ORIGINAL ARTICLE

Relationship between lipid peroxidation or carcinoembryonic antigen and risk factors for non-communicable diseases in women at midlife and beyond

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Abstract

BACKGROUND: Non-communicable diseases (NCDs) constitute leading cause of morbidity, disability and premature mortality. Oxidative processes are involved in the pathogenesis of NCDs. **OBJECTIVES:** To investigate the relationship between lipid peroxidation (LPO), an index of oxidative damage to membrane lipids, or carcinoembryonic antigen (CEA), a tumor marker, and potential risk factors for NCDs in women at midlife and beyond. **METHODS:** Data on lifestyle, such as dietary habits, smoking, physical activity, etc. and medical history, were assessed by a questionnaire in 323 female outpatients of the Regional Centre of Menopause and Osteoporosis – Outpatient Department of Endocrinology, Lodz (Poland), at midlife and beyond. Blood serum LPO and CEA levels, as well as anthropometric measurements were evaluated. **RESULTS:** Positive correlations between LPO level and body mass or body mass index or hip circumference were found. LPO level was increased in women who did not declare regular menstrual cycles. CEA level was increased in women who smoked (and positively correlated with duration of smoking), who consumed pickled food every day and over-consumed animal fats, who had not breastfed in the past, as well as in women with malignancy in anamnesis. Logistic regression analysis has revealed that LPO constitutes the independent positive determinant, whereas CEA constitutes the independent negative determinant, of obesity. Moreover, CEA was independently associated with malignancy in anamnesis, cigarette smoking and animal fat over-consumption. **CONCLUSION:** Both LPO and CEA are independently associated with certain modifiable risk factors for NCDs.

Abbreviations:
BMI - body mass index
CEA - carcinoembryonic antigen
LPO - lipid peroxidation
MDA+4-HDA - malondialdehyde + 4-hydroxyalkenals
NCDs - non-communicable diseases
ROS - reactive oxygen species

INTRODUCTION

Non-communicable diseases (NCDs) (such as malignancy, diabetes, cardiovascular disease, chronic respiratory diseases, stroke and obesity) constitute leading causes of morbidity, disability and premature mortality, at least in developed countries (Abegunde *et al.* 2007). Over the last few decades, the prevalence of NCDs has increased significantly. Numerous studies have shown that many of the risk factors for NCDs are modifiable, and that these diseases are therefore potentially preventable (Alwan *et al.* 2010). It should be also emphasized that women at midlife and beyond are particularly susceptible to the development of NCDs.

There is some evidence that oxidative processes are involved in the pathogenesis of the majority of NCDs and that various antioxidants could prevent development of these diseases (Yoshihara *et al.* 2010). It is also known that cells of living organisms use various antioxidative or defense systems to balance reactive oxygen species (ROS), which result in cells being kept in a state of reduction-oxidation (redox) homeostasis. However, numerous pathological factors may disrupt this balance, leading to loss of redox homeostasis, and finally to conditions referred to as oxidative stress, playing a significant role in the pathogenesis of various diseases (Vendemiale *et al.* 1999). It should be emphasized that lipid peroxidation (LPO) is one of the most frequently examined processes to evaluate oxidative damage to macromolecules (Karbownik *et al.* 2000; Karbownik *et al.* 2001; Karbownik & Lewinski 2003; Podborska *et al.* 2009; Karbownik-Lewinska *et al.* 2010; Kokoszko *et al.* 2010; Stasiak *et al.* 2010; Pelclova *et al.* 2011). LPO products present in the circulation are formed during oxidative damage to membrane lipids (comprising cellular membranes, such as cytosol or reticulum membranes) in all tissues and organs. Importantly, the increased serum level of LPO products was found in different pathological conditions in humans, such as growth hormone deficiency in adults (Kokoszko *et al.* 2006; Karbownik-Lewinska *et al.* 2008), in critically ill patients (Karbownik-Lewinska *et al.* 2007), in hypothyroid thyroid cancer patients (Makarewicz *et al.* 2010), in Alzheimer's disease (Butterfield *et al.* 2010), or in Rett syndrome (Signorini *et al.* 2011).

