) from August 2015 to July 2020, and 86 patients (44 males and 42 females) who underwent a colonoscopy at diagnosis were included in this study. Acromegaly was diagnosed according to the criteria available at the time of diagnosis as follows [14, 15]: 1) evidence of clinical signs and symptoms of the disease; 2) serum IGF-I levels beyond the normal range for age- and sex-matched control individuals, and elevated baseline GH level; 3) maximally suppressed GH levels (GHnadir) during a 75-g oral glucose load test (OGTT) were > 1 ug/L; and 4) evidence of a pituitary tumor on imaging. No patient had a family history of colon cancer.

This study was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Army Medical University (No. 2021-035-01) and registered in the Chinese Clinical Trial Registry (No. ChiCTR1800017714). All the participants provided written informed consent.

Data Collection

Clinical data, including age, sex, height, weight, body mass index (BMI), histological results, site distribution, size, and number of polyps, were collected. Blood samples were obtained after an overnight fast. Glucose metabolic profiles were determined, including fasting blood glucose (FBG) and glycosylated hemoglobin A1c (HbA1c) levels. The automatic biochemical analyzer measured the creatinine (CREA) level, estimated the glomerular filtration rate (EGFR), and measured the levels of uric acid (UA), cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). Growth hormone (GH) and insulin-like growth factor (IGF-1) levels were quantified using chemiluminescent immunoassays. The outcome of the IGF-1 assay in each patient was represented by the IGF-1 index (IGF-1 $\times$ ULN): serum IGF-1/upper limit of IGF-I for age [9]. Each patient consumed a 75-g glucose beverage in 5 min, and blood samples were collected before the start of the test (0 min) and 30, 60, 90, 120, and 180 minutes after the 75-g glucose intake. GH nadir levels during OGTT corresponded to maximally suppressed GH levels during the 180 min-OGTT. The pituitary was imaged with a 3T MRI scanner with or without gadolinium-DTPA (1.0 mmol/kg). The anteroposterior diameter (AD), vertical diameter (VD), and transverse diameter (TD), as well as the Knosp classifications of the GHPA, were evaluated by two experienced radiologists using precision calipers. The GHPA volume was calculated using the formula for approximating the volume of an ellipsoid: $\pi/6 \times AD \times VD \times TD$ [16].

Experienced gastroenterologists performed colonoscopies in acromegalic patients after careful bowel preparation with a 2 L dose of polyethylene glycol electrolyte-based solution (Shenzhen Wanhe Pharmaceutical Co., Ltd., Shenzhen, China). All colonic polyps on colonoscopy were recorded, and if possible, removed for histological examination. Age was divided into a categorical variable with four groups, namely, ≤ 39 , 40–49, 50–59, and ≥ 60 years. The site distribution of polyps was defined as the right colon (the cecum, ascending colon, and hepatic flexure), the left colon (the splenic flexure, descending colon, sigmoid colon, and rectum), and the whole colon (both the right colon and the left colon) [10]. All colonic polyps detected at colonoscopy were grouped into size categories (≤ 0.5 , 0.6–0.9, and ≥ 1.0 cm) depending on endoscopic measurement by the diameter of open biopsy forceps [17]. The number of polyps was divided into a categorical variable (single or multiple (≥ 2)).

Statistical analysis

Analyses were conducted by R studio (version 1.3.1093). The Shapiro-Wilk W test verified the normality of the variable distribution: variable distribution was considered normal if $P \geq 0.05$. According to the distribution of the variables, variables were described either as means $\pm$ SD or medians with interquartile ranges (IQR). For normally distributed variables, we used an independent samples *t*-test to compare variables between two groups, whereas one-way ANOVA, followed by Tukey's multiple comparison test, was used to compare variables among three or more groups. For non-normally-distributed variables, the Mann-Whitney U test was used to compare variables between two groups, whereas the Kruskal-Wallis test, followed by pairwise comparisons using the BWS all-pairs test, was used for multiple subgroups. The relationships between variables were examined using Spearman's correlation analysis. Univariate and multivariate logistic regression analyses were performed to assess the associations of the variables with the diagnosis. A nomogram was created using the predictors from the multivariate analysis for relating the risk of polyp occurrence. The tests were considered statistically significant at $P < 0.05$.

