The influence of surgical treatment and red blood cell transfusion on changes in antioxidative and immune system parameters in colorectal cancer patients

Birutė Surinėnaitė[1], Gražina Prasmickienė[1], Vida Milašienė[1], Eugenijus Stratilatovas[1], Janina Didžiapetrienė[1, 2]

[1]Institute of Oncology, [2]Faculty of Medicine, Vilnius University, Lithuania

Key words: *colorectal cancer; antioxidative system; immune system; surgery; red blood cell transfusion.*

Summary. *Objective. To determine the effect of surgical treatment and red blood cell transfusion on the parameters of antioxidative and immune systems in patients with early and advanced stage colorectal cancer.*

Material and methods. A total of 65 patients with colorectal cancer were included in the study. Three blood serum samples of each patient were tested comparing presurgical and postsurgical periods of 7 and 14 days. Malondialdehyde and total glutathione levels, activity of catalase and glutathione S-transferase were determined spectrophotometrically. The concentration of cytokines TGF-beta1 and TNF-alpha were determined by ELISA.

Results. Malondialdehyde and glutathione levels decreased in surgically treated patients with cancer of both stages while catalase activity decreased in patients with stage III cancer. Cytokine levels did not change after surgery. A decrease in malondialdehyde concentration was observed in the transfused patients with early stage cancer comparing postsurgical periods. Catalase activity was increased after surgery in patients with early stage cancer but was decreased during postsurgical periods in patients with advanced stage cancer. Cytokine levels increased at postsurgical periods in transfused patients with stage III cancer. Correlation between catalase activity and TNF-alpha level and between glutathione S-transferase activity and TGF-beta1 level was determined postsurgically in transfused patients with early stage cancer.

Conclusions. Postsurgical period affected antioxidative system of patients with cancer of both stages while level of cytokines showed no differences. Transfusion determined distinct dynamics of antioxidative parameters due to cancer stage. Elevated cytokine levels in transfused patients with advanced stage cancer showed that the status of immune system was exacerbated. Antioxidative and immune systems were depressed in these patients. Correlation between antioxidative system parameters and cytokines in transfused patients of early stage cancer showed a relationship between two protective systems of the organism against malignant process.

Introduction

Colorectal cancer is one of the most frequent malignancies worldwide and it causes high mortality (1). During the last several years, it is also among the 10 most common cancers for men and women in Lithuania. The problem exists because cancer is often diagnosed at advanced stages and patients undergo surgical treatment of large extent (2).

Oxidative stress as prolonged and abnormal excess of reactive oxygen species (ROS) is one of the main risk factors for cancer. Results of direct measurements of ROS in cells and determination of antioxidative system parameters in cells and in body fluids of cancer patients are still diverse indicating that many factors affect the dynamics of ROS. Oxidative stress is also stimulated by tumor progression and cancer treatment (3, 4).

Surgical intervention induces additional stress also affecting the dynamics of antioxidative system parameters (5). Surgical treatment can deepen already existing injury in the immune system of cancer patients (6) because surgical trauma was shown to determine transient postoperative suppression of the system (7). Surgical treatment of cancer is complicated and usually associated with red blood cell (RBC) transfusion to restore normal physiological functions of the orga-

Correspondence to B. Surinėnaitė, Institute of Oncology, Vilnius University, Baublio 3B, 08406 Vilnius, Lithuania
E-mail: birute.surinenaite@vuoi.lt

nism. Transfusion also alters the state of surgically treated organism, and the increased risk of subsequent transfusion for cancer patients has been shown. Consequently, the procedure should affect status of antioxidative and immune systems (8).

Two protective systems of the organism are closely related in a few aspects. Endogenous antioxidants were found to diminish blood serum levels of TNF-alpha (cachectin) and IL-6 (9). Reduced glutathione level is known to be a crucial factor in the development of the immune response (10). Regulation of this parameter is related to inflammation and to cell sensitivity to TNF-alpha-induced apoptosis as this major proinflammatory cytokine may reduce glutathione level by several mechanisms. Oxidative stress can increase TNF-alpha release (11). Examination of status of both systems in cancer patients is of greatest importance.

