Decreased levels of plasma adiponectin associated with increased risk of colorectal cancer

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Abstract

AIM: To investigate the association between adiponectin levels and risk of colorectal adenoma and cancer (early and advanced).

METHODS: A cross-sectional study in a cohort of hospital-based patients was conducted between January 2004 and March 2006 at Yamagata University Hospital. Male subjects, who had colorectal tumors detected by endoscopic examination, were enrolled according to inclusion and exclusion criteria. Based on the T factor of the TNM system, intraepithelial carcinoma and submucosally invasive carcinoma were defined as early cancer, and invasion into the muscularis propria or deeper was defined as advanced cancer. The plasma levels of glucose, insulin, total cholesterol, triglyceride, high sensitivity C-reactive protein, insulin like growth factor (IGF)-1, IGF binding protein-3, adiponectin, leptin, and resistin were measured. Each factor level was designated low or high, and the risk of adenoma or cancer was estimated by univariate and multivariate logistic regression analysis.

RESULTS: We enrolled 124 male subjects (47 with adenoma, 34 with early cancer, 17 with advanced cancer, and 26 without tumors as controls). In patients with adenoma, high triglyceride and low adiponectin were associated with a significant increase in the odds ratio (OR) by univariate analysis. Only a low adiponectin level was related to increased adenoma risk, with an adjusted OR for low level (< 11 µg/mL) to high (≥ 11 µg/mL) of 5.762 (95% confidence interval (CI): 1.683-19.739, P = 0.005). In the patients with early cancer, high body mass index, high triglyceride, and low adiponectin were associated with a significant increase in OR in univariate analysis. In multivariate analysis, only low adiponectin was significantly associated with early cancer, with an adjusted OR of 4.495 (95% CI: 1.090-18.528, P = 0.038). However, in patients with advanced cancer, low adiponectin was not recognized as a significant risk factor for advanced cancer.

CONCLUSION: A decreased level of adiponectin is strongly associated with an increased risk of colorectal adenoma and early cancer. These data call for further investigation, including a controlled prospective study.

Key words: Adenoma; Early colorectal cancer; Metabolic syndrome; Adipokines; Colonoscopy; Resistin; Leptin; Body mass index

Peer reviewer: Roberto Bergamaschi, MD, PhD, FRCS, FASCRS, FACS, Professor and Chief, Division of Colon & Rectal Surgery, State University of New York, Stony Brook, New York, NY 11794-8191, United States

Otake S, Takeda H, Fujishima S, Fukui T, Orii T, Sato T, Sasaki Y, Nishise S, Kawata S. Decreased levels of plasma adiponectin associated with increased risk of colorectal cancer. World J
INTRODUCTION

Colorectal cancer is the world's third most common type of malignancy. Etiological studies have shown that body/abdominal fat or obesity increases the risk of colorectal cancer[1]. Accumulation of body/abdominal fat is associated with abnormal secretion of adipokines, resulting in either insulin resistance or metabolic syndrome. Metabolic syndrome is clinically defined as an increase in waist circumference and in blood pressure and fasting glucose levels, as well as dyslipidemia[2]. Many other factors, such as insulin, insulin-like growth factor-1 (IGF-1), IGF binding protein-3 (IGFBP-3), high sensitivity C-reactive protein (hsCRP), and inflammatory cytokines are also involved in the pathophysiology of insulin resistance or metabolic syndrome.

Adiponectin is a unique adipokine secreted from abdominal fat tissue and has anti-diabetic, anti-atherosclerotic, and anti-inflammatory effects[3]. Previously, we demonstrated that an increase in visceral fat area and a decrease in plasma adiponectin level were strongly associated with an increased risk of colorectal adenoma[4]. The present study investigated adiponectin levels in patients with colorectal adenoma and cancer. Several studies have previously described the adiponectin levels in patients with colorectal cancer[3,5]. However, most focused on advanced cancer. Although plasma levels of adiponectin were described, evaluations of risk of cancer by multivariate analysis were not conducted. Therefore, the present study attempted to evaluate the risk of colorectal cancer in patients with decreased adiponectin levels, and elucidated the relationship between adiponectin levels and the risk of both early and advanced cancer, in addition to adenoma.

MATERIALS AND METHODS

A cross-sectional study in a cohort of hospital-based patients was conducted between January 2004 and March 2006 at Yamagata University Hospital.

