Total antioxidant status in lung cancer is associated with levels of endogenous antioxidants and disease stage rather than lifestyle factors – preliminary study

Katarzyna Zabłocka-Słowińska[1], Irena Porębska[2], Marcin Gołecki[2], Monika Kosacka[2], Konrad Pawełczyk[3], Lilla Pawlik-Sobecka[4], Katarzyna Zarębska[5], Halina Grajeta[1]

[1]Department of Food Science and Nutrition, Wroclaw Medical University, Poland
[2]Department and Clinic of Pulmonology and Lung Cancers, Wroclaw Medical University, Poland
[3]Department and Clinic of Thoracic Surgery, Wroclaw Medical University, Poland
[4]Department of Professional Training in Clinical Chemistry, Wroclaw Medical University, Poland
[5]Students' Scientific Association of Department of Food Science and Dietetics, Wroclaw Medical University, Poland

Aim of the study: Decreased total antioxidant capacity (TAC) has been reported in different neoplasms, including lung cancer. However, no study concerning the relationship between endogenous antioxidants, lifestyle factors, and TAC has been conducted among lung cancer patients. The purpose of the study was to investigate the associations between endogenous antioxidants, severity of disease, lifestyle factors, and TAC in lung cancer patients.

Material and methods: The study was conducted among 59 lung cancer patients. The levels of total antioxidant status (ATBS method), endogenous antioxidants, and C-reactive protein were measured in patients' sera automatically. Dietary habits of the subjects were evaluated based on the Food Frequency Questionnaire (FFQ) on the day of admission to hospital.

Results: We found a positive correlation between serum albumin, uric acid (UA), and TAC and a negative correlation between CRP and TAC. Moreover, TAC was significantly positively associated with disease stage. We did not find any significant relationship between the frequency of selected food consumption and TAC in lung cancer patients, except for a positive correlation between the frequency of refined cereal products consumption and TAC level. Smoking status did not correlate with TAC.

Conclusions: Total antioxidant status of lung cancer patients results from their disease stage and levels of endogenous antioxidants rather than from lifestyle factors. The lack of influence of diet and smoking on the TAC presumably result from disturbed homeostasis in which cancer, while developing, could determine the redox state to a greater extent than lifestyle factors.

Key words: lung cancer, TAS, albumin, uric acid, CRP, dietary habits.

Contemp Oncol (Pozn) 2016; 20 (4): 302–307
DOI: 10.5114/wo.2016.61850

Introduction

Lung cancer poses serious diagnostic and therapeutic problems. Despite extensive research and development of treatment methods, it has the highest death rates of all cancers [1]. The main risk factors of lung cancer are cigarette smoking, occupational and genetic factors, as well as exposure to carcinogenic substances present in the air [2, 3]. Dietary habits may, to some extent, modify the risk of its development [4, 5].

Lungs are significantly exposed to free radicals because of the role they fulfil. High oxygen pressure, comparable to atmospheric values, promotes oxidation, particularly in the presence of reactive oxygen species (ROS) from tobacco smoke and air pollution [6]. Oxidative stress plays an important role in lung cancer pathogenesis; therefore, protection from ROS seems to be one of the crucial strategies of lung cancer prevention. The total antioxidant capacity (TAC) is determined by the content and activity of systemic exo- and endogenous antioxidant elements, including mainly concentrations of albumin, uric acid, bilirubin, and ascorbic acid [7, 8]. Decreased TAC and depletion of particular elements of the system has been reported in different neoplasms, including lung cancer [9, 10]. Dietary habits and smoking may partially modify TAC, as observed in several studies [11–13]. Nevertheless, similar research has not been conducted yet among lung cancer patients.

Considering the above, the aim of this study was to investigate the association between levels of endogenous antioxidant factors, severity of disease, lifestyle factors, and TAC in lung cancer patients.

Material and methods

Patients

The study was conducted among 59 patients (64.3 ±7.7 years) suffering from lung cancer, before any cancer treatment. The detailed description of patients concerning disease stage, type of lung cancer, and cigarette smoking is presented in Table 1. Patients were interviewed concerning their di-

Table 1. Analyses of biochemical parameters in lung cancer patients [median (min. – max.)]