Changes in lipid peroxidation indices, endogenous antioxidant levels and activities of antioxidative enzymes in cancer patients during postsurgical period serve as prognostic factors of possible forthcoming complications after the treatment (12). Malondialdehyde (MDA) remains the most sensitive parameter of lipid peroxidation (13). Total glutathione (reduced and oxidized forms) is an important parameter as antioxidant defense is regulated by redox pair of GSH/GSSG (14). Catalase (CAT) activity indicates primary antioxidative action while glutathione S-transferase (GST) activity shows detoxication function of glutathione (15).

Cytokine TNF-alpha plays several immunological functions, and it is involved in maintaining homeostasis of the immune system. TGF-beta is a multipotent cytokine and a potent suppressor of immune cells (16). It could be assumed that patients with early stage (II) colorectal cancer possess better reactivity of immunological system.

Considering the known relations among parameters of antioxidative and immune systems, it is important to examine the link of those parameters in patients with cancer of different localizations to provide a better view on status of two protective systems of the organism. Correlation of the parameters can be a factor helping to predict complications in a course of the cancer treatment. However, there is a lack of experimental studies showing reliable data on the relationship between these systems in patients with colorectal cancer.

The aim of the present study was to determine the effect of surgical treatment and RBC transfusion on selected parameters of antioxidative and immune systems in patients with early (II) and advanced (III) stage colorectal cancer.

Materials and methods
Materials
A total of 65 patients diagnosed with primary colorectal cancer in the Department of Abdominal Surgery (Institute of Oncology, Vilnius University, Lithuania) and treated by surgery also following the criteria of age (45–70 years) and Hb before the treatment (exceeding 100 g/L) were included into the study. All patients underwent surgical treatment, and their ECOG (the Eastern Cooperative Oncology Group) performance status was 0–2. Patients were grouped as follows: nontransfused patients with stage II colorectal cancer (n=15; mean age, 57.0±3.0; 9 men and 6 women); nontransfused patients with stage III cancer (n=22; mean age, 59.0±3.7; 13 men and 9 women); RBC transfused patients with stage II cancer (n=9; mean age, 55.0±4.0; 5 men and 4 women); RBC transfused patients with stage III cancer (n=19; mean age, 59.0±3.7; 11 men and 8 women). In all four groups, patients were surgically treated by hemicolectomy, abdominoperineal resection, and rectum resection. The study was approved by the Lithuanian Bioethics Committee, and written informed consent was obtained from all patients. Patients were grouped by cancer stage and requirement for RBC transfusion during the surgery. The patients were considered as transfused if they received 1 or 2 packets of allogenic RBC intrasurgically (RBC loss >500 mL) and received 1 or 2 packets of allogenic RBC during 1–5 days after the treatment. Allogenic RBC transfusions were administered after the surgery if Hb level decreased below 100 g/L. RBC packets were prepared from blood by removing most of the plasma, and red blood cells were suspended in saline-adenine-glucose-mannitol (SAGM) in the National Blood Center of Lithuania. The packets were prepared according to the recommendations of the Council of Europe; leukocyte concentration was $<1.2\times10^9$/L.

Three samples of blood serum of each patient were tested before the treatment and at 7 and 14 days postoperatively. All parameters were determined in blood serum samples and were compared as follows: presurgical versus postsurgical period of 7 days, presurgical versus postsurgical period of 14 days, and postsurgical period of 7 days versus the period of 14 days.