Ethics

This study was approved by the Ethics Committee of Yamagata University Faculty of Medicine, and written informed consent to participate in the study was obtained from every patient and control subject.

Patients

Patients who visited our hospital for colonoscopic examination in that period were screened for this study. The subjects were enrolled according to the following inclusion criteria: (1) male aged at least 31 years; (2) colonoscopic observations of the cecum were performed successfully; (3a) histopathological confirmation by hospital pathologists (in the case of patients with adenoma or cancer) and (3b) confirmation of lack of obvious polyps upon endoscopic examination of the entire colon and rectum (in the case of controls); and the following exclusion criteria: (a) previous gastrointestinal tract surgery; (b) inflammatory bowel disease; (c) patients with cancers in other organs and currently receiving therapy; (d) diabetes mellitus with insulin injection therapy; and (e) lack of consent to participate in the study. In the present study, only male patients were investigated. It has been shown that, in general, the levels of adiponectin, leptin, and resistin in males are significantly lower than in females[7,8]. Also, the criteria for metabolic syndrome differ between males and females[9]. Therefore, for this study, it was considered appropriate to evaluate only males.

Colonoscopy was performed by experienced gastro-intestinal physicians using video-endoscopy (CF-240ZI, PCF-240, PCF-P240AI, or PCF-240Z; Olympus Medical Systems, Tokyo, Japan). The lesions of adenoma or cancer were treated appropriately by endoscopic polypectomy, endoscopic mucosal resection, laparoscopic colectomy, or open surgical colectomy. The degree of cancer invasion was evaluated according to the pathologic T factor of the TNM staging system[9]. Based on the T factor classification, cancer patients were divided into 2 subgroups: early and advanced cancer. Intraepithelial carcinoma (Tim) and submucosally invasive carcinoma (pT1) were defined as the early cancer group. Those with a pathological depth of pT2 or greater (muscularis propria invasion or deeper) were defined as having advanced cancer.

Observed factors and evaluations

All patients were interviewed about their smoking habits, alcohol intake, medications, and medical histories. Persons who had stopped smoking more than 1 year previously were counted as ex-smokers. Any person who was drinking an average of more than 15 g of alcohol daily was defined as a regular alcohol drinker. Body weight, height, and blood pressure were also recorded, and body mass index (BMI) was calculated. And blood samples were collected after overnight fasting. Glucose, insulin, total cholesterol (T-cho), triglyceride (TG), hsCRP, IGF-1, IGFBP-3, adiponectin, leptin, and resistin levels were measured in plasma samples. The homeostatic model assessment of insulin resistance (HOMA-IR) was calculated as: HOMA-IR = fasting glucose × fasting insulin/405. The IGF-1/IGFBP-3 ratio was also calculated. The plasma level of each factor was measured as follows: hsCRP by nephelometry (N Latex CRP II CardioPhase hsCRP, Siemens Healthcare Diagnostics Inc., Tokyo, Japan); IGF-1 by a radioimmunoassay (RIA; IGF-1 IRMA Daiichi, TFB Inc., Tokyo, Japan); IGFBP-3 by an RIA2 antibody method (IGFBP-3 Cosmic, Biocline Australia Pty Ltd., Sydney, Australia); leptin by an RIA2 antibody method (Human Leptin RIA Kit, LONCO Research Inc., St. Charles, USA); resistin by an enzyme-linked immunosorbent assay (ELISA; Human Resistin ELISA, BioVender Inc., Modrice, Czech Republic), and adiponectin by enzyme-linked immunosorbent assay (human adiponectin ELISA kit, WJG | www.wjgnet.com 1253 March 14, 2010 | Volume 16 | Issue 10 |
Otake S et al. Adiponectin levels and colorectal tumors

Otuka Pharmaceuticals Inc., Tokyo, Japan).