Biochemical parameters	Median; min. – max. (n = 59)	Cigarette smokers		Disease stage		Histological type of lung cancer	
		Current (n = 11)	Non-/former (n = 48)	I–III (n = 39)	IV (n = 20)	SCLC (n = 16)	NSCLC (n = 43)
TAS [mmol/l]	1.45; 1.12–2.34	1.41 (1.18–1.92)	1.47 (1.12–2.34)	1.63 (1.23–2.01)[b]	1.39 (1.12–1.63)[b]	1.44 (1.12–2.34)	1.43 (1.12–1.95)
Albumin [g/l]	3.71; 2.52–4.29	3.79 (3.07–4.29)	3.65 (2.52–4.29)	3.97 (2.90–4.29)[a]	3.54 (2.52–4.17)[a]	3.60 (2.52–4.29)	3.58 (2.80–4.29)
UA [mg/dl]	4.77; 2.35–7.91	3.83 (3.50–7.90)	4.81 (2.35–7.91)	5.05 (3.50–7.20)	4.16 (2.35–7.90)	4.42 (2.35–7.91)	4.42 (2.77–7.91)
Bilirubin [mg/dl]	0.36; 0.14–1.38	0.39 (0.24–0.73)	0.36 (0.15–1.38)	0.36 (0.14–1.38)	0.34 (0.15–0.74)	0.36 (0.14–1.38)	0.39 (0.14–1.38)
CRP [mg/l]	14.76; 0.40–166.40	10.0 (0.4–69.0)	16.2 (0.66–166.4)	12.6 (0.4–166.4)	19.2 (1.4–99.5)	14.8 (0.4–166.4)	17.6 (0.4–166.4)

SCLC – small cell lung cancer; NSCLC – non-small cell lung cancer; TAS – total antioxidant status; UA – uric acid; CRP – C-reactive protein
[a]$p < 0.01$; [b]$p < 0.001$

etary habits on the day of admission to the hospital. The next day, blood samples were collected, and serum was separated and then stored at –80°C until analysed. The study was approved by the local Ethics Commission (approval no. 540/2013).

Biochemical measurements

The TAC level was measured in serum by the generation of 2,2'-azino-di-(3-ethylbenzthiazoline sulphonate) (ATBS) radical cation using a kit (TAS, Randox Laboratories). Serum albumin concentration was measured with bromocresol green. Serum uric acid (UA) level was determined based on the oxidation with uricase. TAC, albumin, and UA were evaluated with an auto-analyser (Konelab 20i Thermo-Scientific). The total serum bilirubin concentration was determined with a diazo-coupling method and a serum level of CRP – with a latex-enhanced immunoturbidimetric assay. These measurements were performed with an automated analyser (Cobas e410, Roche Diagnostics).

Lifestyle factors

To evaluate dietary habits, the patients were interviewed using part of a food frequency questionnaire validated in 2005 [14], which included questions concerning the frequency of consumption of selected groups of food products, i.e. wholegrain cereal products, refined cereal products, vegetables in total, raw vegetables, fruit in total, and raw fruit in the previous year. The intake of food products was pooled into five frequency categories: less than 1 portion/day, 1–2 portions/day, 3–4 portions/day, > 4 portions/day. Both raw, frozen, cooked, and canned vegetables were classified as vegetables in total (excluding potatoes). The same classification concerned fruit in total. Fruit and vegetable juices were incorporated into categories of fruit and vegetables in total, respectively. We additionally extracted raw vegetables as well as raw fruit to find the relationship between raw plant food and total antioxidant capacity in lung cancer patients.

Regarding the habit of smoking, individuals were considered to be non-smokers if they had never smoked, and former smokers if they had not smoked for at least four weeks before participation in this study. The remaining subjects were assigned to the current smokers group.

Statistical analysis

All statistical analyses were performed with Statistica ver. 12. Differences in biochemical measurements between the groups of patients relating to their smoking status, disease stage, and histological type of lung cancer were determined with Student's *t*-test or Mann-Whitney *U* test, depending on data distribution. The differences in consumption frequency of food products between patients pooled into two groups based on TAC distribution were determined with χ^2 test. Results were considered statistically significant if $p < 0.05$.