Carcinoembryonic antigen (CEA) is an intracellular glycoprotein which is used as a marker of malignant tumors (Yamashita & Watanabe 2009; Fan & Xiong 2011). This antigen is mainly over-expressed in colorectal cancer but its level can be increased in pancreatic, gastric, lung, breast, prostate, ovary, as well as urinary bladder malignancies. CEA is recommended as a marker of choice for monitoring the response of metastatic disease to systemic therapy in colorectal cancer (Locker *et al.* 2006). Interestingly, CEA levels may be elevated in other nonmalignant conditions, such as ulcerative colitis, pancreatitis, chronic renal failure, hypothyroidism, chronic obstructive pulmonary disease, cirrhosis and also in cigarette smoking.

Thus, increased levels of LPO or CEA may be observed in various pathological conditions. It should be stressed that both these factors are very easy and not expensive to measure. Therefore, it is of interest to evaluate the potential relationship between serum levels of LPO or CEA and potential risk factors for NCDs. This analysis was performed in women at midlife and beyond, a population particularly exposed to the development of NCDs.

Tab. 1. Basic characteristic of female patients.

	The whole group of patients	Non-cancer patients	Cancer patients
n	323	309	14
age [years]	58.9±0.52 (39-83)	58.9±0.53 (39-83)	60.0±2.78 (47-76)

n – number of patients; age is presented as mean ± SEM; ranges of age are shown in parentheses.

MATERIALS AND METHODS

Subjects

Three hundred and twenty three (323) female outpatients of the Regional Centre of Menopause and Osteoporosis – Outpatient Department of Endocrinology, Medical University Hospital No 3 (Lodz, Poland), at midlife and beyond, were enrolled in the study (Table 1), which was carried out in 2005–2006. Fourteen (14) of the whole group of patients had malignancy in anamnesis (breast cancer -6, thyroid cancer -1, ovarian cancer -1, colon cancer -1, skin cancer -1, uterine cancer -1, uterine appendages cancer -1, skin and colon cancer -1, cancer without given localization -1) and all of them had confirmed remission (they are referred to as cancer patients) (Table 1). The remainder of patients (n=309), referred to as non-cancer patients, had no malignancy in anamnesis (Table 1). The procedures used in the study were approved by the Local Ethics Committee of the Medical University of Lodz, and fully informed written consent was obtained from the patients.

Questionnaire and anthropometric parameters

Data on lifestyle and medical history were assessed by a questionnaire designed by us, which was composed of questions related to dietary habits, cigarette smoking, alcohol consumption, physical activity, weight gain (more than 5 kg from the age of 18), use of contraceptive pills, menstrual cycle regularity, hormone replacement

therapy or use of other therapeutic agents, exposure to ionizing radiation, family history, etc. Moreover, anthropometric parameters, such as body height, body mass, waist and hip circumferences, as well as blood pressure, were measured.

Measurement of LPO and CEA level

The concentrations of malondialdehyde + 4-hydroxyalkenals (MDA+4-HDA), as an index of lipid peroxidation (LPO), were measured in blood serum using the LPO-586 kit purchased from Calbiochem (La Jolla, CA). The serum (200 µl) was mixed with 650 µl of a methanol:acetonitrile (1:3, v/v) solution, containing a chromogenic reagent, N-methyl-2-phenylindole, and vortexed. After adding 150 µl of methanesulfonic acid (15.4 M), the incubation was carried out at 45 °C for 40 min. The reaction between MDA+4-HDA and N-methyl-2-phenylindole yields a chromophore, which is spectrophotometrically measured at the absorbance of 586 nm, using a solution of 4-hydroxynonenal (10 mM) as the standard. The level of LPO was expressed as the amount of MDA+4-HDA (nmol) per 1 ml of serum.

Carcinoembryonic antigen (CEA) was measured in blood serum using Elecsys CEA reagent kit (Roche, Germany) in accordance with manufacturer's instruction.