Methods
The status of antioxidative system was evaluated by determination of lipid peroxidation product MDA, antioxidant total glutathione (further indicated as GSH) and enzymes CAT and GST. MDA level was determined by thiobarbituric acid (TBA) assay as

described previously (17). CAT activity was measured as formation of a $H_2O_2/(NH_4)_2MoO_4$ complex (18). GSH amount was detected using recycling system by 5,5'-dithiobis-(2-nitrobenzoic acid, DTNB) and glutathione reductase following the method of (19). GST activity was measured as the rate of formation of GSH/1-chloro-2, 4-dinitrobenzene (CDNB) conjugate as described in (20). All parameters were tested spectrophotometrically. Changes of MDA (nmol/ml), CAT (nmol/L/min), GSH (μmol/mL) and GST (nmol/mL/min) were evaluated comparing values in presurgical and postsurgical periods. Levels of cytokines TNF-alpha and TGF-beta1 were measured according to the supplier instructions indicating the sensitivity of those assays to be 15.6 pg/mL for TGF-beta1 and 3.0 pg/mL for TNF-alpha. Optical density was measured with an ELISA reader (Multiskan EX, Labsystem Oy) at 450 nm.

Statistical analysis was performed by test for paired samples (one-sided test, *P* values for comparative analysis) and *t* test for independent samples (two-sided, *P* values for correlation analysis). Pearson correlation (2-tailed) was employed. The statistical program SPSS 14.0 was used. Differences were considered significant when *P*<0.05.

Results

Surgical treatment and RBC transfusion induce additional stress to cancer patients suffering from the progression of the disease. As a result, certain parameters of antioxidative and immune systems should be affected by both processes. Four indices of antioxidative system were examined in the present study in surgically treated patients with colorectal cancer; in addition, RBC transfusion was considered. Results of the analysis of the parameters in surgically treated patients with stage II (n=15) and stage III (n=22) colorectal cancer are presented in Table 1.

MDA level was significantly decreased in patients with stage II cancer comparing presurgical and both postsurgical periods (*P*=0.003 on day 7 and *P*=0.002 on day 14) and also comparing two postsurgical periods (*P*=0.027); in patients with stage III cancer, it was lower only at postsurgical period of 14 days (*P*=0.003). There were no significant differences in CAT activity in patients with stage II cancer, but CAT activity was decreased in patients with stage III cancer comparing presurgical period and postsurgical period of 14 days (*P*=0.012). GSH level was significantly decreased in patients with both cancer stages comparing presurgical period with both postsurgical periods (*P*=0.007 and *P*=0.024 for stage II and *P*=0.000 and *P*=0.027 for stage III, respectively). No significant changes in GST activity were determined in any case.

Analysis of immune system parameters for patients with colorectal cancer showed that levels of cytokines TGF-beta1 and TNF-alpha did not change significantly either after surgical treatment or at postsurgical periods of 7 and 14 days as compared with presurgical period.

Correlation between parameters of both systems providing defense of the organism against malignancy is a crucial factor to be examined in the course of surgical treatment. No correlation between any indices of antioxidative and immune systems was found in surgically treated patients with early stage colorectal cancer, but the Pearson correlation at the 0.05 level was determined between MDA and GSH amounts at postsurgical period of 7 days. No correlation of any parameters analyzed was found in patients with advanced stage cancer.

A surgically treated patient may show different responses to the treatment after RBC transfusion that rather often follows the operation of colorectal cancer patients. Consequently, this procedure should play a certain role in alterations of antioxidative and immune

***Table 1.* Changes in the levels of lipid peroxidation marker and antioxidative system parameters in surgically treated patients with colorectal cancer**

Pairs	Paired differences	
	Stage II (n=15)	Stage III (n=9)
MDA1 – MDA2 (nmol/mL)	↓ 3.90*	NS
MDA1 – MDA3	↓ 6.12*	↓ 4.96*
MDA2 – MDA3	↓ 3.58*	NS
CAT1 – CAT3 (nmol/L/min)	NS	↓ 7.00*
GSH1 – GSH2 (μmol/mL)	↓ 0.10*	↓ 0.04*
GSH1 – GSH3	↓ 0.08*	↓ 0.05*

1, 2, and 3 indicated each parameter at presurgical period, postsurgical period of 7 days and postsurgical period of 14 days, respectively. *P<0.05 – significant; NS – not significant; ↓ – reduced.