Results

Biochemical measurements in relation to disease stage, histological type of lung cancer, and smoking status

Results concerning biochemical measurements are presented in Table 1. The median of TAC concentration in the lung cancer group was 1.45 mmol/l, in the range between 1.12 mmol and 2.34 mmol/l. The median concentrations of albumin, bilirubin, and uric acid levels were at 3.71 g/l, 0.36 mg/dl, and 4.77 mg/dl, respectively. The median concentration of CRP was 14.76 mg/l, in a wide range between 0.40 and 166.40 mg/l, and was significantly higher than the upper reference value of 5 mg/l. Results of biochemical markers assays did not differ between groups with different histological types of lung cancer and smoking status. However, a trend was observed for a slight decrease in serum UA concentrations in smokers in comparison to the non-smokers and former smokers. The disease stage significantly influenced TAS and albumin levels. The patients at stage IV had significantly lower TAS and albumin levels than the patients with an earlier stage of lung cancer: 1.38 mmol/l vs. 1.60 mmol/l and 3.54 mg/l vs. 3.97 mg/l, respectively. However, the remaining biochemical parameters did not differ as affected by the severity of the disease.

Correlations between endogenous antioxidants, CRP, and TAC

The correlations between levels of serum albumin, uric acid, bilirubin, CRP, and TAC are presented in Table 2. We

Table 2. Correlations between albumin, uric acid (UA), bilirubin, C-reactive protein (CRP), and TAC in lung cancer patients (n = 59)

Biochemical parameters	R	p
Albumin	0.52	< 0.0001
UA	0.59	< 0.0001
Bilirubin	–0.01	0.96
CRP	–0.39	0.013

observed strong positive correlations between albumin, UA, and TAC levels and a significant negative correlation between CRP and TAC levels. There was no correlation between bilirubin and TAC.

Total antioxidant status in relation to dietary habits

The dietary habits of the lung cancer patients are presented in Table 3. The frequency of consumption of wholegrain cereal products was generally low. About half of the group with lower TAC and a similar percentage of patients with a higher value of this marker did not eat wholegrain products regularly (at least once per day). In turn, there was a statistically significant difference between these two groups in the consumption frequency of refined cereal products. Almost 60% of the patients with a lower TAC value consumed these products 3–5 times/day, whereas the same frequency was declared in only about 30% of the subjects from the second group. In turn, we did not observe any statistically significant differences in the frequency of consumption of vegetables and fruit. About 40% of the group with a lower TAC value declared eating vegetables in total 3–4 times/day, while among the patients with a higher TAC value the same declaration was made by a slightly, but not significantly, higher percentage of the group – ca. 48%. The majority of patients from both groups declared consuming 1–2 portions of raw vegetables/day. Similar observations were made for fruit in total and raw fruit consumption; however, a higher percentage of patients from both groups declared consumption of raw fruit compared to raw vegetables.

Discussion

It is obvious that the antioxidant system is disturbed during carcinogenesis. Still little is known, however, on how particular endo- and exogenous factors influence TAC in cancer patients [8]. Therefore, we evaluated correlations between some endogenous antioxidants, severity of disease, as well as selected lifestyle factors and TAC in lung cancer patients. Albumin, UA, and bilirubin have for a long time been recognised as the main endogenous components of extracellular TAC, hence disturbances in TAC can simply reflect their alterations and vice versa, which has mainly been documented in healthy volunteers [7, 15]. However, there are only a few investigations of the above-mentioned relationships, which were conducted on patients suffering from different diseases including cancers [16, 17]. In this study, TAC was found to be significantly positively correlated with albumin and UA. In contrast to other studies [18, 19], no correlation was found between bilirubin and TAC. Albumin is an abundant antioxidant of human extracellular fluids with many different activities against ROS formation, e.g. ligand-binding capacities or free-radical trapping properties [20]. In this study, albumin concentration was generally low; about 44% of the participants had albumin level below the lowest reference value – 3.5 g/l (data not shown), which indicates that the antioxidant capacity of serum might be significantly decreased compared to normal subjects. Indeed, the values of TAC observed in several studies concerning healthy populations were higher [21, 22].

