Original Article

Increased ischemia-modified albumin and malondialdehyde levels in videothoracoscopic surgery

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Abstract:

BACKGROUND: Videothoracoscopic surgery leads to general organ hypoperfusion by reducing mean arterial pressure, systemic vascular resistance, and end-diastolic volume index. Oxidative stress occurs as a result of hypoperfusion. Evaluation of the short-term effects of videothoracoscopic sympathectomy on serum ischemia-modified albumin (IMA), malondialdehyde (MDA), and nitric oxide (NO) levels in patients with primary hyperhidrosis was aimed.

METHODS: Twenty-six patients who underwent videothoracoscopic surgery were contributed in this study. Venous blood samples were obtained from these patients 1 h before and after the surgery. IMA, MDA, and NO levels were measured in serum samples by colorimetric methods. Albumin concentrations were also measured for each sample, and albumin-adjusted IMA levels were calculated.

RESULTS: Postoperative IMA, albumin-adjusted IMA, and MDA values were significantly higher compared to the preoperative values ($P = 0.003$, 0.027, 0.018, respectively). However, postoperative NO levels were lower than the preoperative values ($P = 0.002$). There was no significant difference between pre- and postoperative albumin concentrations, and there was no significant correlation between the parameters tested.

CONCLUSIONS: We can conclude that elevation in MDA and IMA levels after videothoracoscopic surgery was caused by increased oxidative stress due to minimal ischemia-reperfusion injury after the infusion of CO_2 during the surgical process. Videothoracoscopic sympathectomy operation causes a decrease in NO production, and this should be taken in consideration when evaluating nitrosative stress in videothoracoscopic surgery.

Key words:

Ischemia modified albumin, malondialdehyde, nitric oxide, videothoracoscopic surgery

Thoracoscopy was introduced to diagnose primarily pleural and pulmonary diseases by Jacobeus in 1910. The role of thoracoscopy in intrathoracic pathologies has gained importance gradually since that time. The advantages such as minimally invasive approach, less pain, shorter hospitalization, reduction of postoperative morbidity, and better cosmetic results make videothoracoscopic surgery superior to open surgery.[1,2] It has become the primary surgical procedure opted for sympathectomy in primary hyperhidrosis cases through its superiorities.[2,3]

Sweat glands on palms are innervated by sympathetic cholinergic fibers in sympathetic chain. T2 sympathetic ganglion carries out most of the sympathetic innervation of the upper extremities. Therefore, T2 and T3 sympathetic ganglia are excised or cauterized in the treatment of hyperhidrosis. Decrease in heart rate and vascular resistance is observed after sympathectomy since sympathetic cardiac nerves extend from the upper thoracic chain.[4] Moreover, a decrease is observed in end-diastolic pressure and arterial pressure, as well.[5] CO_2 infusion is applied into intrapleural cavity and lungs are collapsed during this operation. Changes are observed in lung function tests, and these changes prolong until postsurgical 2 weeks period.[6]

It is supposed that oxidative stress occurs due to the formation of reactive oxygen species during videothoracoscopic surgery. Reactive oxygen species affect macromolecules in cells

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such as lipids, proteins, DNA, and carbohydrates and cause decomposition in their molecular structure.[7]

In the early 1990s, ischemia-modified albumin (IMA) was introduced as a novel specific indicator of myocardial ischemia.[8] In N-terminal region albumin binds transition elements (cobalt, nickel, copper etc.,).[9] Metal binding capacity of an N-terminal region decreases in pathologic conditions such as oxidative stress and infection. Hypoxia, acidosis, disturbances in sodium-calcium pumps, and tissue damage cause increased production of IMA due to the production of free radicals.[10]

Because lipids contain multiple double bonds, they are frequently exposed to the effect of oxidants. Malondialdehyde (MDA) is one of the end products of lipid peroxidation.[11] MDA is a highly reactive oxidation end product, and it reacts with many biological molecules such DNA and protein.[12]

Nitric oxide (NO) is one of the free radicals which have a role in the modulation of oxidative stress. NO is a cell protector under normal conditions, however, in the case of oxidative stress, high amount of NO synthesis present harmful effects on cells. During oxidative stress, with the degradation of NO, cell-damaging toxic reactive nitrogen products are released.[13] NO is quickly inactivated by oxidation of NO to nitrate. Furthermore, NO can be oxidized to nitrite. However, nitrite is converted into nitrate in a short time by oxidation.[14] Nitrite and nitrate anions are the end product of NO oxidation, and they reflect endogenous NO synthase activity.[15]

There is no data evaluating the effect of videothoracoscopic surgery on oxidative stress parameters in the previous reports. Hence, in our study, we aimed to reveal the short-term effect of videothoracoscopic surgery on serum IMA, MDA and NO levels in patients with primary hyperhidrosis.