Statistical analyses

The data were statistically analysed, using Student's unpaired *t* test or the one-way analysis of variance (ANOVA), followed by Student-Newman-Keuls' test. The results are presented as means ± SEM. Univariate logistic regression analysis was used to determine which continuous variable might determine (predict) or be associated with a dichotomized variable; in order to adjust for several risk factors, multivariate logistic regression analysis was performed with all the variables found to be significant at the univariate analysis. Correlations between analysed parameters were assessed by the Pearson's correlation coefficient. Statistical significance was determined at the level of $p<0.05$.

Tab. 2. Mean values ± SEM of lipid peroxidation (LPO) level in the whole group of patients (n=323) and in non-cancer patients (n=309), exposed to potential risk factors for non-communicable diseases (NCDs).

Risk factors		LPO MDA + 4-HDA (nmol/ml)	*p*-value
THE WHOLE GROUP OF PATIENTS			
regular menstrual cycles	yes	18.68±0.56	0.016*
	no	21.75±1.32	
NON-CANCER PATIENTS			
regular menstrual cycles	yes	18.71±0.57	0.016*
	no	21.86±1.35	

Statistically significant differences were found only for menstrual cycles regularity (shown in Table); *$p<0.05$

RESULTS

In the whole group of patients (non-cancer plus cancer), as well as in non-cancer patients, LPO level was increased in women who did not declare regular menstrual cycles (Table 2). Positive correlations between LPO level and body mass or body mass index (BMI) or hip circumference in the whole group of patients (Table 3), as well as in non-cancer patients (Table 3), were found. Negative correlation between body height and LPO level was observed in the whole group, as well as in non-cancer patients (Table 3). In cancer patients, positive correlations between LPO level and waist circumference (Table 3) or number of smoked cigarettes/day were found (Table 3).

In the whole group of patients, the concentration of CEA was increased in women who smoked (Table 4), and correlated positively with duration of smoking (Table 3). CEA level was also increased in women who consumed pickled food every day and who over-consumed animal fats, as well as in women who did not breastfeed or in women with malignancy in anamnesis (Table 4).

Similarly, in non-cancer patients, CEA level was increased in women who smoked (Table 4), and correlated positively with duration of smoking (Table 3). The level of CEA was also increased in non-cancer patients who over-consumed animal fats (Table 4). Moreover, in this subgroup of patients, CEA level was negatively correlated with body height (Table 3).

In the whole group, as well as in non-cancer patients, women over-consuming animal fats had increased body mass, BMI, waist and hip circumferences (Table 5).

For the whole group of patients, continuous variables such as LPO and CEA levels, as well as age, body mass, BMI, hip circumference, waist circumference, waist/hip ratio, weight gain, body height, number of births, age of menarche, lifetime menstrual activity, age of menopause, duration of postmenopausal life, systolic blood pressure, diastolic blood pressure, number of smoked cigarettes/day, etc., were submitted to a univariate and then to a multivariate logistic regression analysis. The purpose of these analyses was to determine which of those continuous variables might determine (predict) or be associated with a chosen dichotomized variable. Interestingly, LPO did constitute the independent positive determinant of obesity (Table 6). In contrast, CEA constituted the independent negative determinant of obesity (Table 6). LPO was the negative determinant of menstrual cycle regularity (OR=0.97, 95%CI=0.94–0.99, $p=0.018$, data not shown). Additionally, logistic regression analysis has revealed that CEA is independently associated with malignancy in anamnesis (Table 7), cigarette smoking

Tab. 3. Correlations between lipid peroxidation (LPO) or carcinoembryonic antigen (CEA) and selected potential risk factors for non-communicable diseases (NCDs) in the whole group of patients (n=323), in non-cancer patients (n=309) and in cancer patients (n=14).