Table 2. **Changes in the levels of lipid peroxidation marker and antioxidative system parameters in surgically treated and RBC transfused patients with colorectal cancer**

Pairs	Paired differences	
	Stage II (n=22)	Stage III (n=19)
MDA2 – MDA3 (nmol/mL)	↓ 4.97*	NS
CAT1 – CAT2 (nmol/L/min)	↑ 6.60*	NS
CAT2 – CAT3	NS	↓ 6.86*

1, 2, and 3 indicated each parameter at presurgical period, postsurgical period of 7 days and postsurgical period of 14 days, respectively. *$P<0.05$ – significant; NS – not significant; ↓ – reduced; ↑ – increased.

system parameters. The analysis was also performed for RBC transfused patients with stage II (n=9) and stage III (n=19) colorectal cancer. Results of changes in antioxidative system parameters are presented in Table 2.

In contrast to nontransfused patients with colorectal cancer, MDA level was decreased in transfused patients with early stage cancer only during postsurgical period ($P=0.008$). CAT activity was increased in transfused patients with stage II cancer on day 7 after the surgery as compared with presurgical period, but it was decreased in transfused patients with stage III cancer comparing both postsurgical periods. No significant changes in GSH level and GST activity were determined in transfused patients.

Comparison of patients' groups who received RBC transfusion or not showed that subsequently transfused patients with stage II cancer had a relatively lower initial MDA concentration and higher GST activity, and analogous patients with stage III cancer had a reduced GSH level.

Analysis of changes in immune system parameters showed that levels of both cytokines TGF-beta1 and TNF-alpha did not change significantly in RBC transfused patients with stage II colorectal cancer after surgical treatment. In transfused patients with stage III cancer, TGF-beta1 concentration was significantly increased at postsurgical period of 14 days and TNF-alpha level was increased at postsurgical periods of 7 and 14 days as compared with presurgical period (Table 3).

Examination of both surgically treated and RBC transfused patients with cancer could allow determination of greater operative stress and correlations between indices. In our study, the Pearson correlation at the 0.05 level was determined between CAT2 activity and TNF2 concentration and between GST2 activity and TGF2 concentration in RBC transfused patients with stage II colorectal cancer. Despite these parameters did not change significantly at postsurgical period of 7 days, the correlation between their changes

Table 3. **Changes in cytokine TGF-beta1 and TNF-alpha levels in surgically treated and RBC transfused patients with colorectal cancer**

Pairs	Paired differences
	Stage III (n=19)
TGF1 – TGF2 (ng/mL)	NS
TGF1 – TGF3	↑ 3470.4*
TGF2 – TGF3	NS
TNF1 – TNF2 (pg/mL)	↑ 11.4*
TNF1 – TNF3	↑ 7.4*
TNF2 – TNF3	NS

1, 2, and 3 indicated each parameter at presurgical period, postsurgical period of 7 days and postsurgical period of 14 days, respectively.
*$P<0.05$ – significant; NS – not significant;
↑ – increased.

was seen during that period. No correlation among any indices in patients with advanced stage cancer was found.

Discussion

Parameters reflecting antioxidative system status can indicate complications of surgical treatment in cancer patients and should serve as biomarkers of the organism, next to molecular biomarkers, indicating prognosis of the disease. A decrease in MDA level, comparing postsurgical periods of 7 and 14 days in RBC transfused patients with stage II cancer, shows the weaker oxidative stress, which is reflected by reduced lipid peroxidation. Postsurgical period of 7 days possibly was insufficient for significant changes in this parameter. In addition, RBC transfusion in combination with surgery of patients with advanced stage colorectal cancer can mean poor prognosis of the treatment as lipid peroxidation was not decreased as indicated by not significant changes in MDA level.