Table 3. Dietary habits of lung cancer patients divided into two groups based on TAC distribution

Group of food products	Consumption frequency [no of portions/d]	TAC ≤ 1.44 mmol/l (n = 32) [% of group]	TAC > 1.44 mmol/l (n = 27) [% of group]	p
Whole grain cereal products	0	46.9	44.4	0.72
	1-2	28.1	37.0	
	3-4	25.0	18.6	
Refined cereal products	0	12.5	11.1	0.04
	1-2	28.1	59.3	
	3-5	59.4	29.6	
Vegetables in total	0	0.0	3.7	0.35
	1-2	59.4	48.1	
	3-4	40.6	48.1	
Raw vegetables	0	3.1	14.8	0.24
	1-2	81.3	74.1	
	3-4	15.6	11.1	
Fruit in total	0	9.4	18.5	0.57
	1-2	50.0	48.1	
	3-4	40.6	33.3	
Raw fruit	0	9.4	18.5	0.58
	1-2	59.4	55.5	
	3-4	31.2	25.9	

Like albumin, UA is one of the most powerful antioxidants circulating in human blood. About 50% of human blood antioxidant capacity is attributable to UA activity [23]. On the other hand, a high UA level may exert a pro-oxidative effect [24]. Moreover, UA is postulated as a marker of oxidative stress and rises under oxidative conditions. It is, therefore, difficult to clearly determine its role in the antioxidant barrier of the body. The highest correlation for TAC was found with serum UA, which clearly demonstrates the important role of this parameter in TAC levels of lung cancer patients. According to this information, low levels of the main components of TAC (albumin, UA) in lung cancer are especially undesired because chemo- and/or radiotherapy may additionally reduce the concentrations of albumin, UA, and other antioxidants, and thus significantly escalate TAC depletion [25]. The strong correlation found between TAC and UA allows us to conclude that TAC of lung cancer patients may significantly decrease during chemotherapy due to, for example, renal loss of UA [25]. Moreover, the radio- and chemotherapy, especially with platin-based cytostatics, is expected to significantly enhance ROS formation from lipid peroxidation [26]. Therefore, UA, which takes part in cell protection against ROS, may be significantly disturbed under treatment conditions. With current knowledge it is, however, hard to evaluate whether low TAC before oncological treatment may improve or worsen therapy outcome. High TAC may prevent cytotoxicity induced by chemo- or radiotherapy in normal cells but it may also protect cancer cells from damage and, therefore, may decrease the efficacy of anticancer agents. Further studies are, therefore, needed to evaluate the relationship between TAC and oncological treatment efficacy.

Bilirubin possesses strong antioxidant properties and may decrease the risk of oxidant-related diseases [18, 19], including cancers [27]. A significant correlation between bilirubin level and TAC was observed in several studies [18, 28], in contrast to our findings. Some behavioural factors can negatively influence levels of bilirubin, e.g. smoking, while others, e.g. alcohol consumption, may increase its concentration [29]. During smoking, which is the main risk factor of lung cancer, the bilirubin is wasted. Moreover, smoking is responsible for alterations of other endogenous and exogenous components of TAC [13]. However, the influence of smoking on TAC is inexplicit [30]. The effects of cancer development and smoking may vary as affected by changes in concentrations of particular antioxidant components. Thus the changes of other antioxidant molecules might influence changes of TAC to a greater extent than bilirubin disturbances. However, we did not observe any influence of smoking on TAC and main antioxidant endogenous components, such as serum total bilirubin, albumin, and UA.

In addition, in order to better understand the conditions that disturb TAC in lung cancer patients, we determined the association between TAC and CRP, which was significantly negative. Similar correlations were also observed in other studies between inflammatory and antioxidant status in cancers [31] as well as in other diseases [32]. Systemic inflammation is a well-known factor affecting depletion of individual components of TAC. For example, in inflammatory disorders, ROS-mediated damage leads to fragmentation and a loss of some antioxidant molecules [31]. Additionally, inflammation causes hypoalbuminaemia due to attenuated albumin synthesis [33].