Risk factors	LPO [MDA + 4-HDA (nmol/ml)]		CEA (ng/mL)	
THE WHOLE GROUP OF PATIENTS				
	r	*p*-value	r	*p*-value
body height	–0.12	0.03*	–0.09	0.103
body mass	0.16	0.004*	–0.09	0.095
body mass index (BMI)	0.23	<0.001*	–0.06	0.286
hip circumference	0.19	<0.001*	–0.09	0.099
duration of smoking	0.01	0.889	0.17	0.045*
NON–CANCER PATIENTS				
body height	–0.13	0.019*	–0.13	0.026*
body mass	0.15	0.007*	–0.1	0.094
body mass index (BMI)	0.22	<0.001*	–0.05	0.415
hip circumference	0.18	0.001*	–0.09	0.131
duration of smoking	0.00	0.973	0.22	0.01*
CANCER PATIENTS				
waist circumference	0.59	0.028*	0.20	0.485
number of smoked cigarettes/day	0.96	0.038*	–0.41	0.586

r - Pearson's correlation coefficient; *p<0.05

Tab. 4. Mean values ± SEM of carcinoembryonic antigen (CEA) level in the whole group of patients (n=323) and in non-cancer patients (n=309), exposed to selected potential risk factors for non-communicable diseases (NCDs) (shown are only risk factors, for which statistically significant differences were found).

Risk factors		CEA (ng/mL)	*p*-value
THE WHOLE GROUP OF PATIENTS			
smoking (currently or in anamnesis)	yes	1.99±0.12	<0.001*
	no	1.39±0.06	
consumption of pickled food	every day	2.82±1.97	0.005*
	never	1.52±0.1	
over-consumption of animal fats	yes	2.22±0.31	0.002*
	no	1.62±0.06	
breastfeeding in anamnesis	yes	1.55±0.08	0.042*
	no	1.85±0.12	
malignancy in anamnesis	yes	2.69±0.94	0.004*
	no	1.67±0.06	
NON-CANCER PATIENTS			
smoking (currently or in anamnesis)	yes	1.91±0.1	<0.001*
	no	1.38±0.06	
over-consumption of animal fats	yes	1.97±0.2	0.04*
	no	1.62±0.06	

*p<0.05

(Table 8) and with animal fat over-consumption (Table 9). In univariate logistic regression analysis, CEA concentration was associated [at the borderline significance level (OR=1.31, 95%CI=0.99–1.73, p=0.056, data not shown)] with everyday consumption of pickled food.

In the whole group, as well as in non-cancer patients, body mass correlated positively with waist circumference (r=0.79, p<0.001; r=0.80, p<0.001, respectively) or hip circumference (r=0.83, p<0.001 both) or waist/hip ratio (r=0.27, p<0.001; r=0.28, p<0.001, respectively) or weight gain (r=0.73, p<0.001 both) or number of births (r=0.16, p=0.004; r=0.14, p=0.015, respectively) (data not shown). Similarly, in cancer patients, body mass correlated positively with waist circumference (r=0.73, p=0.003) or hip circumference (r=0.82, p<0.001) or weight gain (r=0.91, p=0.004), as well as with BMI (r=0.92, p<0.001) (data not shown). In the whole group of patients, body mass was negatively correlated with duration of postmenopausal life (r=–0.14, p=0.03) (data not shown). In cancer patients, negative correlation between age and body mass was observed (r=–0.54, p=0.044) (data not shown).

In the whole group, as well as in non-cancer patients, systolic blood pressure correlated positively with waist circumference (r=0.23, p<0.001; r=0.24, p<0.001, respectively) or hip circumference (r=0.14, p=0.015; r=0.15, p=0.007, respectively) or waist/hip ratio (r=0.19, p<0.001; r=0.19, p=0.001, respectively) or body mass (r=0.16, p=0.003; r=0.19, p=0.001, respectively) or BMI (r=0.24, p<0.001; r=0.26, p<0.001, respectively) (data not shown). Similarly, in the whole group, as well as in non-cancer patients, diastolic blood pressure correlated positively with waist circumference (r=0.26, p<0.001; r=0.27, p<0.001, respectively) or hip circumference (r=0.17, p=0.002; r=0.18, p=0.001, respectively) or waist/hip ratio (r=0.19, p=0.001; r=0.18, p=0.001, respectively) or body mass (r=0.22, p<0.001; r=0.24, p<0.001, respectively) or BMI (r=0.25, p<0.001; r=0.26, p<0.001, respectively) (data not shown).

Decreased values of systolic blood pressure were found in women taking oral contraception (OC) as compared with women who did not take OC, when both the total group of 323 patients and the subgroup of non-cancer patients (n=309) (p=0.009 both, data not shown) were considered.