Results

Clinical features of acromegalic patients with colonic polyps A total of 86 acromegalic patients (mean age, 43.53 ± 11.78 years; sex, 48.8% females) underwent complete colonoscopy. Of the 86 patients, 35 patients (18 females, 17 males) were found to have one or more polyps, with a higher prevalence (40.7%) than a general Asian population (17.6–23.9%) of comparable age [17–20]. The prevalence of polyps increased with age, reaching a peak at ≥ 60 years. The prevalence rates of polyps in acromegalic patients aged ≤ 39 , 40–49, 50–59, and ≥ 60 years were 30, 32, 50, and 77.8%, respectively (Fig. 1). Of the 35 patients, 13 (37.2 %) and 22 (62.8%) patients had a single polyp and multiple polyps, respectively. The mean diameter of the polyps was in most cases ≤ 5 mm (71.4%), and the maximum diameter of the polyps was ≥ 10 mm. With respect to the different site distributions of the colonic polyps, 4 (11.4%) patients had polyps in the right colon, 19 (54.3%) patients had polyps in the left colon, and 12 (34.3%) patients had polyps in the whole colon. Colonic polyps were more frequently detected in the sigmoid colon and rectum. In addition, only 5 cases of colonic polyps were biopsied, and all of them were histologically confirmed to be adenomas. Furthermore, 21 patients were observed to have hemorrhoids, and 1 patient was observed to

have chronic colitis. There were no patients with colorectal carcinoma (Table 1). At diagnosis, 79 (92%) patients had pituitary macroadenoma, 3 (3%) patients had pituitary microadenoma, and 4 (5%) patients had no data on the pituitary tumor diameter. Hypertension, impaired glucose metabolism (diabetes mellitus and impaired glucose tolerance), and dyslipidemia were separately diagnosed in 24 (28%), 47 (55%), and 34 (40%) patients, respectively (Table 1). Characteristics of colonic polyps associated with hormone levels The results showed that acromegalic patients with colonic polyps were older and had higher IGF-1×ULN levels than those without colonic polyps ($P=0.005$ and $P=0.03$, respectively, Table 1). No significant differences were found between acromegalic patients with or without colonic polyps regarding sex, BMI, FBG levels, dyslipidemia, hypertension, diabetes mellitus, GHPA volumes, Knosp classifications, UA levels, GH levels, GHnadir levels during OGTT, and IGF-1 levels (Table 1 and Supplementary Table 1). Although GH levels and GHnadir levels during OGTT were similar in patients with or without colonic polyps, GHPA volumes and IGF-1 levels tended to be higher in those with polyps, although there were no statistical differences between the two groups (Table 1). As shown in Table 2, with respect to the different site distribution of polyps, GH levels, and GHnadir levels during OGTT in patients with polyps in the right colon were higher than those in patients with polyps in the whole colon ($P=0.023$ and $P=0.037$, respectively). Interestingly, compared with polyp diameters >5 mm, GH levels were significantly higher in patients with polyp diameters ≤5 mm ($P=0.031$, Table 2). Apart from the BMI ($P=0.013$), we did not identify relevant clinical indicators between the two groups with single polyps and multiple polyps (Table 2). GHPA volumes, IGF-1 levels, and IGF-1×ULN levels were similar among subjects with different site distribution, size, and number of polyps. In addition, with respect to the different site distribution of polyps, hypertension and diabetes mellitus had a significant association with the polyps in the right colon, left colon, and whole colon ($P = 0.003$ and $P = 0.008$, respectively, Table 2). However, FBG and HbA1c had observed no difference with respect to three different site distributions of polyps (Supplementary Table 2). Next, to investigate the effect of IGF-1×ULN in acromegalic patients with polyps, we further divided the subjects into IGF-1×ULN-quantile subgroups according to the IGF-1×ULN level (Table 3). Age, GH levels, and GHnadir levels during OGTT were significantly higher in acromegalic patients with the highest IGF-1×ULN levels than those with the lowest IGF-1×ULN levels in the first quantile ($P<0.05$ for Q1 vs Q4). Compared to patients with lower IGF-1×ULN levels in the second quantile, UA levels were significantly higher in patients with the highest IGF-1×ULN levels ($P<0.05$ for Q2 vs Q4). Notably, there were changes in the IGF-1×ULN-quantile subgroups with respect to acromegalic patients with or without colonic polyps, GHPA volumes groups, and IGF-1 levels ($P<0.05$, Table 3). Prognostic model for colonic polyps in acromegalic patients In univariate analysis, age, especially 60 years and older, and the IGF-1×ULN level predicted polyp occurrence in acromegalic patients as shown in Table 4. Furthermore, in multivariate analysis, these variables showed that GHPA volumes (OR: 1.09, 95% CI: 1.01–1.20; $P=0.039$) and IGF-1×ULN Q2 levels (OR: 6.51, 95% CI: 1.20–44.60; $P = 0.038$) were independently associated with polyp occurrence (Table 4). IGF-1×ULN Q3 and IGF-1×ULN Q4 cloud also are independent risk predictors, although no significant difference was found. Thus, univariate and multivariate analyses revealed that GHPA volumes and IGF-1×ULN levels could be independent risk factors for polyps in acromegalic patients. In addition, a nomogram for predicting acromegalic patients with polyp risk was constructed using the variables (Fig 2). According to the prognostic model, a man with a GHPA volume of 3.5 cm³ and an IGF-1×ULN level of 5.5 was predicted to have an 80% probability of polyps.