The measured values of each factor in control patients were divided into 2 categories (Low and High), and the odds ratio (OR) (High vs Low) for adenoma or cancer was evaluated by univariate and multivariate logistic regression analysis. Criteria determining Low and High categorization were appropriately determined; the actual categorizations for each factor are described as follows. BMI was categorized as Low (< 22.5 kg/m²) and High (≥ 22.5 kg/m²), systolic blood pressure (BP-S) as < 120 mmHg and ≥ 120 mmHg, diastolic BP (BP-D) as < 80 mmHg and ≥ 80 mmHg, glucose as < 100 mg/dL and ≥ 100 mg/dL, insulin as < 4.5 U/mL and ≥ 4.5 U/mL, HOMA-IR as < 2 and ≥ 2, T-cho as < 180 mg/dL and ≥ 180 mg/dL, TG as < 120 mg/dL and ≥ 120 mg/dL, hsCRP as < 500 ng/mL and ≥ 500 ng/mL, IGF-1/IGFBP-3 ratio as < 60 and ≥ 60, adiponectin as ≥ 11 µg/mL and < 11 µg/mL, leptin as < 3 ng/mL and ≥ 3 ng/mL, and resistin as < 42 ng/mL and ≥ 42 ng/mL. Only adiponectin was inversely categorized (High and Low).

Statistical analysis
The SPSS statistical software package for Windows version 11.0J (SPSS Inc, Tokyo, Japan) was used for all statistical analyses. Distributions were evaluated by the χ² test. Comparisons of mean values among groups were tested by analysis of variance, and Dunnett's test was applied as an additional multiple comparison after the equality of variance had been confirmed. Risks were tested by univariate and multivariate logistic regression. Differences at P < 0.05 were considered to be significant. The exact P values are indicated when statistically significant.

RESULTS
Clinical background of patients
The study included 124 male subjects (47 with adenoma, 34 with early cancer, 17 with advanced cancer, and 26 without tumors as controls). The early cancer group included 14 Tim and 20 pt1 cases. The advanced cancer group included 6 pT2, 10 pT3, and one pT4 cases.

The clinical backgrounds of the controls and patients are shown in Table 1. There were no significant differences in mean age or blood pressure among the 4 groups (control, adenoma, early cancer, and advanced cancer). There were also no significant differences in the distribution of the numbers of diabetic patients, current smokers, ex-smokers, habitual alcohol drinkers, NSAID users, and other medicine users. Angiotensin II receptor antagonists, angiotensin converting enzyme inhibitors, and statin type anti-hyperlipidemia medicines were designated as other medicines. The BMI in the control group was 21.8 ± 3.1 kg/m². Those in the adenoma, early cancer, and advanced cancer groups were 23.2 ± 3.2 kg/m², 24.4 ± 3.8 kg/m², and 22.7 ± 3.8 kg/m², respectively. The BMI was highest in the early cancer group, and the difference was significant (Dunnett's test, P = 0.015). The BMI in patients with advanced cancer was lower than that in patients with early cancer.

| Table 1 Background of the male patients examined by colonoscopy n (%) |
|---------------------------------------------------|
| Control (n = 26) | Adenoma (n = 47) | Early cancer (n = 14) | Advanced cancer (n = 17) | P-value |
|------------------|------------------|----------------------|------------------------|---------|
| Age (yr)         | 67.9 ± 12.4      | 65.1 ± 11.7          | 67.0 ± 8.8             | 66.5 ± 7.8 | 0.810 |
| Diabetes         | 1 (3.8)          | 6 (12.8)             | 2 (5.9)                | 2 (11.8)  | 0.523 |
| Smokers          |                  |                      |                        |          |
| Current-smokers  | 9 (34.6)         | 18 (38.2)            | 13 (38.2)              | 7 (41.8)  | 0.977 |
| Ex-smokers       | 6 (23.4)         | 14 (29.8)            | 10 (28.6)              | 2 (11.8)  | 0.480 |
| Alcohol          | 15 (57.7)        | 30 (63.8)            | 27 (79.4)              | 14 (82.4) | 0.151 |
| NSAIDs           | 2 (7.7)          | 2 (4.3)              | 1 (3.0)                | 0 (0)     | 0.631 |
| Other meds       | 6 (23.1)         | 11 (23.4)            | 8 (23.5)               | 3 (17.6)  | 0.965 |
| BMI (kg/m²)      | 21.8 ± 3.1       | 23.2 ± 3.2           | 24.4 ± 3.8             | 22.7 ± 3.8 | 0.025 |
| BP-S (mmHg)      | 123 ± 14         | 129 ± 14             | 129 ± 13               | 133 ± 20  | 0.193 |
| BP-D (mmHg)      | 76 ± 12          | 76 ± 10              | 78 ± 10                | 81 ± 11   | 0.331 |

NSAIs: Non-steroid anti-inflammatory drug; Other meds: Other medicines such as angiotensin receptor antagonists, angiotensin converting enzyme inhibitors, or HMG-CoA reductase inhibitors; BMI: Body mass index; BP-S: Systolic blood pressure; BP-D: Diastolic blood pressure. Age, BMI, BP-S and BP-D are expressed as the mean ± SD and P-value was evaluated by analysis of variance. BMI was additionally evaluated by Dunnett's test (P = 0.015). Diabetes (without insulin injections), current smoker, ex-smoker, alcohol habit (ethanol intake more than 15 g/d on average) and NSAID users and Other Meds. users are expressed as the number of patients, and P values were evaluated by χ² test.