Women who gave birth to at least one child (n=282) had increased body mass as compared with women who had never given birth (n=41) (p=0.038, data not shown). Women with malignancy in anamnesis (n=14) had decreased body mass as compared with women without malignancy in anamnesis (n=309) (p=0.031, data not shown).

Tab. 5. Mean values ± SEM of body mass, body mass index (BMI), waist circumference and hip circumference in the whole group of patients (n=323) and in non-cancer patients (n=309) over-consuming of animal fats.

		THE WHOLE GROUP OF PATIENTS			
		body mass (kg)	**BMI (kg/m^2)**	**waist circumference (cm)**	**hip circumference (cm)**
over-consumption of animal fats	yes	72.08±2.07	27.77±0.67	89.02±1.68	107.79±1.58
	no	66.97±0.7	26.25±0.26	84.29±0.65	103.77±0.58
p-value		0.005*	0.024*	0.004*	0.008*
		NON-CANCER PATIENTS			
		body mass (kg)	BMI (kg/m^2)	waist circumference (cm)	hip circumference (cm)
over-consumption of animal fats	yes	72.85±2.2	28.07±0.7	89.33±1.81	108.5±1.67
	no	67.31±0.71	26.33±0.27	84.46±0.67	103.93±0.6
p-value		0.004*	0.013*	0.005*	0.004*

*p<0.05

Tab. 6. Univariate and multivariate logistic regression analysis of the univariate obesity (for BMI value > 30 kg/m^2) determinants (variables), performed in the whole group of patients (n=323).

Variable	**Univariate regression**			**Multivariate regression**		
	OR	**95%CI**	***p*-value**	**OR**	**95%CI**	***p*-value**
CEA (ng/mL)	0.73	0.53–0.99	0.043*	0.68	0.49–0.95	0.025*
LPO [MDA + 4-HDA (nmol/ml)]	1.05	1.02–1.08	0.001*	1.05	1.02–1.09	<0.001*
body height (cm)	1.00	0.96–1.05	0.844	–	–	–
waist circumference (cm)	1.27	1.20–1.35	<0.001*	–	–	–
hip circumference (cm)	1.29	1.21–1.37	<0.001*	–	–	–
waist/hip ratio	26508	247–2.84×10^6	<0.001*	–	–	–
systolic blood pressure (mm Hg)	1.02	1.01–1.03	0.004*	1.01	0.99–1.03	0.292
diastolic blood pressure (mm Hg)	1.03	1.01–1.06	0.015*	1.03	0.98–1.07	0.206
age (years)	1.00	0.97–1.03	0.972	–	–	–
duration of smoking (years)	0.99	0.95–1.03	0.636	–	–	–
number of smoked cigarettes/day	1.04	0.99–1.10	0.138	–	–	–
age of menarche (years)	0.96	0.82–1.11	0.58	–	–	–
age of menopause (years)	1.04	0.96–1.13	0.285	–	–	–
lifetime menstrual activity (years)	1.06	0.98–1.15	0.147	–	–	–
duration of postmenopausal life (years)	0.99	0.95–1.02	0.463	–	–	–
number of pregnancies	1.05	0.87–1.26	0.606	–	–	–
number of births	1.36	0.97–1.89	0.072	–	–	–

OR - odds ratio; CI - confidence interval; *p<0.05.

DISCUSSION

Oxidative stress plays an important role in the pathogenesis of numerous disorders (Vendemiale *et al.* 1999). Besides earlier mentioned disorders (such as growth hormone deficiency in adults or Alzheimer's disease, among others) (Kokoszko *et al.* 2006; Karbownik-Lewinska *et al.* 2007; Karbownik-Lewinska *et al.* 2008; Butterfield *et al.* 2010; Makarewicz *et al.* 2010; Signorini *et al.* 2011), the level of oxidative stress is also increased in obesity in humans (Vincent & Taylor 2006). Moreover, enhanced oxidative stress was observed in rats with high-fat diet–induced obesity (Dobrian *et al.* 2001). In the present study, positive correlations between LPO level and three parameters related to obesity criteria, namely: body mass, body mass index (BMI) and hip circumference, were found. Furthermore, the logistic regression analysis has revealed that

Tab. 7. Univariate and multivariate logistic regression analysis of the univariate malignancy in anamnesis (with confirmed remission) determinants (variables), performed in the whole group of patients (n=323).