Statistically insignificant correlations between TAC and dietary habits of lung cancer patients are consistent with several other studies performed with normal subjects [34, 35]. We found only that the frequency of consumption of refined cereal products may be significantly associated with TAC value. Refined cereal products have a high glycaemic index, thus leading to high serum glucose concentration [36]. According to literature data [37], abnormal serum glucose concentration may influence ROS formation via generation of NADPH, which directly explains the correlation between high frequency of refined cereal product consumption and low TAC. Moreover, lung cancer patients often suffer from carbohydrate metabolism disorders, high insulin concentration, and elevated insulin resistance [38]. These metabolic disturbances additionally potentiate the rise of glucose concentration after the intake of refined cereal products. Several studies have been conducted to show the relationship between consumption of plant products and TAC in different populations. For example, Record *et al.* [34] evaluated the impact of consumption of high amounts of fruits and vegetables on TAC in healthy volunteers. The high-antioxidant diet did not influence TAC, although concentrations of some antioxidant components were increased. In turn, Young *et al.* [35] showed no influence of blackcurrant and apple juice drinking on TAC in healthy subjects. Controlled drinking of juices caused only an increase in urinary excretion of quercetin, plasma ascorbate, and glutathione peroxidase activity. The studies presented above suggest that an antioxidant-rich diet may influence the activity of particular antioxidant enzymes and other markers without affecting TAC. In turn, Pitsavos *et al.* [39] and Telegawkar *et al.* [40] demonstrated a positive impact of the Mediterranean diet and high vegetable and fruit consumption on TAC of participants. In contrast to the previous studies [34, 35], these studies [39, 40] used in-depth research models in which data were adjusted for smoking status [40] and participants with chronic and inflammatory diseases were excluded [39]. In our study, the subjects suffered from lung cancer – a serious, chronic, inflammatory disease, which is moreover often diagnosed in an advanced stage. The severity of the disease reflects TAS, as was observed in this study. A lack of association between dietary habits and TAC could be due to disturbances of endogenous components of TAC resulting from the underlying disease. Besides this, consumption frequency of antioxidant-rich products was low among the surveyed patients. Therefore, we additionally consider that the consumption of products rich in antioxidants might have been too low to permanently influence TAC in lung cancer patients.

Limitations

Several limitations need to be acknowledged. Firstly, it is a small study (only 59 cases) from a single centre. Statistical analysis in this case is very limited. We need a prospective, more advanced trial with clearly more rigorous reporting and data monitoring or more cases from other centres. Moreover, the influence of dietary factors on TAC in lung cancer patients was evaluated based on a food frequency questionnaire, which could not clearly define the impact of diet on this parameter, especially under lung cancer conditions, where changes in overall homeostasis might disturb metabolism and utility of nutritional components important in TAC. Therefore, further, more in-depth studies based on more detailed methods are needed to assess these associations.

In conclusion, the total antioxidant status of lung cancer patients is associated with disease stage and endogenous antioxidant factors rather than with the frequency of consumption of selected food products and smoking. The slight correlation between dietary habits and total antioxidant capacity in lung cancer patients presumably results from the disturbed homeostasis in which cancer, while developing, could determine the redox state to a greater extent than dietary habits. However, it is likely that the consumption of the antioxidant-rich food products with a higher frequency could lead to the improvement of TAC in lung cancer patients. However, further studies are needed to determine the factors that predominantly influence TAC in lung cancer patients.

The authors declare no conflict of interest.