Cancer stage most probably was one of the factors that caused reduced MDA level comparing both postsurgical periods in both RBC transfused and non-

transfused patients with colorectal cancer. On the other hand, RBC transfusion depressed antioxidative system as MDA level did not change significantly comparing two postsurgical periods with presurgical period in transfused patients with stage II and III cancer while it was lower even 7 days after surgical treatment in nontransfused patients with early stage cancer and 14 days after the treatment in patients with advanced stage cancer. Increased MDA level in patients with primary colorectal cancer was shown by other authors (21). It is necessary to investigate the relationship between changes in MDA level and clinical biomarkers in order to provide reliable prognosis of surgical treatment.

We found that changes in CAT activity depended on cancer stage and also varied in two groups of patients considering requirement for RBC transfusion. Conflicting results were found in comparison of transfused and nontransfused patients. Transfusion probably contributed to higher enzymatic activity in patients with stage II cancer after 7 days following surgery and resulted in nonsignificant change of the parameter for patients with stage III cancer 14 days after the treatment.

It was shown that GSH level was decreased in both groups of nontransfused patients with stage II and III cancer. This decrease most probably could be a consequence of operative stress rather than the reduced function of antioxidative system because it is known that GSH is a crucial modulator of immune system and detoxication agent as well (10). On the other hand, in case of oral squamous cell carcinoma, it was shown that GSH level was decreased in red blood cells of cancer patients but in contrast it was increased in the cells of tumor tissue (9). It can be assumed that our results are not favorable indicating a possible increase in GSH level in tumor cells, but simultaneous analysis of the parameter in blood and tumor cells is necessary to support or deny the suggestion.

RBC transfusion most probably caused the fact that no significant changes in GSH level and GST activity were detected in transfused patients. GST activity reflects detoxication function of GSH. Most probably, the alteration of GST activity should be related to changes of GSH as the enzyme substrate. On the other hand, detoxication process should accelerated in cancer. Consequently, investigations combining enzymatic and molecular levels are necessary to evaluate the function of GST as it has been already shown that genetic polymorphism of GST is associated with cancer risk and GST activity increases depending on tumor stage (22).

The results of the present study indicated that changes in the levels of multipotent cytokines TGF-

beta1 and TNF-alpha might be determined by RBC transfusion because the levels of both cytokines were significantly increased in transfused cancer patients after surgical treatment and did not change significantly in nontransfused patients. TGF-beta is a potent suppressor of immune cells and also plays an important role in late-stage carcinogenesis by stimulating the invasive process of cancer cells, promoting neoangiogenesis, and helping cancer cells to escape surveillance by the immune system (16). TNF-alpha is responsible for several immunologic functions. It is suggested that this cytokine causes cachexia and anemia and is involved in the maintenance of homeostasis of the immune system. TNF-alpha level is often increased in cancer patients and it may promote tumor growth and invasion (23). We showed that TGF-beta1 and TNF-alpha levels were significantly increased after RBC transfusion only in patients with stage III colorectal cancer. Our data support results of other authors (14) that allogenic RBC transfusion might exert immunomodulatory effects. Moreover, improved reactivity of the immune system probably was more favorable for patients with early stage colorectal cancer; therefore, RBC transfusion caused no significant changes in the levels of cytokines. Consequently, cytokines TGF-beta1 and TNF-alpha could be important in cancer prognosis, and increased levels of these cytokines after allogenic RBC transfusion determined in the present study could show a negative influence on disease treatment and poor prognosis.

The role of RBC transfusion in surgically treated cancer patients can be discussed in the aspect of changes in parameters analyzed considering differences within groups of transfused and nontransfused patients. It was shown that antioxidative system was probably depressed in RBC transfused patients with stage III cancer. This effect is related to the increased level of both parameters of the immune system in transfused patients with advanced stage cancer, and this may show a poor prognosis and additional stress caused by RBC transfusion. Relatively lower initial MDA level and higher GST activity in subsequently transfused patients with stage II cancer and lower GSH level in analogous patients with stage III cancer indicate that changes in these parameters could predict the risk of requirement of subsequent RBC transfusion. More data on relationship between antioxidative and immune system parameters considering RBC transfusion in patients with colorectal cancer are needed because transfusion was shown to influence outcome of surgical cancer treatment, which might be both unfavorable (24) and favorable (25). On the

other hand, more patients with early stage colorectal cancer should be included in the analysis in order to provide reasonable conclusions considering the influence of RBC transfusion on changes in the parameters of both systems.

