VARIATIONS OF ADIPOKINE PROFILE IN PATIENTS DIAGNOSED WITH RECTAL CARCINOMA

A. Florescu¹, S. Bilha¹, I. Grigoras², D. Branisteanu^{1,*}

“Gr. T. Popa” University of Medicine and Pharmacy - ¹Endocrinology, ²Intensive Care, Iasi, Romania

Abstract

Background. Adipokine secretion is influenced by various disease conditions.

Purpose. We wanted to check the impact of rectal carcinoma (RC) on adipokine profile.

Patients and methods. We evaluated serum leptin and adiponectin levels in 24 RC patients (12 males and 12 females) as well as in the same number of age, sex and weight-matched healthy controls.

Results. Adipokines were oppositely correlated with body weight (BW) in controls and RC patients. Women had higher adipokine levels than men. Healthy controls had higher leptin (37.6 ± 7.8 vs. 7.9 ± 2.6 ng/mL in women and 11.9 ± 4.6 vs. 1.4 ± 0.34 ng/mL in men, $p=0.0016$ and 0.043) and lower adiponectin levels (9.3 ± 1.1 vs. 14.9 ± 1.1 µg/mL in women and 7.9 ± 0.9 vs. 11.1 ± 0.9 µg/mL in men, $p=0.012$ and 0.017) than RC patients.

Conclusion. Adipokine profiles of patients with RC differ from the healthy population, possibly reflecting an adaptation to the disease rather than a triggering factor. These differences may find clinical applications for the prognosis of disease evolution.

Key words: adipokines, leptin, adiponectin, rectal carcinoma.

respect to their carcinogenetic potential (4). It is also known that the two adipokines, although both correlated with BW and fat tissue mass (major BW contributor in most individuals), they are influenced oppositely by weight and fat tissue distribution, with an increase of leptin and a decrease of adiponectin with weight and visceral fat tissue gain (5). Leptin is generally considered oncogenic, being a stimulator of malignant angiogenesis, whereas adiponectin inhibits inflammation and angiogenesis, being considered protective against malignancy (6). These two adipokines and others are also taken into consideration as biomarkers in colorectal cancer (CRC) (4-6). Clinical data have, however, a large variability among studies (4, 6, 7). These differences may be caused by distinctive tumour types, localizations along the digestive tract, or disease severity and impact upon the weight of patients (3, 8-10). We aimed to observe the difference in serum leptin and adiponectin levels between patients diagnosed with cancer located exclusively in the rectal region and not accompanied by significant weight loss or cachexia and healthy age and weight-matched controls.

PATIENTS AND METHODS

The study was approved by the Ethical Committee of Clinical Research of the Regional Institute of Oncology of Iasi (nr. 167 from 30/06/2017). All study participants signed a written informed consent.

Study participants

We performed a cross sectional study which included 24 Caucasian patients (12 females and 12 males) consecutively diagnosed with stage 2 and 3 digestive cancer located exclusively in the rectal region (rectal carcinoma, RC), between January and June 2018 and programmed for surgical intervention at the Regional Institute of Oncology of Iasi (the RC groups)

INTRODUCTION

Besides genetic predisposal, environmental factors, e.g. diet and obesity, were described to influence the risk of various disorders, such as cardiovascular disease (1), but also CRC (2).

Adipokines are hormones secreted by fat tissue cells having a regulator role in important processes, such as puberty onset, bone acquisition, glucose metabolism but also inflammation, which is directly involved in the pathogenesis of malignancy (3). The risk of various types of digestive cancer was also related to weight gain and the variation of adipokine secretion. Leptin and adiponectin are adipokines extensively studied with

*Correspondence to: Dumitru Branisteanu PhD, “Gr.T.Popa” University of Medicine and Pharmacy, Endocrinology, 18 Vasile Conta Street, Iasi, 700106, Romania, E-mail: dumitru_branisteanu@yahoo.com

and 24 age- and weight-matched healthy controls (12 females and 12 males) recruited from the St. Spiridon Hospital, Iasi, with no history of malignancy or autoimmune diseases (the HC groups). We chose only patients with RC, because this type of cancer is known to be diagnosed at earlier stages, with less weight loss and higher chance of survival (11). Many of the enrolled RC patients were older and overweight, but they were compared with age and BW-matched HC volunteers (Table 1). Two criteria of exclusion from both groups were obesity (a BMI above 30 kg/m²) and overt type 2 diabetes mellitus, since both situations can independently influence adipokine secretion.