Methods

Subjects

Twenty-six patients (15 male and 11 female) with primary hyperhidrosis and hospitalized for videothoracoscopic sympathectomy between January and December 2014 in Clinics of Thoracic Surgery in Hospital of Selcuk University Faculty of Medicine were contributed in this study. The protocol of the study was approved by the Ethics Committee of our institute. Informed consents were obtained from the patients who accepted to participate in this study. None of the patients included in the study have diabetes, hypertension, malignant disease, chronic renal failure, liver failure, and chronic inflammatory diseases and under medication for any chronic disease.

Videothoracoscopic sympathectomy was performed under general anesthesia by using a single lumen endotracheal tube. Patients lie down in the semi-prone position, same side arm in abduction and anti-trendelenburg position. Ports were opened from third intercostal space on the preaxial line. Intrapleural CO_2 insufflation was started, and lung was collapsed. An intrapleural pressure was applied as 10 mmHg at the beginning and then decreased to 5 mmHg to prevent tension pneumothorax.

Biochemical analysis

Prior to surgery and within the 1st h after surgery, venous blood samples of these patients were taken and was centrifuged at 1500 g for 10 min. After centrifugation, serum portions were separated and stored at −20° until the day of analysis.

Serum MDA levels were determined by the method of Draper and Hadley[16] based on the reaction of MDA with thiobarbituric acid (TBA). In this reaction, MDA and TBA react and form a colored pigment, and the results are obtained by analyzing the color of pigment spectrophotometrically at 532 nm, and the results are reported as µM MDA. Serum NO levels were measured with colorimetric method using nitrate/nitrite assay (Cayman Chemical Company, USA), and the results were reported as µM. IMA levels were determined with the colorimetric method described by Bar–Or *et al*.[17] Results were reported in absorbance units. Serum albumin concentrations were measured with bromcresol green method using Cobas Intgra 400 analyzer (Roche, Germany). Results were expressed as mg/dl. Adjusted IMA levels were calculated with the formula defined by Lippi *et al*. This formula is as follows: ([Individual serum albumin concentration/median albumin concentration of the group] × individual IMA value).[18]

Statistical analysis

Statistical analysis of all data was performed with SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). Shapiro–Wilk test was used for the distribution analysis of the numeric data. In addition to descriptive analysis (mean, standard deviation [SD]), paired t-test was used to compare means between preoperative and postoperative values. Wilcoxon test was used for comparison of medians from nonparametric data. Spearman and Pearson correlation analysis were performed for testing the relations between the tested parameters. Multivariate analysis of variance was also performed to test the effect of independent variables on dependent variables. The results were expressed as mean ± (mean ± SD) and $P < 0.05$ was considered as statistically significant.

Results

Demographic characteristics and routine laboratory tests are presented in Table 1. Postoperative IMA and albumin-adjusted

Table 1: Demographic characteristics and preoperative routine laboratory tests of patients undergoing videothoracoscopic surgery

Parameter	Mean±SD
Age (year)	30.5±14.3
Albumin (g/dL)	3.57±0.13
AST (U/L)	18.81±5.70
ALT (U/L)	18.57±11.19
Glucose (mg/dl)	95.75±14.14
Creatinine (mg/dL)	0.72±0.11
BUN (mg/dL)	25.68±9.20
WBC (K/uL)	7.60±2.67
CRP (mg/L)	10.40±20.19

Data are presented as means±SD. AST = Aspartate transaminase, ALT = Alanine transaminase, BUN = Blood urea nitrogen, WBC = White blood cell count, CRP = C-reactive protein, SD = Standard deviation

IMA levels were significantly higher compared to the preoperative values ($P = 0.003, 0.027$, respectively). Postoperative MDA levels were significantly higher than preoperative levels ($P = 0.018$). However, postoperative NO levels were lower than the preoperative values ($P = 0.002$). Pre- and postoperative albumin concentrations were similar ($P > 0.05$). Pre- and postoperative IMA, albumin-adjusted IMA, MDA, and NO levels were presented in Table 2 and Figure 1.

There was no significant correlation between the parameters tested ($P > 0.05$) and none of the parameters had significant effect on pre- and postoperative IMA levels due to the results of multivariate analysis of variance ($P > 0.05$).

