EJMI

DOI: 10.14744/ejmi.2018.64936
EJMI 2018;2(3):168–171

Research Article

Investigation of Prevalence of Insulin Resistance and Metabolic Syndrome in Patients with Gastric and Colon Carcinoma

Mehmet Celik, Erdal Akyer, Elif Yorulmaz, Hilmi Ciftci, Veli Cakici, Osman Kostek

Department of Internal Medicine, Istanbul Medeniyet University Goztepe Training and Research Hospital, Istanbul, Turkey

Abstract

Objectives: The aim of this study was to determine the relationship between insulin resistance, metabolic syndrome (MetS) and the development of gastrointestinal system tumors.

Methods: This study included 29 gastric cancer patients and 29 colorectal cancer patients who had been histopathologically diagnosed, and 30 healthy individuals. The patients and the control participants were evaluated for the presence of MetS using the International Diabetes Federation criteria. Insulin resistance was calculated using the Homeostasis Model Assessment of insulin resistance. The tomography results of subjects who were diagnosed with cancer were recorded according to presence of liver metastasis.

Results: Overall, 27 (30%) of the patients were found to have MetS. MetS was confirmed for 31% of the gastric cancer group and 62.1% of the colon cancer group. The insulin resistance of colon cancer patients was significantly greater than that of gastric cancer patients ($p<0.05$).

Conclusion: The frequency of MetS and insulin resistance in colon cancer patients was greater than that of the healthy population.

Keywords: Colon cancer, gastric cancer, insulin resistance, metabolic syndrome

Gastrointestinal system (GIS) cancers are the second most common noncutaneous cancers and the second most common cause of cancer-related deaths.[1] The basis of carcinogenesis is non-fatal genetic damage. These genetic damage can be divided into 4 groups. These include the activation of protooncogenes that trigger cell proliferation, the inactivation of tumor suppressor genes that control cell proliferation, the inactivation of genes that regulate apoptosis, and the inactivation of DNA repair enzymes. In carcinogenesis, the disruption of these control mechanisms leads to uncontrolled cell growth and proliferation, proliferation to surrounding tissues, and metastasis to distant organs.[2] Metabolic syndrome (MetS) A metabolic syndrome (MetS) is a syndrome that is associated with an increase in the risk of cardiovascular disease (CVD) in the clinical table, including glucose tolerance disorder, diabetes mellitus, central obesity, essential hypertension, dyslipidemia, proinflammatory and prothrombotic items, prematurity atherosclerosis risk factor group.[3] The pathomechanisms thought responsible are obesity, other growth factors such as cytokines (released from excessive amounts from the adipose tissue), persistent and postprandial hyperglycaemia, hyperinsulinism and insulin resistance, proinsulin, insulin-like growth factor-1, reactive oxygen containing substances, angiogenesis, inflammation and inflammatory cytokines active. Both the receptors activated

Address for correspondence: Mehmet Celik, MD. Istanbul Medeniyet Universitesi Goztepe Egitim ve Arastirma Hastanesi, Ic Hastaliklari Anabilim Dali, Istanbul, Turkey
Phone: +90 533 561 87 06 **E-mail:** drmehmetcelik@hotmail.com
Submitted Date: February 07, 2018 **Accepted Date:** March 12, 2018 **Available Online Date:** November 14, 2018

by peroxisome proliferators and the ubiquitin proteasome system have proven to play important roles in coordinating cell proliferation and angiogenesis with insulin resistance. These mechanisms in MetS are also risk factors for atherosclerosis and cancer. This emerging new knowledge can open a new era in the treatment and prevention of the above pathological processes.[4] In this study, the relationship between insulin resistance, MetS frequency and liver metastasis was investigated in newly diagnosed gastric and colon cancer patients.

Methods

Patient Population

A detailed history of 30 newly diagnosed gastric cancer (20 males, 10 females), 29 colon cancer (15 males, 14 females) and 30 healthy individuals (16 males, 14 females) were studied and physical examinations were performed. Patients' age, gender, occupational backgrounds, habits, known chronic disease history, family member's malignancy, and the drugs they used were questioned and recorded. Patients with previously known acute and chronic liver disease, those with operation history, those with chemotherapy and radiotherapy history due to malignancy were excluded from the study. The endoscopic, biochemical, radiological and pathological results of the patients were examined and results of liver metastases and unexplained cases were recorded separately.

Laboratory Method

Biochemical tests of patients who were examined by hospital admission were measured in our hospital biochemistry laboratory, Roche E170 ECL model, Chemiluminescence method. The results are given as numerical values.

Statistical Analysis

For the statistical analyzes, SPSS (Statistical Package for Social Sciences) for Windows 17.0 program was used. In the comparison of descriptive statistical methods (Mean, Standard deviation, Frequency, Percentage) as well as Quantitative data; One-way analysis of variance (One-way ANOVA) and Multivariate ANOVA (Univariate ANOVA) were used in the comparison of parameters between groups. Correlation analysis was used in interpreting the relationship between variables and the severity. The results were evaluated in a 95% confidence interval and a significance level of $p<0.05$.