Discussion

According to several population-based studies, the incidence of colon cancer in patients with acromegaly ranges from 0.9 to 2.4% [12, 21, 22]. However, the risk of colon cancer in acromegaly is still controversial. Colonoscopy screening can reduce the mortality from colorectal cancer by early detection and removal of pre-existing adenomatous polyps. In this study, we ascertained a high prevalence of colonic polyps was 40.7% in acromegalic patients. IGF-1×ULN levels were higher in patients with polyps than in those without polyps. GHPA volumes and IGF-1×ULN levels were found to be independent risk factors for polyps.

Colonic polyps had a high prevalence in acromegalic patients. In this study, the overall prevalence of colonic polyps was 40.7%. The prevalence of colonic polyps in the acromegalic population was significantly higher than in the Asian general population. In the non-acromegalic population, the prevalence of polyps ranged from 17.6 to 23.9% [17–20]. The prevalence of colonic polyps also varied in different acromegalic populations. One of the largest datasets from 14 centers across Europe indicated that the prevalence of polyps in a fourth of acromegalic patients (820/3173) who had a colonoscopy was 13% [23]. Furthermore, the prevalence of polyps in patients with acromegaly was 32% in an Italian single-center study [24]. In contrast, French national registry data reported that the prevalence of colonic polyps ranged from 27–55% [22]. The different prevalence of colonic polyps may be due to differences in genetic predisposition, environmental backgrounds, and lifestyle (including dietary habits). The prevalence of multiple polyps was 62.8% compared to earlier reports by Bogazzi (50%) [9] and Colao (72.1%) [8]. A colonic polyp diameter > 10 mm is generally considered a high risk of colorectal carcinoma and thought to take more than ten years. A recent study reported the frequency of polyps ≥ 10 mm was 15.2%, and 5 patients were detected colorectal cancer [25]. However, the maximum diameter of colonic polyps was < 10 mm, and most colonic polyps were at early stages ≤ 5mm (71.4%), which may explain why no colorectal cancer was found in our study.