Discussion

In our study, which aimed to reveal the short-term effect of videothoracoscopic surgery on the oxidative and nitrosative stress parameters in patients with primary hyperhidrosis, we observed that postoperative IMA, adjusted IMA, and MDA levels were significantly higher, and NO levels were lower than the preoperative values.

When we have searched medical databases, we did not meet any report evaluating the effect of videothoracoscopic surgery on oxidative stress. However, there are some reports available that demonstrated the effects of laparoscopic surgery which was performed by insufflation of CO_2 into peritoneum instead of pleura using similar pressures with videothoracoscopic surgery. In some of these studies, the researchers compared the effects of open surgery and laparoscopic surgery on oxidative stress. Zulfikaroglu *et al*.[19] evaluated plasma MDA and NO levels of 50 patients with either laparoscopic or open cholecystectomy and measured these parameters for three times preoperatively, 24 h after surgery, and during the operation. They reported that MDA levels decreased 30 min after the beginning of the laparoscopic surgery. NO levels in laparoscopic surgery were lower than the values of open surgery, but this difference was not statistically significant. Ozmen *et al*.[20] demonstrated that there was a minimal increase in NO and MDA levels of the patients undergoing laparoscopic cholecystectomy when compared to the patients operated with open surgery and this increase was not statistically significant. After open cholecystectomy, they did not observe any significant change in NO and MDA levels. Bukan *et al*.[21] stated that NO and MDA levels were increased in both open and laparoscopic cholecystectomy but the rate of the increase in open cholecystectomy was higher than the laparoscopic cholecystectomy. In another study by Aran *et al*.,[22] they have evaluated MDA and IMA levels of 33 patients with laparoscopic ovarian cystectomy. They measured MDA and IMA levels of these patients three times: Preoperatively, 10 min after

Table 2: Preoperative and postoperative concentrations of IMA, ADJ-IMA, MDA, and NO in patients undergoing videothoracoscopic surgery

Parameters	Mean±SD		*P*
	Preoperative	Postoperative	
IMA (absorbance units)	0.73±0.05	0.91±0.04	0.003
ADJ-IMA (absorbance units)	0.75±0.06	0.89±0.04	0.027
MDA (μM)	2.59±0.59	2.92±0.79	0.018
NO (μM)	6.85±2.98	4.78±2.10	0.002

IMA = Ischemia modified albumin, ADJ-IMA = Albumin adjusted-ischemia modified albumin, MDA = Malondialdehyde, NO = Nitric oxide, SD = Standard deviation

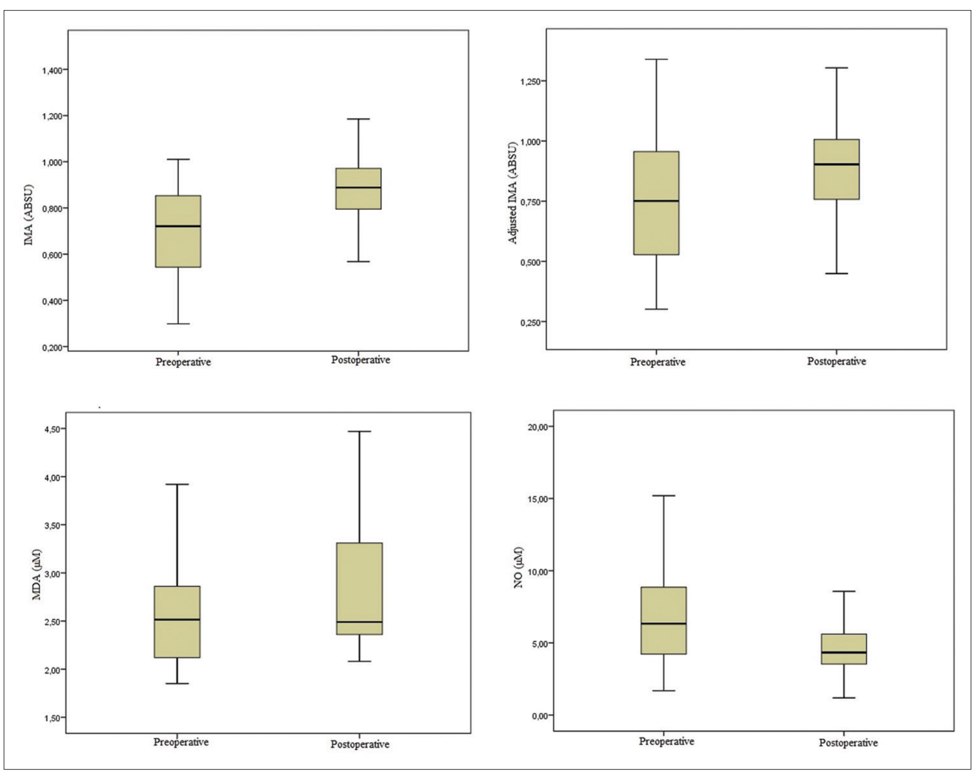

Figure 1: Preoperative versus postoperative values of ischemia modified albumin, albumin adjusted ischemia modified albumin, malondialdehyde, and nitric oxide in videothoracoscopic surgery

induction of anesthesia, 30 min after CO_2 insufflation. It was observed that IMA levels significantly increased, and MDA levels did not change 30 min after CO_2 insufflation.