Evaluation of risk for adenoma, early cancer and advanced cancer
In the patients with adenoma, TG [OR: 3.990, 95% confidence interval (CI): 1.173-13.574, P = 0.027] and adiponectin [OR: 6.667, 95% CI: 2.190-20.295, P = 0.001] levels revealed significant associations in univariate analysis (Table 2). Multivariate analysis (adjusted for age, BMI, BP-S, TG, and adiponectin) showed that only adiponectin was a significant risk factor for adenoma (OR: 5.762, 95% CI: 1.683-19.739, P = 0.005). The other factors including glucose, insulin, HOMA-IR, T-cho, hsCRP, IGF-1/IGFBP-3 ratio, leptin and resistin were not significant risk factors for adenoma.

In the patients with early cancer, BMI [OR: 4.200, 95% CI: 1.344-13.128, P = 0.014], TG [OR: 3.958, 95% CI: 1.103-13.574, P = 0.035], and adiponectin [OR: 6.300, 95% CI: 1.847-21.485, P = 0.003] showed significant associations in univariate analysis (Table 3). Multivariate analysis (adjusted for age, BMI, BP-S, TG, and adiponectin) showed that only adiponectin was a significant risk factor for early cancer (OR: 4.995, 95% CI: 1.090-18.524, P = 0.038). As was the case for adenoma, none of the other factors, including glucose, insulin, HOMA-IR, T-cho, hsCRP, IGF-1/IGFBP-3 ratio, leptin and resistin leptin and resistin, were significant risk factors for early cancer.

In the patients with advanced cancer, only BP-D [OR: 4.950, 95% CI: 1.289-19.014, P = 0.020] revealed a significant OR in univariate analysis (Table 4). Unlike adenoma and early cancer, changes in adiponectin, BMI, and TG were not associated with a significantly increased risk. Multivariate analysis (adjusted for age, BP-D, hsCRP, and adiponectin) still recognized BP-D as a risk factor for advanced cancer (OR: 5.015, 95% CI: 1.159-21.696, P = 0.031).
Table 2  Evaluation of risks for adenoma

| Criteria                          | (Case/Cont) | Univariate analysis | Multivariate analysis |
|-----------------------------------|-------------|---------------------|-----------------------|
| | Low         | High        | OR (95% CI)         | P value | OR (95% CI) | P value |
| BMI (kg/m²)                       | < 22.5, ≥ 22.5 | 18/14, 32/18 | 2.256 (0.828-6.145) | 0.112 | 1.432 (0.434-4.729) | 0.556 |
| BP-S (mmHg)                       | < 120, ≥ 120 | 14/14, 33/12 | 1.030 (0.998-1.074) | 0.073 | 1.576 (0.463-5.370) | 0.467 |
| BP-D (mmHg)                       | ≥ 80, < 80  | 32/18, 15/8   | 1.050 (0.375-2.967) | 0.920 |                      |        |
| Glucose (mg/dL)                   | ≥ 100, < 100 | 27/14, 19/10 | 0.992 (0.976-1.008) | 0.328 |                      |        |
| Insulin (mg/mL)                   | < 4.5, ≥ 4.5 | 12/12, 35/14 | 1.033 (0.989-1.091) | 0.249 |                      |        |
| HOMA-IR                           | > 2, ≤ 2    | 27/15, 19/9   | 1.173 (0.426-3.232) | 0.758 |                      |        |
| T-cho (mg/dL)                     | ≥ 180, < 180 | 19/13, 27/10 | 1.005 (0.992-1.019) | 0.449 |                      |        |
| TG (mg/dL)                        | ≥ 120, < 120 | 25/19, 21/4   | 3.990 (1.173-13.570) | 0.027 | 2.715 (0.707-10.410) | 0.146 |
| hsCRP (mg/mL)                     | ≥ 500, < 500 | 20/16, 27/10 | 2.160 (0.811-5.750) | 0.123 |                      |        |
| IGF-1/IGFBP-3                     | ≥ 60, < 60  | 29/15, 18/11  | 0.846 (0.319-2.245) | 0.074 |                      |        |
| Adiponectin (µg/mL)               | > 11, ≤ 11  | 40/12, 7/14   | 6.667 (2.190-20.300) | 0.001 | 5.762 (1.683-19.739) | 0.005  |
| Leptin (ng/mL)                    | < 3, ≥ 3    | 17/13, 50/30  | 1.765 (0.668-4.665) | 0.252 |                      |        |
| Resistin (ng/mL)                  | > 42, ≤ 42  | 17/13, 30/13  | 1.184 (0.524-3.642) | 0.514 |                      |        |