The relation of parameters of both protective systems of the organism against malignant process is crucial to be examined for cancer patients. Antioxidant treatment has been shown to reduce the level of TNF-alpha in cancer patients. In our study, the correlation between MDA2 and GSH2 levels was found in nontransfused patients with early stage colorectal cancer 7 days after surgical treatment. It shows the link between lipid peroxidation and the pool of essential antioxidant, and it may indicate that tumor cells most probably utilize GSH to scavenge lipid peroxides in such way decreasing their amount in blood serum (9).

Correlation between CAT activity and TNF-alpha level at the same postsurgical period of 7 days determined for transfused patients with stage II colorectal cancer may indicate that these parameters of antioxidative and immune systems could be presumed as markers of postoperative period without complications considering antioxidative defense and level of the cytokine involved in tumorigenesis. Another significant correlation between GST activity (detoxication) and TGF-beta1 level (regulation of the cell cycle including trigger of apoptosis) at early postsurgical period could also be considered to help prediction of the treatment. No correlation between indices in patients with advanced stage colorectal cancer most probably indicates that in tumor progression, other factors affect dynamics of both system parameters.

Conclusions

Postsurgical period has an influence on changes in the antioxidative system parameters, which were analyzed in patients with colorectal cancer of both stages, while levels of cytokines TGF-beta1 and TNF-alpha showed no differences in cancer patients after surgery. Red blood cell transfusion during the treatment determined distinct dynamics of antioxidative system parameters in patients with cancer of both stages but more patients with early stage cancer should be included in the analysis for reasonable conclusions considering the effect of the transfusion. Elevated levels of TGF-beta1 and TNF-alpha in transfused patients with advanced stage cancer show that status of the immune system is exacerbated when cancer is more advanced, and surgical stress is combined with additional invasion to the organism. Correlation between catalase activity and TNF-alpha level as well as between glutathione S-transferase activity and TGF-beta1 level 7 days after surgery in transfused patients with early stage cancer showed the relation of two protective systems of the organism against malignant process. Red blood cell transfusion worsened parameters of both systems in patients with advanced stage colorectal cancer showing that additional invasion enhances operative stress resulting in depressed antioxidative and immune defense against the progressing tumor.

Chirurginio gydymo ir eritrocitų masės transfuzijos įtaka sergančiųjų storosios žarnos vėžiu antioksidacinės ir imuninės sistemų rodiklių pokyčiams

Birutė Surinėnaitė[1], Gražina Prasmickienė[1], Vida Milašienė[1], Eugenijus Stratilatovas[1], Janina Didžiapetrienė[1, 2]

Vilniaus universiteto [1]Onkologijos institutas, [2]Medicinos fakultetas

Raktažodžiai: storosios žarnos vėžys, antioksidacinė sistema, imuninė sistema, operacija, eritrocitų masės transfuzija.

Santrauka. *Tikslas.* Nustatyti sergančiųjų II ir III stadijų storosios žarnos vėžiu antioksidacinės bei imuninės sistemų pokyčius po chirurginio gydymo ir eritrocitų masės transfuzijos.

Medžiaga ir metodai. Į tyrimą įtraukti 65 pacientai. Antioksidacinės ir imuninės sistemos rodikliai ištirti sergančiųjų kraujo serume prieš operaciją ir praėjus 7 bei 14 dienų po operacijos. Malono dialdehido ir bendrojo glutationo kiekiai, katalazės ir glutationo S-transferazės aktyvumai nustatyti specifiniais metodais spektrofotometriškai. Citokinų TGF-beta1 ir TNF-alfa kiekiai nustatyti ELISA metodu.