Body weight (BW), leptin and adiponectin evaluation

After overnight fasting, all patients and healthy volunteers were weighed with the same weighing scale. A 10 mL blood sample was further collected and the separated serum aliquots were stored at -20°C until assessment of serum leptin and adiponectin with Luminex technology (Luminex Screening Assay, R&D Systems Inc., MN, USA).

Statistical analysis

Differences between groups were tested using the Student's t test. Correlation analysis was performed using Pearson analysis for normally distributed data and Spearman rank correlation for skewed data. Differences were considered significant at p values < 0.05.

RESULTS

The characteristics and adipokine levels of

enrolled participants are depicted in Table 1.

RC and HC females and males were matched with respect to age and BW (Table 1). Irrespective of the belonging to HC or RC groups, females had higher mean levels of both leptin and adiponectin than the corresponding males (Table 1). Leptin and adiponectin were oppositely correlated with BW – directly for leptin and inversely for adiponectin for both HC and RC women and men (Table 2). Significance was however reached only in HC males for leptin whereas in the same group adiponectin was not correlated with BW, while significantly correlated in the other three groups (Table 2).

When compared to HC, both RC female and male patients had significantly lower leptin (Table 1).

DISCUSSION

Our study confirmed that leptin and adiponectin levels were directly and respectively inversely correlated with BW in HC or RC males and females. However, these correlations did not always reach significance, possibly due to the small number of volunteers.

These observations implied the investigation of a possible role of adipokines as prognostic markers in CRC. Women showed higher adipokine levels than their paired men groups, fact also observed by others (5). Further comparison between RC and HC participants was therefore made separately for each gender.

In contrast to other investigators (5) we found significantly lower leptin and higher adiponectin in RC patients when compared to sex, BW and age matched HC. These results suggest that RC may impose

Table 1. Characteristics and serum levels of RC and HC patients, expressed as mean ± SEM. * and # - p < 0.05 compared to HC and to males of the same group category, respectively. ** and ## - p < 0.01 compared to controls and to males of the same group category, respectively

Parameter	HC		RC	
Gender	Females	Males	Females	Males
Number	12	12	12	12
Age (years)	67.3±2	65±2.1	67.3±2.6	69.8±2.9
BW (kg)	76.3 ±3.9	81±5.9	71.6±3.9	74.8±3.4
Leptin (ng/mL)	37.6±7.8 ##	11.9±4.6	7.9±2.6 ** #	1.4±0.34 *
Adiponectin (µg/mL)	9.3±1.1	7.9±0.9	14.9±1.1 * #	11.1±0.9 *

Table 2. Correlations of leptin and adiponectin with body weight (BW) in HC (healthy control) and RC (rectal carcinoma) patients. R = correlation coefficient. P = significance. Significance was considered to be reached when P values were lower than 0.05 (bold, italic)

Parameter		HC		RC	
Gender		Females	Males	Females	Males
Correlation	Leptin and BW	R = 0.073	R = 0.676	R = 0.434	R = 0.517
		P = 0.822	<i>P = 0.016</i>	P = 0.159	P = 0.086
	Adiponectin and BW	R = -0.602	R = -0.158	R = -0.691	R = -0.596
		<i>P = 0.039</i>	P = 0.624	<i>P = 0.013</i>	<i>P = 0.041</i>

adipokine spectrum modifications as an adaptation to malignancy and plead against a direct involvement of adipokines in RC onset.

It is not clear how these differences observed by us may find application for disease prognosis. Surgical intervention may also be accompanied by further acute and long-run modifications of leptin and adiponectin levels, possibly reflecting the impact of surgical stress and subsequent cure or persistence of malignancy. The variation of adipokine secretion and its potential prognostic application was already tested in other surgical conditions (12). Our group is presently involved in organizing such prospective studies concerning adipokine dynamics after surgery for RC.

The current study is original by the homogeneity of tumor localization and severity ranking but included, however, a limited number of participants. Another limitation is that other adipokines or fat tissue-related markers proposed as prognosis parameters by others, such as the soluble leptin receptor, adiponectin isoforms, resistin or fat tissue mass and distribution (4, 5) were not assessed in our study.

In conclusion, patients diagnosed with RC seem to adapt to disease by displaying lower pro-oncogenic leptin and higher anti-oncogenic adiponectin levels than healthy controls. The two adipokines, possibly together with other fat tissue endocrine markers, may find practical application in the evolution prognosis of RC or other malignancies.

Conflict of interest

The authors declare that they have no conflict of interest.

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