References

1. Malvezzi M, Bertuccio P, Rosso T, Levi F, La Vecchia C, Negri E. European cancer mortality predictions for the year 2015: does lung cancer have the highest death rate in EU women? Ann Oncol 2015; 26: 779-86.
2. Lo YL, Hsiao CF, Chang GC, et al. Risk factors for primary lung cancer among never smokers by gender in a matched case-control study. Cancer Causes Control 2013; 24: 567-76.
3. Szeszenia-Dąbrowska N, Wilczyńska U. Occupational diseases in Poland – an overview of current trends. Int J Occup Med Environ Health 2013; 26: 457-70.
4. Zabłocka-Słowińska K, Porebska I, Gołecki M, et al. Dietary habits of lung cancer patients from the Lower Silesia region of Poland. Contemp Oncol (Pozn) 2015; 19: 391-5.
5. Gnagnarella P, Maisonneuve P, Bellomi M, Rampinelli C, Bertolotti R, Spaggiari L, Palli D, Veronesi G. Nutrient intake and nutrient patterns and risk of lung cancer among heavy smokers: results from the COSMOS screening study with annual low-dose CT. Eur J Epidemiol 2013; 28: 503-11.
6. Guz J, Dziaman T, Szpila A. Czy witaminy antyoksydacyjne mają wpływ na proces kancerogenezy? Postępy Hig Med Dośw 2007; 61: 185-98.
7. Lamont J, Campbell J, FitzGerald P. Measurement of individual vs total antioxidants. Clin Chem 1997; 43: 852-4.
8. Serafini M, Del Rio D. Understanding the associations between dietary antioxidants, redox status and disease: is the Total Antioxidant Capacity the right tool? Redox Rep 2004; 9: 145-52.
9. Battisti V, Maders LDK, Bagatini MD, et al. Oxidative stress and antioxidant status in prostate cancer patients: Relation to Gleason score, treatment and bone metastasis. Biomed Pharmacother 2011; 65: 516-24.
10. Erhola M, Niemlnen MM, Kellokumpu-Lehtinen P, Metsä-Keelä T, Poussa T, Alho H. Plasma peroxyl radical trapping capacity in lung cancer patients: a case-control study. Free Rad Res 1997; 26: 439-47.
11. Cao G, Russell RM, Lischner N, Prior RL. Serum antioxidant capacity is increased by consumption of strawberries, spinach, red wine or vitamin C in elderly women. J Nutr 1998; 128: 2383-90.
12. Whitehead TP, Robinson D, Allaway S, Syms J, Hale A. Effect of red wine ingestion on the antioxidant capacity of serum. Clin Chem 1995; 41: 32-5.
13. Tsuchiya M, Asada A, Kasahara E, Sato EF, Shindo M, Inoue M. Smoking a single cigarette rapidly reduces combined concentrations of nitrate and nitrite and concentrations of antioxidants in plasma. Circulation 2002; 105: 1155-7.
14. Ilow R, Królicka O, Regulska-Ilow B, Pluta J. Validation of food frequency questionnaire for dietary intake estimation among students from Wrocław. Bromat Chem Toksykol 2005; 3: 203-9.
15. Kampa M, Nistikaki A, Tsaousis V, Maliaraki N, Notas G, Castanas E. A new automated method for the determination of the Total Antioxidant Capacity (TAC) of human plasma, based on the crocin bleaching assay. BMC Clin Pathol 2002; 2: 3.
16. Nieto FJ, Iribarren C, Gross MD, Comstock GW, Cutler RG. Uric acid and serum antioxidant capacity: a reaction to atherosclerosis? Atherosclerosis 2002; 148: 131-9.
17. Ching S, Ingram D, Hahnel R, Beilby J, Rossi E. Serum levels of micronutrients, antioxidants and total antioxidant status predict risk of breast cancer in a case control study. J Nutr 2002; 132: 303-6.
18. Lin JP, O'Donnell CJ, Schwaiger JP, Cupples LA, Lingenhel A, Hunt SC, Yang S, Kronenberg F. Association between the UGT1A1* 28 allele, bilirubin levels, and coronary heart disease in the Framingham Heart Study. Circulation 2006; 114: 1476-81.
19. Cheriyath P, Gorrepati VS, Peters I, Nookala V, Murphy ME, Srouji N, Fischman D. High total bilirubin as a protective factor for diabetes mellitus: An analysis of NHANES data from 1999-2006. J Clin Med Res 2010; 2: 201-6.
20. Roche M, Rondeau P, Singh NR, Tarnus E, Bourdon E. The antioxidant properties of serum albumin. FEBS Lett 2008; 582: 1783-7.
21. Jozanov-Stankov O, Durić J, Dobutović B, Isenović ER. Determination of total antioxidant status (TAS) as a biochemical parameter in control of workers' health. Arch Biol Sci 2009; 61: 375-82.
22. Szulińska M, Piorunek T, Suliburska J, Pupek-Musialik D, Kupsz J, Drzymala-Czyż S, Bogdański P. Evaluation of insulin resistance, tumor necrosis factor alpha, and total antioxidant status in obese patients smoking cigarettes. Eur Rev Med Pharmacol Sci 2013; 17: 1916-22.
23. Horsfall LJ, Nazareth I, Petersen I. Serum uric acid and the risk of respiratory disease: a population-based cohort study. Thorax 2014; 69: 1021-6.
24. Kumar AN, Aruna P, Naidu JN, Kumar R, Srivastava AK. Review of concepts and controversies of uric acid as antioxidant and pro-oxidant – an uncertainty. Arch Med Rev J 2015; 24: 19-40.
25. Weijl NI, Wipkink-Bakker A, Lentjes EG, Berger HM, Cleton FJ, Osanto S. Cisplatin combination chemotherapy induces a fall in plasma antioxidants of cancer patients. Ann Oncol 1998; 9: 1331-7.
26. Barrera G. Oxidative stress and lipid peroxidation products in cancer progression and therapy. ISRN Oncology 2012; 2012: 137289.
27. Jirásková A, Novotný J, Novotný L, et al. Association of serum bilirubin and promoter variations in HMOX1 and UGT1A1 genes with sporadic colorectal cancer. Int J Cancer 2012; 131: 1549-55.
28. Erel O. A novel automated direct measurement method for total antioxidant capacity using a new generation, more stable ABTS radical cation. Clin Biochem 2004; 37: 277-85.
29. Lim JE, Kimm H, Jee SH. Combined effects of smoking and bilirubin levels on the risk of lung cancer in Korea: The Severance Cohort Study. PLoS One 2014; 9: e103972.
30. Kim M J, Kim OH, Kim JH. The effects of smoking, drinking and exercise on antioxidant vitamin intakes and plasma antioxidant status elderly people living in Ulsan. Korean J Community Nutr 2002; 7: 527-38.
31. Talwar D, Ha TK, Scott HR, Cooney J, Fell GS, O'Reilly DS, Lean ME, McMillan DC. Effect of inflammation on measures of antioxidant status in patients with non-small cell lung cancer. Am J Clin Nutr 1997; 66: 1283-5.
32. Dandana A, Gammoudi I, Ferchichi S, Chahed H, Limam HB, Addad F, Miled A. Correlation of oxidative stress parameters and inflam-