Rezultatai. Pooperaciniu laikotarpiu sumažėjo malono dialdehido ir glutationo kiekiai pacientams, sergantiems II ir III stadijų storosios žarnos vėžiu, o katalazės aktyvumas – tik sergantiesiems III stadijos vėžiu. Citokinų kiekis po operacijos nepakito. Po eritrocitų masės perpylimo malono dialdehido kiekis pooperaciniu laikotarpiu žymiai sumažėjo II stadijos vėžiu sergantiems pacientams, o katalazės aktyvumas –

sergantiesiems III stadijos vėžiu. Po eritrocitų masės perpylimo III stadijos vėžiu sergantiems pacientams žymiai padidėjo TGF-beta1 ir TNF-alfa kiekiai. II stadijos vėžiu sergantiems pacientams, kuriems gydymo metu buvo perpilta eritrocitų masė, praėjus septynioms dienoms po operacijos, nustatyta koreliacija tarp kata-lazės aktyvumo ir TNF-alfa kiekio, taip pat tarp glutationo S-transferazės aktyvumo ir TGF-beta kiekio.

Išvados. Pooperaciniu laikotarpiu nustatyta abiejų stadijų storosios žarnos vėžiu sergančiųjų antioksidacinės sistemos pokyčių, o citokinų kiekiai nepakito. Eritrocitų masės perpylimas lėmė skirtingus antioksidacinės sistemos rodiklių pokyčius, lyginant II ir III vėžio stadijas. Citokinų kiekiai padidėjo vėlyvosios ligos stadijos pacientams po perpylimo ir šiuo atveju antioksidacinė ir imuninė organizmo sistemos buvo nuslopintos. Koreliacija tarp antioksidacinės sistemos rodiklių ir citokinų ankstyvosios vėžio stadijos pacientams po eritrocitų masės perpylimo rodo reikšmingą dviejų apsauginių organizmo sistemų sąsają kovojant su piktybiniu procesu.

Adresas susirašinėti: B. Surinėnaitė, VU Onkologijos institutas, Baublio 3B, 08406 Vilnius
El. paštas: birute.surinenaite@vuoi.lt