Variable	Univariate regression			Multivariate regression		
	OR	95%CI	*p*-value	OR	95%CI	*p*-value
CEA (ng/mL)	1.34	1.04–1.72	0.023*	1.30	1.02–1.67	0.036*
LPO [MDA + 4-HDA (nmol/ml)]	0.99	0.93–1.05	0.676	–	–	–
body mass (kg)	0.94	0.88–0.99	0.033*	0.94	0.88–1.00	0.045*
body height (cm)	0.93	0.85–1.02	0.108	–	–	–
BMI (kg/m^2)	0.89	0.77–1.02	0.099	–	–	–
waist circumference (cm)	0.98	0.93–1.03	0.454	–	–	–
hip circumference (cm)	0.95	0.89–1.01	0.132	–	–	–
waist/hip ratio	6.24	0.00–21576	0.658	–	–	–
systolic blood pressure (mm Hg)	1.01	0.98–1.03	0.603	–	–	–
diastolic blood pressure (mm Hg)	0.99	0.94–1.05	0.830	–	–	–
age (years)	1.01	0.96–1.07	0.651	–	–	–
weight gain (kg)	0.93	0.82–1.06	0.269	–	–	–
duration of smoking (years)	1.02	0.95–1.11	0.546	–	–	–
number of smoked cigarettes/day	0.91	0.77–1.08	0.292	–	–	–
age of menarche (years)	1.11	0.82–1.51	0.506	–	–	–
age of menopause (years)	0.98	0.84–1.15	0.847	–	–	–
lifetime menstrual activity (years)	0.98	0.84–1.14	0.82	–	–	–
number of pregnancies	0.73	0.44–1.21	0.225	–	–	–
number of births	0.63	0.32–1.25	0.186	–	–	–
age of first childbirth (years)	0.84	0.68–1.03	0.098	–	–	–

OR - odds ratio; CI - confidence interval; *$p<0.05$.

LPO may constitute the independent determinant (predictor) of obesity. It has been consistently shown in previous studies that body mass is significantly associated with increased oxidative damage to macromolecules in postmenopausal women (Szosland *et al.* 2010). Therefore, on the basis of these findings, one could conclude that the relationship between LPO and the aforementioned anthropometric parameters reported here might be expected.

Reeves *et al.* (2007) reported that increased BMI was associated with a significant increase in the risk of development of cancer in postmenopausal women. Similarly, increased BMI was associated with enhanced risk of development of various malignancies (Renehan *et al.* 2008). Taking into account the fact that increased oxidative stress level may be associated with the process of carcinogenesis (Valko *et al.* 2006), the positive correlation between LPO and BMI (and certainly body mass), as seen in the present study, may also be expected in that context.

The mechanism of the strong association between oxidative damage and obesity, documented in the present study, remains to be examined. It can be hypothesized that this increased oxidative stress results from many factors, such as increased accumulation of body fat, bad dietary habits and decreased physical activity, which is typical for obese patients. Motykova *et al.* (2011) have recently shown that lifestyle modification (physical activity and reduction of energy intake) may lead to decrease of lipoprotein associated phospholipase A2, which is an independent marker of inflammation and risk of atherosclerosis, in obese children.

In the present study, LPO level was increased in women who did not report regular menstrual cycles. Any hormonal disturbances which can be observed in women with irregular menstrual cycles may lead to redox imbalance, and as a result of that, to increased oxidative damage to macromolecules. For example, malondialdehyde (MDA) level in ovary follicular fluid was increased in women with polycystic ovary syndrome (PCOS), a disorder which is characterized by various disturbances of the menstrual cycle (Yildirim *et al.* 2007). Importantly, PCOS may be associated with development of endometrial, ovarian and breast cancer (de Franca Neto *et al.* 2010). Thus, in the context of the above-mentioned observations, it is not excluded that

Tab. 8. Univariate and multivariate logistic regression analysis of the univariate cigarette smoking determinants (variables), performed in the whole group of patients (n=323).