In laparoscopic surgery, similar with the videothoracoscopic surgery, CO_2 insufflation is performed at a pressure of 10–15 mmHg during the process. Contrary to abdominal laparoscopic surgery in which CO_2 insufflation is applied into the peritoneal cavity, in videothoracoscopic surgery, into the pleural cavity. The only difference between these two methods is processing time; approximately, 1 h for laparoscopic abdominal surgery, while videothoracoscopic surgery can take up to 30–45 min. In these pressure levels, ischemia forms in the gaps, with the termination of insufflation process, reperfusion occurs. In ischemia-reperfusion models, oxidative stress occurs in ischemia-reperfusion period, but free oxygen radicals and their effects are more obvious during reperfusion.[23]

In our study, we observed that there was a significant increase in IMA and MDA levels which are the indicators of ischemia and oxidative stress in the postoperative 1st day of videothoracoscopic surgery. Our findings are different from the results of laparoscopic surgery. However, in the study of Bukan *et al*.,[21] they observed significant increase in MDA levels in perioperative period (ischemia period), however in the postoperative period (perfusion period), MDA levels decreased back to the preoperative levels. In the study of Aran *et al*.,[22] they reported that IMA levels increased 30 min after insufflation, but they did not observe a significant difference in MDA levels. However, a period of 30 min may not be sufficient for a significant increase in MDA levels. In addition, this period can be evaluated as perioperative period, so the effects of reperfusion were not evaluated. The study of Bukan *et al.* is the only one which is similar to our study. However, the results of the research which were conducted by Cevrioglu *et al*.[23] on 32 rats supported our findings. In this study, it was intended to compare the impact of ischemic preconditioning and low-pressure pneumoperitoneum on reducing ischemia-reperfusion injury, and for this purpose rats were divided into four groups. For first and second groups pneumoperitoneum was established for 60 min at 15 mmHg and 10 mmHg, respectively. In the third group, after ischemic preconditioning at 15 mmHg for 10 min, pneumoperitoneum was established for 60 min at 15 mmHg. The fourth group was the control group formed from anesthetized rats. MDA levels of all groups were evaluated in the perioperative period, and the highest levels were observed in the first group; and the concentrations decreased gradually in third, second, and fourth groups.

In our study, we observed that after videothoracoscopic surgery there is a significant decrease in NO levels compared to the preoperative values. Instead of evaluating these findings as a decrease of nitrosative stress due to increasing of oxidative stress during surgical operation we considered that this is the effect of sympathectomy which is performed by videothoracoscopic surgery. When we have reviewed the literature about the effects of sympathectomy on vascular endothelial function, we observed that the results are conflicting. Kars *et al*.[24] demonstrated the effect of cervical and periarterial sympathectomy on endothelium-dependent vasodilatation by examining common carotid artery *in vitro* medium in rabbits. They argued that endothelium-dependent dilatation is inhibited selectively and strongly and this may be caused by decrease in NO synthesis or desensitization of muscle cells to NO. In another study, to demonstrate the effects of sympathectomy to endothelium-independent dilatation by dissecting common carotid artery of the rabbits cervical and periarterial sympathectomy were performed. Endothelium-dependent dilatation which is provided by substance P is inhibited so they argued that this situation may be a result of decreased NO secretion.[25] These findings claim the decrease in NO secretion after sympathectomy and support our findings.

According to our study, it can be concluded that elevated levels of MDA and IMA after videothoracoscopic surgery, is caused by minimal ischemia-reperfusion injury due to CO_2 inflation during surgical operation and increased oxidative stress during this process. We suggest that decreased NO levels after videothoracoscopic sympathectomy is the consequence of sympathectomy. Further experimental and clinical investigations are needed to clarify the underlying mechanisms of the relation between oxidative stress and this type of operation. We can also conclude that reducing the time of ischemia-reperfusion or supplementation of antioxidants may be helpful in decreasing oxidative stress during this type of surgery.

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Conflicts of interest

There are no conflicts of interest.

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