OR: Odds ratio; CI: Confidence interval; TG: Triglyceride; T-cho: Total cholesterol; hs-CRP: High sensitivity C-reactive protein; HOMA-IR: Homeostatic model assessment of insulin resistance; IGF-1/IGFBP-3: Ratio of insulin-like growth factor-1 and IGF binding protein-3; Cont: Numbers of control persons; Case: Numbers of patients. The OR (High vs Low) was evaluated by univariate and multivariate logistic regression analysis. Only the OR of adiponectin was inversely evaluated (Low vs High). Multivariate analysis included age, BMI, BP-S, TG, and adiponectin. *P < 0.05, **P < 0.01.

Table 3  Evaluation of risks for early cancer

| Criteria                          | (Case/Cont) | Univariate analysis | Multivariate analysis |
|-----------------------------------|-------------|---------------------|-----------------------|
| | Low         | High        | OR (95% CI)         | P value | OR (95% CI) | P value |
| BMI (kg/m²)                       | < 22.5, ≥ 22.5 | 8/14, 24/10 | 4.200 (1.344-13.128) | 0.014 | 2.814 (0.746-10.620) | 0.127 |
| BP-S (mmHg)                       | < 120, ≥ 120 | 11/14, 22/12 | 2.333 (0.810-6.718) | 0.116 | 1.702 (0.461-6.281) | 0.425 |
| BP-D (mmHg)                       | ≥ 80, < 80  | 21/18, 12/8   | 1.286 (0.431-3.839) | 0.653 |                      |        |
| Glucose (mg/dL)                   | ≥ 100, < 100 | 15/14, 18/10 | 1.680 (0.581-4.859) | 0.338 |                      |        |
| Insulin (mg/mL)                   | ≥ 4.5, < 4.5 | 12/13, 21/14 | 1.500 (0.526-4.276) | 0.448 |                      |        |
| HOMA-IR                           | < 2, ≥ 2    | 13/15, 7/9   | 1.771 (0.608-5.173) | 0.296 |                      |        |
| T-cho (mg/dL)                     | ≥ 180, > 180 | 13/15, 18/8 | 1.560 (0.534-4.557) | 0.416 |                      |        |
| TG (mg/dL)                        | ≥ 120, < 120 | 18/19, 15/4  | 3.958 (1.103-14.201) | 0.035 | 2.705 (0.596-12.283) | 0.197 |
| hsCRP (mg/mL)                     | ≥ 500, < 500 | 16/17, 17/10 | 1.700 (0.598-4.830) | 0.319 |                      |        |
| IGF-1/IGFBP-3                     | ≥ 60, < 60  | 18/15, 15/11  | 1.136 (0.403-3.205) | 0.809 |                      |        |
| Adiponectin (µg/mL)               | < 11, ≥ 11  | 27/12, 5/14   | 6.300 (1.847-21.485) | 0.003 | 4.495 (1.090-18.528) | 0.036  |
| Leptin (ng/mL)                    | < 3, ≥ 3    | 8/14, 24/13  | 3.000 (0.989-7.100) | 0.052 |                      |        |
| Resistin (ng/mL)                  | > 42, ≤ 42  | 14/12, 16/14 | 0.980 (0.324-2.808) | 0.969 |                      |        |

The OR (High vs Low) was evaluated by univariate and multivariate logistic regression analysis. Only the OR of adiponectin was inversely evaluated (Low vs High). Multivariate analysis included age, BMI, BP-S, TG, and adiponectin. *P < 0.05, **P < 0.01.