Variable	Univariate regression			Multivariate regression		
	OR	95%CI	*p*-value	OR	95%CI	*p*-value
CEA (ng/mL)	1.75	1.34–2.27	<0.001*	1.81	1.30–2.52	<0.001*
LPO [MDA + 4-HDA (nmol/ml)]	1.00	0.98–1.02	0.979	–	–	–
body mass (kg)	1.00	0.98–1.02	0.824	–	–	–
body height (cm)	1.01	0.98–1.05	0.498	–	–	–
BMI (kg/m^2)	1.00	0.95–1.05	0.954	–	–	–
waist circumference (cm)	1.00	0.98–1.02	0.657	–	–	–
hip circumference (cm)	1.00	0.97–1.02	0.776	–	–	–
waist/hip ratio	12.12	0.38–383.1	0.155	–	–	–
systolic blood pressure (mm Hg)	0.99	0.98–1.00	0.201	–	–	–
diastolic blood pressure (mm Hg)	0.99	0.97–1.01	0.289	–	–	–
age (years)	0.94	0.91–0.96	<0.001*	0.88	0.81–0.96	0.003*
weight gain (kg)	1.00	0.96–1.03	0.863	–	–	–
age of menarche (years)	0.87	0.77–1.00	0.043*	0.91	0.76–1.09	0.313
age of menopause (years)	0.94	0.88–1.00	0.062	–	–	–
lifetime menstrual activity (years)	0.97	0.91–1.03	0.367	–	–	–
duration of postmenopausal life (years)	0.94	0.91–0.97	<0.001*	1.04	0.96–1.13	0.295
number of pregnancies	1.06	0.90–1.24	0.469	–	–	–
number of births	0.75	0.57–0.99	0.039*	0.74	0.52–1.04	0.082
age of first childbirth (years)	0.95	0.89–1.00	0.063	–	–	–

OR - odds ratio; CI - confidence interval; *p<0.05.

Tab. 9. Univariate and multivariate logistic regression analysis of the univariate animal fat over-consumption determinants (variables),

increased LPO level in women with irregular menstrual cycles may contribute to cancer initiation.

In our present study, CEA level was found to be increased in women who smoked and correlated positively with duration of smoking. Furthermore, logistic regression analysis found CEA to be independently associated with cigarette smoking. These findings may confirm the well-known observation that smoking is a modifiable risk factor for cancer. Ha *et al.* (2012) have recently shown that prolonged cigarette smoking is an independent predictor for hepatocellular carcinoma in patients with chronic liver disease. Cigarette smoking is also strongly associated with squamous cell carcinoma of the skin (Rollison *et al.* 2012). Our findings are consistent with the results of other studies. For example, higher CEA level was observed in cigarette smokers as compared to non-smokers, and CEA level increased with the number of daily smoked cigarettes (Sajid *et al.* 2007).

In this study, CEA level was found to be increased in women who over-consumed animal fats. Furthermore, CEA was independently associated with animal fat over-consumption, as revealed in regression analysis. It is well known that a high-fat diet may lead to the development of obesity. Lee *et al.* (2011) have recently shown that CEA level increases consistently with each additional component of metabolic syndrome. However, we documented in regression analysis that CEA is independently inversely associated with obesity. Thus, on the basis of our observations we can hypothesize that animal fat over-consumption may be considered as a factor which could increase CEA level. Further analysis is needed to broaden our knowledge about the potential relationship between CEA level, fat over-consumption and obesity and about the importance of this association in clinical practice.

We also found that CEA level was increased in women who consumed pickled food every day, and an independent association was noted between these two variables (however, of borderline significance). Numerous studies have shown that consumption of pickled food may lead to the development of various malignancies (Islami *et al.* 2009; Yu *et al.* 2010). Therefore, further studies are needed to determine to what extent the increased CEA level, as seen in the present study, results from the influence of ingredients used for pickling, and

performed in the whole group of patients (n=323).