References

1. Polite BN, Dignam JJ, Olopade OI. Colorectal cancer model of health disparities: understanding mortality differences in minority populations. J Clin Oncol 2006;24:2179-87.
2. Cancer Register, Institute of Oncology Vilnius University. Major results of aid in oncology in Lithuania. Vilnius; 2006. p. 1-44.
3. Černe D, Lukač-Bajalo J. Oxidative stress assays for disease risk stratification. Acta Pharm 2006;56:1-17.
4. Valko M, Rhodes CJ, Moncol J, Izakovic M, Mazur M. Free radicals, metals and antioxidants in oxidative stress-induced cancer. Chem Biol Interact 2006;160:1-40.
5. Corsi MM, Pagani D, Iorio EL, Dogliotti G, Verna R, Sambataro G, et al. RBC reactive oxygen metabolites (ROMs) and total antioxidant status (TAS) in patients with laryngeal squamous cell carcinoma after surgical treatment. Clin Chem Lab Med 2006;44:1047-8.
6. Wang YX, Su WL, Zhu WX. Correlation of the changes of lymphocyte phenotype to tumor stage and operative pattern of gastric cancer. Ai Zheng 2004;23:1065-8.
7. Korenaga D, Takesue F, Kido K, Yasuda M, Inutsuka A, Honda M, et al. Impaired antioxidant defense system of colonic tissue and cancer development in dextran sulfate sodium-induced colitis in mice. J Surg Res 2002;2:144-9.
8. Edgren G, Hjalgrim H, Reilly M, Tran TN, Rostgaard K, Shanwell A, et al. Risk of cancer after RBC transfusion from donors with subclinical cancer: a retrospective cohort study. Lancet 2007;369:1724-30.
9. Fiaschi AI, Cozzolino A, Ruggiero G, Giorgi G. Glutathione, ascorbic acid and antioxidant enzymes in the tumor tissue and RBC of patients with oral squamous cell carcinoma. Eur Rev Med Pharmacol Sci 2005;9:361-7.
10. Bounous G, Molson JH. The antioxidant system. Anticancer Res 2003;23:1411-5.
11. Rahman I, Antonicelli F, Macnee W. Molecular mechanism of the regulation of glutathione synthesis by tumor necrosis factor-alpha and dexamethasone in human alveolar epithelial cells. J Biol Chem 1999;274:5088-96.
12. Misthos P, Katsaragakis S, Milingos N, Kakaris S, Sepsas E, Athanassiadi K, et al. Postresectional pulmonary oxidative stress in lung cancer patients. The role of one-lung ventilation. Eur J Cardiothorac Surg 2005;27:379-83.
13. Bakan E, Taysi S, Polat MF, Dalga S, Umudum Z, Bakan N, et al. Nitric oxide levels and lipid peroxidation in plasma of patients with gastric cancer. Jpn J Clin Oncol 2002;32:162-6.
14. Miller LT, Watson WH, Kirlin WG, Ziegler TR, Jones DP. Oxidation of the glutathione/glutathione disulfide redox state is induced by cysteine deficiency in human colon carcinoma HT29 cells. J Nutr 2002;132:2303-6.
15. Saygili EI, Akcay T, Konukoglu D, Papila C. Glutathione and glutathione-related enzymes in colorectal cancer patients. J Toxicol Environ Health A 2003;66:411-5.
16. Nikiteas NI, Tzanakis N, Gazouli M, Rallis G, Daniilidis K, Theodoropoulos G. Serum IL-6, TNFα and CRP levels in Greek colorectal cancer patients: prognostic implications. World J Gastroenterol 2005;11:1639-43.
17. Surinėnaitė B, Kazbarienė B, Prasmickienė G, Krikštaponienė A, Didžiapetrienė J, Jankevičius F, et al. Surgical stress induced alterations of antioxidative and immune system parameters. Biologija 2006;2:76-9.
18. Goth L. A simple method for determination of serum catalase activity, and revision of reference range. Clin Chim Acta 1991;196:143-52.
19. Baker MA, Cerniglia GJ, Zaman Z. Microtiter plate assay for the measurement of glutathione and glutathione disulfide in large numbers of biological samples. Anal Biochem 1990; 190:360-5.
20. Galli F, Rovidati S, Benedetti S, Buoncristiani U, Covarelli C, Floridi A, et al. Overexpression of erythrocyte glutathione S-transferase in uremia and dialysis. Clin Chem 1999;45: 1781-8.
21. Skrzydlewska E, Sulkowski S, Koda M, Zalewski B, Kan-czuga-Koda L, Sulkowska. Lipid peroxidation and antioxidant status in colorectal cancer. World J Gastroenterol 2005;11: 403-6.
22. Peklak-Scot C, Townsend AJ, Morrow CS. Dynamics of glutathione conjugation and conjugate efflux in detoxification of the carcinogen, 4-nitroquinoline 1-oxide: contributions of glutathione, glutathione S-transferase, and MRP1. Biochemistry 2005;44:4426-33.
23. Balkwill F. Tumor necrosis factor or tumor promoting factor? Cytokine Growth Factor Rev 2002;13:135-41.
24. Spirtos NM, Westby CM, Averette HE, Soper JT. Blood transfusion and the risk of recurrence in squamous cell carcinoma of the cervix: a gynecologic oncology group study. Am J Clin Oncol 2002;25:398-403.
25. Fergusson D, Khanna MP, Tinmouthn A, Hébert PC. Transfusion of leukoreduced red RBC cells may decrease postoperative infections: two meta-analyses of randomized controlled trials. Can J Anaesth 2004;51:417-25.