We found a significant association between polyp occurrence and hormone values. In detail, IGF-1×ULN levels in patients with polyps were higher than those without polyps, consistent with previous findings [22]. Although GH and GHnadir levels during OGTT were similar in patients with or without colonic polyps, IGF-1 levels and GHPA volumes tended to be higher in those with polyps. Nevertheless, few studies have consistently suggested that IGF-1 levels are significantly related to polyp prevalence [24, 26]. This study also indicated that GH and GHnadir levels during OGTT were higher in patients with polyps in the right colon and a diameter ≤ 5 mm. As a result, we hypothesize that GH levels may play different roles in different stages of polyp development. The findings in patients with acromegaly suggest a higher prevalence of polyps in the left colon, similar to Battistone et al. [27]. In the general population, previous literature also reported that the site distribution of polyps was detected mainly in the left colon [17, 28]; however, several studies observed polyps in the cecum and ascending colon [29–31]. Additionally, the acromegalic patients with multiple polyps were higher BMI levels than those with single polyps. Compared to patients without polyps, the age in patients with polyps was higher. Simultaneously, the prevalence of colonic polyps increased significantly with age ≥ 50 years ($> 50\%$). Bogazzi [9] and Parolin [24] also reported similar trends in polyp prevalence when patients were ≥ 50 years old. Although the recent guidelines recommend the initiation of colonoscopy screening at 50 years of age for the average-risk non-acromegalic population [32, 33], this may be inadequate for patients with acromegaly. A few guidelines have suggested that the initial colonoscopy should be performed at the age of 40 years to early detect precancerous polyps in acromegaly [31, 34, 35]. However, we observed that several patients younger than 40 years of age had colonic polyps. Similarly, Terzolo et al. reported younger acromegalic patients had a higher risk of colonic neoplasia than those with age-matched controls [7]. Therefore, colonoscopic surveillance should be performed at the time of diagnosis in acromegaly as recent guideline recommendations [36–39].

GHPA volumes may be a reliable predictor for polyp occurrence in acromegaly. According to univariate analysis and clinical parameters, the final diagnostic model was decided using age, height, GHPA volumes, and IGF-1×ULN levels. To our knowledge, this is the first study reporting that GHPA volumes (OR: 1.09, 95% CI: 1.01–1.20; $P = 0.039$) were an independent risk factor for colonic polyp occurrence. However, GHPA volumes did not differ significantly between patients with or without polyps. We speculate that the larger GHPA volumes were indicative of long-term and uncontrolled secretion of GH and IGF-1 contributing to the higher risk of polyp occurrence. Meanwhile, we found that IGF-1×ULN levels (OR: 6.51, 95% CI: 1.20–44.60; $P = 0.038$) were a predictor for polyp occurrence similar to the results of Gonzalez [26]. Therefore, we established a polyp risk prediction model according to GHPA volumes and IGF-1×ULN levels. For example, a woman with a GHPA volume of 3.5 cm³ and an IGF-1×ULN level of 5.5 was predicted to have a probability of polyps by approximately 80%.

In this study, alone standard intestinal preparation resulted in inadequate intestinal cleansing in most acromegalic patients, seriously affecting the detection of colonoscopy (data not shown). Previous studies have suggested two consecutive bowel preparations or an increased dose of PEG solution for acromegalic patients [40], and the time required to reach the cecum during colonoscopy was significantly prolonged [41]. Furthermore, we acknowledge several limitations in our study. First, this study was relatively small, and the absence of a control group. Second, this was a retrospective analysis, and selectivity bias was impossible to avoid. Third, most polyps with a diameter > 5 mm were not biopsied. Further long-term prospective studies involving acromegalic patients may determine whether colonic polyps have a similar tendency to develop into colon cancer as in the general population.

In conclusion, we confirmed the high prevalence of colonic polyps in patients with acromegaly. Older age, multiple, and usually occurring in the left colon were the clinical features of acromegalic patients with colonic polyps. In addition, GHPA volumes and IGF-1×ULN levels might predict colonic polyp occurrence in the acromegalic population.

Declarations

Ethics declarations

Disclosure Statement: There were no conflicts of interest to declare.

Statement of Ethics: This study was approved by the Medical Ethics Committee of The Second Affiliated Hospital of Army Medical University.

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Informed consent: Informed consent was obtained from all individual participants included in the study.

Author Contributions

GL.P., P.H., and YL.Z.: acquired the data; RF.S. and L.Z.: M.R. imaging assessment; YY.Z., JY.B., and GL.P.: colonoscopy assessment; GL.P., X.L., RF.S.: did the statistical data analysis and draft the manuscript; L.Z., MY.L., YL. Z. And WX.L.: interpreted the data, contributed to the methods, and performed the laboratory analyses; M.L., HT.Z., and Z.S.: revised the manuscript; RF.S. and M.L.: obtained the study funding and supervised the study. All authors read and approved the manuscript for publication.