Variable	Univariate regression			Multivariate regression		
	OR	95%CI	*p*-value	OR	95%CI	*p*-value
CEA (ng/mL)	1.32	1.07–1.63	0.01*	1.40	1.12–1.76	0.004*
LPO [MDA + 4-HDA (nmol/ml)]	0.99	0.96–1.02	0.532	–	–	–
body mass (kg)	1.03	1.01–1.06	0.006*	1.05	0.98–1.11	0.153
body height (cm)	1.03	0.98–1.08	0.291	–	–	–
BMI (kg/m^2)	1.08	1.01–1.15	0.025*	0.92	0.78–1.09	0.348
waist circumference (cm)	1.04	1.01–1.07	0.005*	1.03	0.98–1.08	0.288
hip circumference (cm)	1.04	1.01–1.07	0.01*	1.03	0.98–1.08	0.305
waist/hip ratio	13.33	0.14–1265	0.263	–	–	–
systolic blood pressure (mm Hg)	1.01	1.00–1.03	0.153	–	–	–
diastolic blood pressure (mm Hg)	1.02	0.99–1.05	0.142	–	–	–
age (years)	0.97	0.94–1.01	0.12	–	–	–
weight gain (kg)	1.03	0.98–1.07	0.197	–	–	–
duration of smoking (years)	1.04	0.99–1.08	0.094	–	–	–
number of smoked cigarettes/day	1.02	0.96–1.07	0.548	–	–	–
age of menarche (years)	0.98	0.83–1.15	0.78	–	–	–
age of menopause (years)	1.02	0.94–1.12	0.571	–	–	–
lifetime menstrual activity (years)	1.04	0.95–1.13	0.407	–	–	–
duration of postmenopausal life (years)	0.96	0.92–1.00	0.053	–	–	–
number of pregnancies	1.04	0.86–1.27	0.671	–	–	–
number of births	1.02	0.71–1.46	0.905	–	–	–
age of first childbirth (years)	0.93	0.85–1.01	0.085	–	–	–

OR - odds ratio; CI - confidence interval; *p<0.05.

to clarify the potential association between pickled food consumption, increased CEA and cancer.

In the present study, CEA level was increased in women who did not breastfeed. Breastfeeding is considered as a factor which may reduce the risk of breast cancer. However, this hypothesis is not fully confirmed. In some studies, significant protection against breast cancer has been shown (Awatef *et al.* 2010), whereas other studies have failed to confirm the beneficial effects of breastfeeding in reducing breast cancer incidence (Yang & Jacobsen 2008). Therefore, our observation could support the hypothesis that breastfeeding may decrease the risk of breast cancer development.

Positive correlations between systolic or diastolic blood pressure and waist or hip circumference, or waist/hip ratio or body mass or BMI were found in the present study. Increased waist circumference as well as BMI associated with high blood pressure was reported (Hu *et al.* 2011). Thus, our findings may confirm an important, and after all well documented, role of body mass reduction in the prevention of NCDs, including cardiovascular disease.

Decreased values of systolic blood pressure were found in women taking oral contraception. The use of older generation oral contraceptives was associated with the risk of increased blood pressure. Fortunately, oral contraceptives of the newer generation are safer and do not affect certain components of the renin-angiotensin-aldosterone system, possibly even triggering a decrease in their levels (Wiegratz *et al.* 2003). Therefore, the present findings may confirm the safety of recently and currently used oral contraceptives.

Intriguingly, a negative correlation between body height and LPO level was observed in our study. Similarly, CEA level was also inversely correlated with this anthropometric parameter. These observations seem to be difficult to explain in the context of results showing positive associations between body height and susceptibility to the development of various neoplasms, including testicular germ-cell tumor (Lerro *et al.* 2010) or breast cancer (John *et al.* 2011), among others. Therefore, further studies are needed to determine the significance of the above observation.

In conclusion, LPO and CEA are independently associated with numerous, yet differing, modifiable risk factors for NCDs. Therefore, taking into account the fact that both LPO and CEA are very easy and inexpensive to measure, one could conclude that these assessments could serve as supporting tools in clinical practice in the prevention and detection of NCDs.

Declaration of interest

There is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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