Results

A total of 89 patients and healthy individuals were included in the study, ranging in age from 37 to 86 years (49 men, 51%) and 40 women (49%). Of the patients included in the study, 27 (30%) had metabolic syndrome (Table 1). The rate of metabolic syndrome was 31% in stomach cancer, whereas this rate was 62.1% in colon cancer. The incidence of metabolic syndrome was higher in colon cancer patients than in gastric cancer patients. The relationship between the disease and the metabolic syndrome was statistically significant ($p<0.05$). 17 (19%) of the patients participating in the study had liver metastasis. It was observed that the frequency of liver metastases in colon ca patients and stomach ca patients did not differ (Table 2). It can be said that the relation between disease and liver metastasis was not statistically significant ($p>0.05$). The presence of metabolic syndrome in participants with different disease groups (stomach ca, colon ca, control group) differs according to the Homa-IR variable ($p<0.05$) (Table 3). It can be said that the difference between Homa-IR values of stomach ca patients according to their liver metastases was not statistically significant at $p>0.05$ level. The difference between the Homa-IR values according to the presence or absence of liver metastases in the colon ca patients is statistically significant at the level of $p<0.05$. There was a weak linear relationship between insulin and age in the positive direction ($r=0.274$). As age increases, the level of insulin may also increase.

Table 1. Metabolic Syndrome in Colon Cancer and Gastric Cancer

		Metabolic Syndrome	
		N	%
Gastric Cancer	-	20	69
	+	9	31
	Total	29	100
Colon Cancer	-	11	37.9
	+	18	62.1
	Total	29	100

Table 2. Liver Metastasis in Colon Cancer and Gastric Cancer Patients with MetS

Hastalık				Liver Metastasis -	Liver Metastasis +	Total
Gastric Cancer	M etS	-	N	14	6	20
			%	73.7	60	69
		+	N	5	4	9
			%	26.3	40	31
	Total		N	19	10	29
			%	100	100	100
Colon Cancer	MetS	-	N	10	1	11
			%	45.5	14.3	37.9
		+	N	12	6	18
			%	54.5	85.7	62.1
	Total		N	22	7	29

Table 3. HOMA-IR values according to liver metastasis in patients with gastric cancer and colon cancer

			N	Mean	Std. Deviation	Std. Error	P
Gastric	Liver	-	19	2.9763	3.86711	0.88718	
Cancer	Metastasis	+	10	1.7080	3.05592	0.96637	
		Total	29	2.5390	3.60441	0.66932	0.377
Colon	Liver	-	22	2.9518	2.38608	0.50871	
Cancer	Metastasis	+	7	6.0486	4.99509	1.88796	
			29	3.6993	3.38163	0.62795	0.032

Independent variable: HOMA-IR

Discussion

The metabolic syndrome is a population of risk factors associated with increased risk of cardiovascular disease, which is based on insulin resistance, including a premature atherosclerosis involving glucose tolerance disorder, diabetes mellitus, central obesity, essential hypertension, dyslipidemia, proinflammatory and prothrombotic items in the clinical table.[3] Over the past 20 years, there has been a worldwide increase in the number of patients with metabolic syndrome, closely related to the increased prevalence of obesity and cancer.[4, 5]

Insulin resistance is a common risk factor for the two most dangerous group of diseases seen in humans; these are cardiovascular diseases and malignancy. There are five basic criteria for insulin resistance syndrome: hyperglycemia, visceral obesity, high serum triglycerides, low HDL cholesterol level (dyslipidemia) and hypertension. Each of these criteria is a risk factor for cancer alone, and a combination of all means multiple risks. Insulin has different metabolic effects and is a growth factor at the same time. It increases the production and mitogenic activity of other insulin-like growth factors and leads to pathological cell proliferation. Hyperglycaemia occurs when the insulin resistance is unbalanced, which leads to tumor formation in various ways. Elevated serum glucose levels provide an advantage in enhancing DNA synthesis in tumor cells. It leads to the release of free radicals, which degrades the enzymes involved in DNA and repair mechanisms. Hyperglycaemia leads to nonenzymatic glycation of protein structures, glycated products increase the release of free radicals, cytokines and growth factors. Insulin resistance is an increased risk factor for breast, pancreas, liver, colon, bladder, prostate and oral cavity cancers. Even if there is no type 2 diabetes indication, the partially elevated fasting glucose level is also a risk factor for breast, stomach, and colon cancers. Insulin resistance also increases tumor growth. In cancer patients with hyperglycaemia or type 2 diabetes, tumor recurrence, metastatic spread and mortality rates are higher than cancer patients without metabolic disease.