DISCUSSION

The present data for adenoma were similar to those of our previous study[9], and it was also revealed that a decreased level of adiponectin was a strong risk factor for early colorectal cancer. Furthermore, we were able to demonstrate that a low adiponectin level was a stronger risk factor than high TG or BMI in patients with adenoma and early cancer. However, other adipokines, including leptin and resistin, were not direct risk factors for colorectal tumors in this study. In contrast to adenoma and early cancer, a low adiponectin level was not recognized as a significant risk factor for advanced cancer.

In the present study, the mean BMI was significantly higher in the early cancer group than in the control group. However, the mean BMI in the advanced cancer group was lower than that in the early cancer group and nearly equal to that in the controls. One reason may be a reduction of BMI as a result of nutritional deficiencies in some patients with advanced cancer. Generally, the adiponectin level is known to increase with a reduction in body weight[10]. Thus the reduction of BMI may have been related to the fact that a low adiponectin level was not a significant risk factor for advanced cancer. As the number of patients with advanced cancer in the present study was relatively small, the low adiponectin level observed in this group must be evaluated carefully in further investigations.

Recently, 2 reports addressing adiponectin levels in patients with colorectal cancer were published. Kumor et al[13] and Erarslan et al[14] revealed that serum adiponectin levels were significantly low in patients with cancer. In fact, our present study revealed results consistent with those reports. Our results enhanced the strength of their data. However, we were able to add some information. Our study evaluated the risk of colorectal tumors, focusing on patients with early-stage colorectal cancer. Besides these 2 reports, Levy et al[15] also reported adiponectin levels in patients with colorectal cancer, and demonstrated that...
adiponectin levels were not influenced by cancer stage, including the early stage. However, their study did not consider the adiponectin levels in normal controls or adenoma patients.

While some reports have indicated a positive relationship between adiponectin and cancer, Lukanova et al.[12] reported that the serum adiponectin level was not associated with the risk of colorectal cancer in a case control study in males. Also, Fukumoto et al.[13] demonstrated only a weak correlation between large adenoma and adiponectin level in males working in the Japanese Self-Defense Forces. However, Wei et al.[14] demonstrated that low levels of adiponectin were associated with a significantly increased risk of colorectal cancer in a prospective cohort study in males, with a mean follow-up period of 4.5 years. In addition to these epidemiologic studies, genetic polymorphisms of the adiponectin gene in patients with colorectal cancer have been investigated, and these showed that single nucleotide polymorphism of the adiponectin gene was associated with an increased risk of colorectal cancer[15,16].

So far, several interesting reports on the molecular mechanism connecting adiponectin and colorectal tumors have been published. Fujisawa et al.[17] reported that adiponectin normalized the expression of adenosine monophosphate-activated protein kinase (AMPK) and suppressed colonic epithelial cell proliferation via inhibition of the mammalian target of the rapamycin (mTOR) pathway. Moreover, a direct inhibitory effect of adiponectin on colorectal cancer cells via the AMPK-mTOR pathway has been demonstrated[18]. Thus, the relationship between a decreased plasma adiponectin level and colorectal tumorigenesis is a major issue that needs to be investigated further.

Many studies have noted that a high TG level is associated with colorectal adenoma[19,20]. Otake et al.[21] have also reported that the OR (highest vs lowest quintile) of TG was significantly increased to 1.5 in Japanese patients. The present study revealed a significantly increased OR of TG in patients with adenoma and early cancer by univariate analysis. The systemic inflammatory marker, hsCRP, is a factor associated with metabolic syndrome[22]. The hsCRP levels were relatively increased in patients with advanced cancer (OR: 3.520, P = 0.062), but the difference was not statistically significant. CRP levels are increased by inflammatory cytokines. Kim et al.[23] found that circulating levels of interleukin-6 and TNF-α were associated with colorectal adenoma risk. Association of inflammatory cytokines with colorectal cancer is also an interesting issue. The circulating IGF-1 level has been discussed in relation to colorectal adenoma and cancer[24,25]. However, the relationship between IGF-1 and colorectal tumors is still obscure. In the present study, the IGF-1/IGFBP-3 ratio did not show a significant OR.

In our previous study, HOMA-IR was a significant risk factor for adenoma[9]. However, HOMA-IR was not recognized as a risk factor for adenoma or cancer in the present study. This factor seemed not to be consistent. However, cohorts of both studies were different, and mean age and gender in the both cohorts were also different. To investigate this issue, further studies involving patients with wide age ranges must be performed.