matory markers in Tunisian coronary artery disease patients. Int J Biomed Sci 2011; 7: 6-13.
33. Moshage HJ, Janssen JA, Franssen JH, Hafkenscheid JC, Yap SH. Study of the molecular mechanism of decreased liver synthesis of albumin in inflammation. J Clin Invest 1987; 79: 1635.
34. Record IR, Dreosti IE, McInerney JK. Changes in plasma antioxidant status following consumption of diets high or low in fruit and vegetables or following dietary supplementation with an antioxidant mixture. Brit J Nutr 2001; 85: 459-64.
35. Young JF, Nielsen SE, Haraldsdóttir J, et al. Effect of fruit juice intake on urinary quercetin excretion and biomarkers of antioxidative status. Am J Clin Nutr 1999; 69: 87-94.
36. Bell SJ. Glycemic index for the management of chronic disease: why certain foods like raisin may be beneficial. Open Nutr J 2011; 5: 7-12.
37. Stief T. Glucose initially inhibits and later stimulates blood ROS generation. J Diab Mel 2013; 3: 15-21.
38. Petridou ET, Sergentanis TN, Antonopoulos CN, Dessypris N, Matsoukis IL, Aronis K, Efremidios A, Syrigos C, Mantzoros CS. Insulin resistance: an independent risk factor for lung cancer? Metabolism 2011; 60: 1100-6.
39. Pitsavos C, Panagiotakos DB, Tzima N, Chrysohoou C, Economou M, Zampelas A, Stefanadis C. Adherence to the Mediterranean diet is associated with total antioxidant capacity in healthy adults: the ATTICA study. Am J Clin Nutr 2005; 82: 694-9.
40. Talegawkar SA, Beretta G, Yeum KJ, Johnson EJ, Carithers TC, Taylor HA Jr, Russell RM, Tucker KL. Total antioxidant performance is associated with diet and serum antioxidants in participants of the diet and physical activity substudy of the Jackson Heart Study. J Nutr 2009; 139: 1964-71.

Address for correspondence

Katarzyna Zabłocka-Słowińska PhD
Department of Food Science and Dietetics
Wroclaw Medical University
Borowska 211
50-556 Wrocław, Poland
tel. +48 71 784 02 14
e-mail: katarzynazablocka0112@gmail.com

Submitted: 12.01.2016
Accepted: 25.05.2016