The relationship between insulin resistance and tumor development presents new possibilities for cancer prevention and treatment. Healthy diet, physical activity and weight loss increase insulin sensitivity and reduce both cardiovascular and malignancy risk.[6] Hyperinsulinemia is also considered a biological risk factor for the development of colorectal cancer. Compared to distal colon or rectal adenomas, the increased risk for proximal lesions was more pronounced and almost only in large lesions (5 mm diameter). Therefore, it can be said that metabolic syndrome is important in preventing both colorectal cancer and cardiovascular diseases and type 2 diabetes.[7]

Large quantities of epidemiological data collected over the last 10 years indicate that the risk of colon cancer is increased by metabolic syndrome. This evidence is based on the risk of colon cancer or adenomas, the indicators of metabolic syndrome (obesity, abdominal fat tissue accumulation and physical inactivity), clinical consequences of this syndrome (type 2 diabetes and hypertension), plasma or serum components of the definition of metabolic syndrome (hypertriglyceridemia, (insulin, C-peptide), which is the metabolic disorder underlying the metabolic syndrome, and insulin resistance (hyperinsulinemia). The mechanism underlying these relationships is unknown, but may involve the effect of hyperinsulinemia on increasing free or beneficial concentrations of insulin-like growth factor-1. Future studies to better assess which aspects of the insulin resistance are most closely related to colon neoplasia should be based on better measurements of insulin resistance, beta cell depletion, and insulin response.[8]

Metabolic syndrome is associated with colorectal adenoma. Abdominal obesity, a component of the metabolic syndrome, is an important risk factor for colorectal adenoma.[9]

In this study, metabolic syndrome was found in 31% of patients with stomach cancer and 62.1% in patients with colon cancer. The metabolic syndrome was more prominent in the group with colorectal cancer ($p<0.005$). This finding coincided with previous studies.[9] Metastatic syndrome was present in 14.3% of the cases without liver metastasis and 85.7% of metastatic cases had metabolic syndrome in the gastric cancer group ($p=0.197$). There was a significant difference in the presence of metabolic syndrome among the patients with and without liver metastasis ($p<0.005$) in the colorectal cancer group. This finding was consistent with previous studies.[9]

In this study, the presence of metabolic syndrome in participants of different disease groups (gastric ca, colon ca, control group) was found to vary according to the Homa-IR

variable. ($p<0.05$).

It can be said that the difference between Homa-Ir values was not statistically significant at the level of $p>0.05$ according to whether hepatic metastases were present in gastric cavernous patients. The difference between Homa-IR values according to the presence or absence of liver metastases in patients with colorectal cancer was statistically significant at $p<0.05$ ($p=0.007$). In the literature, no similar publication was found to explain this situation. However, in a study conducted by Giovannucci E., colon cancer suggests that Riskin is elevated in metabolic syndromes.[5] This evidence is based on the risk of colon cancer or adenomas, the indicators of metabolic syndrome (obesity, abdominal fat tissue accumulation and physical inactivity), clinical consequences of this syndrome (type 2 diabetes and hypertension), plasma or serum components of the definition of metabolic syndrome (hypertriglyceridemia, HDL cholesterol) and hyperinsulinemia, a metabolic disorder underlying the metabolic syndrome, and markers of insulin resistance (insulin C-peptide). The mechanism underlying these associations is unknown, but may involve the effect of hyperinsulinemia on increasing free or beneficial concentrations of insulin-like growth factor-1.[5] This study overlaps with the results of Giovannuci E.'s study.

Conclusion

The incidence of MetS was higher in colon cancer patients than in the normal population. In addition, insulin resistance was significantly higher in all colon cancer cases with and without liver metastasis.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship contributions: Concept – M.C., E.Y.; Design – M.C., E.Y.; Supervision – E.A., O.K.; Materials – M.C., V.C.; Data collection &/or processing – H.C., O.K., M.C., V.C.; Analysis and/or interpretation – E.Y., M.C., H.C., E.A.; Literature search – M.C.; Writing – M.C.; Critical review – E.Y., H.C.

References

1. Braunwald E, Fauci A, Kasper D, Hauser S, Longo D, Jameson J. Harrison's principles of internal medicin. 15th ed. McGraw-Hill; 2001. p. 578–88
2. Cotran RS, Kumar V, Robbins SL. Biology of Tumor Growth, Neoplasia In: Schoen FJ, editor. Robbin's Pathology. 5th ed. WB Saunders; 1992. p. 293–6.
3. Fulop T, Tessier D, Carpentier A. The metabolic syndrome. Pathologie Biologie 2006;54:375–86. [CrossRef]
4. Halmos T, Suba I. The metabolic syndrome and type-2 diabetes mellitus as conditions predisposing for malignant tumors. [Article in Hungarian]. Orv Hetil 2008;149:2403–11. [CrossRef]
5. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. Nature 2001;414:782–7. [CrossRef]
6. Suba Z, Ujpál M. Correlations of insulin resistance and neoplasms. [Article in Hungarian]. Magy Onkol 2006;50:127–35.
7. Morita T, Tabata S, Mineshita M, Mizoue T, Moore MA, Kono S. The metabolic syndrome is associated with increased risk of colorectal adenoma development: the Self-Defense Forces health study. Asian Pac J Cancer Prev 2005;6:485–9.
8. Giovannucci E. Metabolic syndrome, hyperinsulinemia, and colon cancer: a review. Am J Clin Nutr 2007;86:s836–42. [CrossRef]
9. Kim JH, Lim YJ, Kim YH, Sung IK, Shim SG, Oh SO, et al. Is metabolic syndrome a risk factor for colorectal adenoma? Cancer Epidemiol Biomarkers Prev 2007;16:1543–6. [CrossRef]