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Tables

Table 1. Clinical characteristics of the study patients with acromegaly.

	Total Patients (n = 86)	Patients without polyps = 51)	(n	Patients with polyps = 35)	(n	P value
Age (years)	43.53 ±11.78	40.63 ±11.58		47.77 ±10.88		0.005*
Sex, female, n (%)	42 (49)	24 (47)		18 (51)		0.858
BMI (Kg/m2)	26.1 ±3.05	25.96 ±3.05		26.31 ±3.09		0.602
GHPA Volumes (cm ³)	2.47 (1.15, 6.44)	2.2 (1.17, 4.87)		3.19 (1.15, 7.31)		0.305
Basal GH levels (ug/L)	18.3 (8.08, 34.5)	17.8 (5.94, 29.8)		19.3 (9.7, 52.5)		0.153
GHnadir levels during OGTT (ug/L)	12.1 (5.24, 30.9)	12 (4.41, 25.2)		13 (6.54, 40.85)		0.18
Basal IGF-1 levels (ng/mL)	762.56 ±259.66	733.73 ±259.89		804.57 ±257.24		0.215
IGF-1×ULN	2.53 (1.94, 3.01)	2.22 (1.79, 2.88)		2.73 (2.1, 3.2)		0.03*
FBG (mmol/L)	5.07 (4.4, 5.96)	4.95 (4.38, 5.82)		5.33 (4.54, 6.29)		0.34
Hemorrhoids,n (%)	21(24)	7(20)		14(27)		0.403
Hypertension, n (%)	24 (28)	15 (29)		9 (26)		0.896
Diabetes mellitus, n (%)						0.708
non-diabetes mellitus	25 (29)	14 (27)		11 (31)		
IGT	39 (45)	25 (49)		14 (40)		
DM	22 (26)	12 (24)		10 (29)		

Data are shown as mean ± SD for variables of normal distribution, and median with the interquartile range (25-75%) for skewed variables.

BMI: body mass index; GHPA Volume: growth hormone (GH)-secreting pituitary adenoma volume; GH: growth hormone; GHnadir levels during OGTT: the maximal suppression of GH levels during 180-OGTT, IGF-1: insulin-like growth factor; ULN = upper limit of normal; FBG: fasting blood glucose; IGT: impaired glucose tolerance; DM: diabetes mellitus.

P value for Patients without polyps vs Patients with polyps, * p<0.05.

Table 2. Clinical characteristics of acromegalic patients with polyps.