In conclusion, our study has investigated risk factors for adenoma, early cancer, and advanced cancer. A decreased level of adiponectin was recognized as a strong risk factor for both colorectal adenoma and early cancer. The present results were similar to our previous data for adenoma, and we also demonstrated that a decreased adiponectin level was associated with an increased risk of early cancer. On the basis of these data, we consider that further investigations to clarify the relationship between low adiponectin and colorectal tumors, including controlled prospective studies, are warranted.

**ACKNOWLEDGMENTS**

We are indebted to Junji Yokozawa, Yayoi Sasaki, Koji Suzuki, Shinya Hirata, Katsuyoshi Ishihama, and Hideki Saito for their valuable contributions to this study.

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| Criteria | (Case/Cont) | Univariate analysis OR (95% CI) | P value | Multivariate analysis OR (95% CI) | P value |
|----------|-------------|--------------------------------|---------|---------------------------------|---------|
| Low | High | | | | |
| BMI (kg/m²) | < 22.5, ≥ 22.5 | 8/14 | 8/10 | 1.400 (0.392-4.997) | 0.604 |
| BP-S (mmHg) | < 120, ≥ 120 | 6/14 | 10/12 | 1.944 (0.545-6.940) | 0.306 |
| BP-D (mmHg) | < 80, ≥ 80 | 5/19 | 11/8 | 4.950 (1.289-19.014) | 0.020* |
| Glucose (mg/dL) | <100, ≥ 100 | 6/15 | 10/10 | 2.333 (0.638-8.538) | 0.201 |
| Insulin (µU/mL) | < 4.5, ≥ 4.5 | 5/12 | 11/14 | 1.885 (0.510-6.978) | 0.342 |
| HOMA-IR | < 2, ≥ 2 | 10/15 | 6/9 | 1.000 (0.271-3.694) | 1.000 |
| T-cho (mg/dL) | < 180, ≥ 180 | 7/13 | 9/10 | 1.671 (0.462-6.051) | 0.434 |
| TG (mg/dL) | < 120, ≥ 120 | 10/19 | 6/4 | 2.850 (0.650-12.305) | 0.165 |
| hsCRP (mg/mL) | < 500, ≥ 500 | 5/16 | 11/10 | 3.520 (0.941-13.174) | 0.062 |
| IGF-1/IGFBP-3 | < 60, ≥ 60 | 7/14 | 9/11 | 1.753 (0.499-6.165) | 0.382 |
| Adiponectin (µg/mL) | < 11, ≥ 11 | 11/12 | 5/14 | 2.567 (0.644-9.498) | 0.158 |
| Leptin (ng/mL) | < 60, ≥ 60 | 7/14 | 9/11 | 3.355 (0.729-15.451) | 0.120 |
| Resistin (ng/mL) | < 2, ≥ 2 | 9/12 | 7/14 | 0.667 (0.190-2.334) | 0.526 |

The OR (High vs Low) was evaluated by univariate and multivariate logistic regression analysis. Only the OR of adiponectin was inversely evaluated (Low vs High). Multivariate analysis included age, BP-D, hsCRP, and adiponectin. *P < 0.05.
March 14, 2010 | Volume 16 | Issue 10 |

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S-Editor Tian L  L-Editor Cant MR  E-Editor Lin YP

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COMMENTS

Background

Many biological factors vary according to accumulation of body/abdominal fat. Etiological studies have shown that body/abdominal fat or obesity increases the risk of colorectal cancer. What factors are strongly associated with colorectal tumors?

Research frontiers

Adiponectin is secreted from abdominal fat tissue, and has anti-diabetic, anti-atherosclerotic, and anti-inflammatory effects. A decrease in plasma adiponectin level may be strongly associated with an increased risk of colorectal adenoma or cancer.

Innovations and breakthroughs

The present study investigated the adiponectin levels in patients with colorectal adenoma and cancer (early and advanced). A low adiponectin level was a stronger risk factor than triglyceride or body mass index in patients with early cancer. However, a low adiponectin level was not recognized as a significant risk factor for advanced cancer. 

Applications

The study enhanced the strength of previous data. Further investigations to clarify the relationship between low adiponectin levels and colorectal tumors, including controlled prospective studies, are warranted.

Peer review

The author investigate the association of adiponectin levels with risk of colorectal adenoma and cancer (early and advanced). It is a good paper and should be accepted with revision.