	the site distribution of polyps			<i>P</i> value	the size of polyps		<i>P</i> value	the number of polyps		
	right colon	left colon	whole colon		≤5mm	>5mm		Single polyp	Multiple polyps	<i>P</i> value
	(n = 4)	(n = 19)	(n = 12)		(n = 25)	(n = 10)		(n = 13)	(n = 22)	
Age (years)	49.25 ±13	44.58 ±10.47	52.33 ±9.95	0.148	47 ± 11.43	49.7 ± 9.62	0.486	43.23 ±11.73	50.45 ±9.62	0.056
Sex (Female), n (%)	4 (100)	8 (42)	6 (50)	0.164	13 (52)	5 (50)	1	7 (54)	11 (50)	1
BMI (kg/m ²)	27.09 ±3.74	26.19 ±3.56	26.24 ±2.19	0.873	25.95 ± 3.42	27.2 ± 1.91	0.182	24.66 ±3.25	27.28 ±2.6	0.013*
GHPA Volumes (cm ³)	4.83 (3.55, 5.88)	3.48 (1.3, 12.63)	1.83 (0.96, 6.91)	0.531	3.48 (1.25, 6.75)	2.22 (0.54, 8.81)	0.615	3.59 (1.81, 7.46)	2.95 (1.05, 6.86)	0.366
Basal GH levels (ug/L)	127.5 (70.33, 189.5) ^c	17 (13.05, 33.95)	11.95 (7.8, 33.08)	0.023*	26.6 (14.5, 61.4)	9.7 (8.08, 19.1)	0.031*	35.3 (14, 82)	16.45 (8.2, 27.57)	0.142
GHnadir levels during OGTT (ug/L)	73.9 (44.7, 111.1) ^c	12.4 (8.59, 37.2)	8.75 (5.02, 24.25)	0.037*	21.2 (8.76, 48)	8.7 (4.52, 12.32)	0.05	21.2 (10.3, 48)	11.25 (4.43, 28.23)	0.124
Basal IGF-1 (ng/mL)	731.75 ±261.15	869 ±267.81	726.83 ±229.95	0.279	802.56 ± 271.42	809.6 ± 231.27	0.939	808.54 ±247.11	802.23 ±268.75	0.945
IGF-1×ULN	2.92 (1.84, 3.93)	2.83 (2.22, 3.2)	2.59 (2.36, 2.97)	0.764	2.84 ± 1.05	2.94 ± 0.85	0.773	2.72 (2.08, 3.16)	2.78 (2.42, 3.22)	0.585
Hypertension, n (%)	1 (25) ^{a,b}	1 (5) ^c	7 (58)	0.003*	6 (24)	3 (30)	0.694	1 (8)	8 (36)	0.109
DM, n (%) ^{a,b, c}	0.008*						0.33			0.455
Non-DM	0 (0)	11 (58)	3 (25)		12 (48)	2 (20)		6 (46)	8 (36)	
IGT	0 (0)	6 (32)	4 (33)		6 (24)	4 (40)		2 (15)	8 (36)	
DM	4 (100)	2 (11)	5 (42)		7 (28)	4 (40)		5 (38)	6 (27)	

Data are shown as mean ± SD for variables of normal distribution, and median with the interquartile range (25-75%) for skewed variables.

BMI: body mass index; GHPA Volume: growth hormone (GH)-secreting pituitary adenoma volume; GH: growth hormone; GHnadir levels during OGTT: the maximal suppression of GH levels during 180-OGTT, IGF-1: insulin-like growth factor; ULN = upper limit of normal;

*: P<0.05.

a: P<0.05 for right colon vs left colon. b: P<0.05 for right colon vs whole colon. c: P<0.05 for left colon vs whole colon.

Table 3. Clinical characteristics and biochemical variables in acromegalic patients of different IGF-1×ULN quartiles.

IGF-1×ULN quartiles	Q1 (n = 21)	Q2 (n = 21)	Q3 (n = 22)	Q4 (n = 22)	P value
Age (years)	37.38 ± 13.35 ^c	45.19 ± 12.02	45 ± 10.18	46.36 ± 9.96	0.048*
Sex, n (%)					0.72
Male	9 (43)	10 (48)	12 (55)	13 (59)	
Female	12 (57)	11 (52)	10 (45)	9 (41)	
BMI (Kg/m2)	25.11 ± 2.92	25.76 ± 3.46	26.37 ± 2.88	27.1 ± 2.78	0.174
GHPA Volumes (cm ³)	5.19 (0.83, 7.95)	2.33 (1.19, 3.38)	2.73 (1.72, 6.5)	1.81 (1.12, 4.33)	0.779
Basal GH levels (ug/L)	9.12 (4.87, 21.8) ^c	17 (10.5, 29.5)	17.15 (8.08, 29.42)	27.45 (19.25, 55.95)	0.018*
GHnadir levels during OGTT (ug/L)	5.85 (2.83, 12.5) ^c	13.8 (11.3, 26.5)	8.59 (5.53, 22.78)	27.25 (10.83, 43.38)	0.023*
Basal IGF-1 levels (ng/mL)	501.24 ± 133.91 ^{a,b,c}	653.19 ± 131.4 ^{d,e}	807.36 ± 134.64 ^f	1071.59 ± 197.13	< 0.001*
IGF-1×ULN	1.59 (1.33, 1.8) ^{a,b,c}	2.11 (2.03, 2.32) ^{d,e}	2.81 (2.72, 2.88) ^f	3.85 (3.16, 4.2)	< 0.001*
UA (umol/L)	259.4 (220.7, 348.8)	259.1 (221.6, 299.5) ^e	301.2 (238.48, 389.7)	332.6 (279.68, 389.88)	0.048*
Patients with polyps, n (%)	3 (14) ^{a,b,c}	10 (48) ^{d,e}	10 (45) ^f	12 (55)	0.038*
GHPA Volume group(cm ³), n (%) ^{a,b,c, d,e, f}					0.018*
<1	7 (33)	3 (14)	3 (14)	4 (18)	
1–4	2 (10)	13 (62)	11 (50)	11 (50)	
≥ 4	12 (57)	5 (24)	8 (36)	7 (32)	

Data are shown as mean ± SD for variables of normal distribution, and median with the interquartile range (25-75%) for skewed variables.

BMI: body mass index; GHPA Volume: growth hormone (GH)-secreting pituitary adenoma volume; GH: growth hormone; GHnadir levels during OGTT: the maximal suppression of GH levels during 180-OGTT, IGF-1: insulin-like growth factor; ULN: upper limit of normal.

*: P<0.05.

a. P<0.05 for Q1 vs Q2; b. P<0.05 for Q1 vs Q3; c. P<0.05 for Q1 vs Q4; d. P<0.05 for Q2 vs Q3; e. P<0.05 for Q2 vs Q4; f. P<0.05 for Q3 vs Q4.

Table 4. Univariate and multivariable logistic regression analysis of associations between clinical and biochemical variables and polyps.

	Univariate analysis		Multivariate analysis	
	OR (CI 95%)	<i>P</i> value	OR (CI 95%)	<i>P</i> value
Age	1.06 (1.02, 1.11)	0.007	1.05 (0.99, 1.12)	0.11
sex	1.19 (0.50, 2.84)	0.691	-	-
Height	0.02 (0.00, 2.03)	0.102	0.03 (0.00, 16.03)	0.286
Weights	0.98 (0.94, 1.02)	0.397	-	-
BMI	1.04 (0.90, 1.20)	0.597	-	-
GHPA Volumes	1.06 (0.99, 1.15)	0.136	1.09 (1.01, 1.20)	0.039
Basal GH levels	1.00 (1.00, 1.01)	0.278	-	-
GHnadir levels during OGTT	1.00 (1.00, 1.01)	0.22	-	-
Basal IGF-1 levels	1.00 (1.00, 1.00)	0.216	-	-
IGF-1×ULN	1.65 (1.04, 2.75)	0.04	1.47 (0.88, 2.55)	0.151
FBG	1.07 (0.86, 1.34)	0.548	-	-
TG	0.84 (0.50, 1.10)	0.394	-	-
TC	0.77 (0.49, 1.10)	0.21	-	-
HDL	1.96 (0.33, 12.46)	0.459	-	-
LDL	0.89 (0.47, 1.64)	0.71	-	-
UA	1.00 (1.00, 1.01)	0.702	-	-
Age Group		0.011		
≤39	1		1	
40–50	1.10 (0.34, 3.48)	0.873	-	-
50–60	2.33 (0.75, 7.53)	0.147	-	-
>60	8.17 (1.61, 62.58)	0.019	-	-
IGF-1×ULN Quartile		0.015		
Q1	1		1	
Q2	5.45 (1.34, 28.54)	0.026	6.51 (1.20, 44.60)	0.038
Q3	5.00 (1.24, 25.93)	0.033	5.82 (0.71, 55.33)	0.106
Q4	7.20 (1.80, 37.50)	0.009	10.52 (0.42, 300.62)	0.152

OR, odd ratio; CI, confidence interval.

Figures

Figure 1

Association between age (years) and Prevalence of polyps (%). Age was parsed into a categorical variable with four groups: ≤ 39 , 40–49, 50–59, and ≥ 60 years. Prevalence (%) of polyposis according to Renehan, et al. [30]; Matano, et al. [42]; Yamamoto, et al. [43] and this study.

Figure 2

Constructed colonic polyp incidence risk nomogram. The colonic polyp risk was constructed with the features, including GHPA volume, IGF-1× ULN. GHPA Volume: growth hormone (GH)-secreting pituitary adenoma volume; IGF-1: insulin-like growth factor; ULN: upper limit of normal.

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