Myocardial protection during elective coronary artery bypasses grafting by pretreatment with omega-3 polyunsaturated fatty acids

Zaštita srca tokom operacije revaskularizacije srčanog mišića primenom omega-3 nezasićenih masnih kiselina

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Abstract

Background/Aim. Despite recent advances in coronary artery bypass grafting (CABG), cardioplegic cardiac arrest and cardiopulmonary bypass (CPB) are still associated with myocardial injury. Accordingly, the efforts have been made lately to improve the outcome of CPB by glucose-insulin-potassium, adenosine, Ca2+-channel antagonists, L-arginine, N-acetylcysteine, coenzyme Q10, diazoxide, Na+/H+ exchange inhibitors, but with an unequal results. Since omega-3 polyunsaturated fatty acids (PUFAs) have shown remarkable cardioprotection in preclinical researches, the aim of our study was to check their effects in prevention of ischemia reperfusion injury in patients with CPB. Methods. This prospective, randomized, placebo-controlled study was performed with parallel groups. The patients undergoing elective CABG were randomized to receive preoperative intravenous omega-3 PUFAs infusion (n = 20) or the same volume of 0.9% saline solution infusion (n = 20). Blood samples were collected simultaneously from the radial artery and the coronary sinus before starting CPB and at 10, 20 and 30 min after the release of the aortic cross clamp. Lactate extraction/excretion and myocardial oxygen extraction were calculated and compared between the two groups. The levels of troponin I (TnI) and creatine kinase–myocardial band (CK-MB) were determined between the two groups. The levels of TnI, 4 and 24 h after CPB, was significantly higher in the control group compared to PUFAs group, with statistically significant differences (11.4 vs 5.9, p < 0.008, respectively). The level of lactate extraction 30 minutes after reperfusion was not statistically different between the two groups (6.9% vs 4.2%, p < 0.54). Oxygen extraction in the PUFAs group was statistically significantly higher compared to the control group after 10, 20 and 30 min of reperfusion (35.5% vs 50.4%, p < 0.0004; 25.8% vs 48.7%, p < 0.0001 and 25.8% vs 45.6%, p < 0.0002, respectively). The level of TnI, 4 and 24 h after CPB, was significantly higher in the control group compared to PUFAs group, with statistically significant differences (11.4 vs 6.6, p < 0.009 and 12.7 vs 5.9, p < 0.008, respectively). The level of CK-MB, 4 h after CPB, was significantly higher in the control group compared to PUFAs group (61.9 vs 37.7, p < 0.008), but its level, 24 h after CPB, was not statistically different between the two groups (58.9 vs 40.6, p < 0.051). Conclusion. Treatment with omega-3 PUFAs administered preoperatively promoted early metabolic recovery of the heart after elective CABG and improved myocardial protection. This study showed that omega-3 emulsion should not be considered only as a nutritional supplement but also as a clinically safe and potent cardioprotective adjunct during CPB.

Key words: fatty acids, omega-3, myocardial reperfusion; coronary artery bypass; surgical procedures, elective.

Apstrakt

Uvod/Cilj. Uprkos tehnološkom napretku srčani zastojav zazvan kardioplegijskom i vantelesni krvotok (cardiopulmonary bypass – CPB) tokom operacije revaskularizacije srčanog mišića i dalje dovode do oštećenja srčanog mišića. Napor da se poboljša

ishod posle CPB primenom glukoze-insulin-kalijuma, adenosina, blokatora Ca2+-kanala, L-arginina, N-acetylcistesteina, koenzima Q10, diazoksida, inhibitora razmene Na+/H+ nije dao željene rezultate. Omega-3 nezasićene masne kiseline (polyunsaturated fatty acids – PUFAs), u prekličnim ispitivanjima, pokazale su značajno kardioprotektivno dejstvo. Cilj

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ovog rada bio je ispitivanje efekata primene PUFAs u prevenciji ischemično-hipertrofnih oštećenja srčanog mišića nakon revaskularizacije sa primenom CPB. Metode. Ova prospektivna, randomizovana, placebo-kontrolisana studija sprovedena je na paralelnim grupama. Bolesnici sa elektivnim operacijama revaskularizacije srčanog mišića slučajnim izborom podjeljeni su u dve grupe. Prva grupa (n = 20) preoperativno je dobijala infuziju PUFAs (PUFAs grupa), dok je kontrolna grupa (n = 20) dobijala istu količinu 0,9% rastvora NaCl. Uzorci krvi su istovremeno uziman iz radijalne arterije i koronarnog sinususa pre početaka CPB i 10, 20 i 30 minuto posle skidanja kleme sa aorte. Ekstrakcija laktata i kiseonika iz srčanog mišića izvedena je promenom poznatih formula. Nivo troponina I (TnI) i miokardne frakcije kreatin-kinaze (CK-MB) određivana je pre početka CPB i 4 i 24 h posle operacije. Rezultati. Demografiske i operativne karakteristike, uključujući trajanje CPB i klenovanja aorte, bili su slični u oba grupe. Nivo ekskrecije laktata 10 i 20 min nakon deklemenovanja aorte imao je negativne vrednosti u kontrolnoj grupi, dok su vrednosti u PUFAs grupi bile pozitivne, sa statistički značajnom razlikom (-19.6% prema 7.9%, p < 0.001 i -19.9% prema 8.2%, p < 0.008, respektivno). Nivo ekstrakcije laktata 30 min nakon skidanja kleme sa aorte bio je bez statistički značajne razlike između dve grupe (6.9% prema 4.2%, p < 0.54). Ekstrakcija kiseonika 10, 20 i 30 min posle skidanja kleme sa aorte bila je veća u PUFAs grupi sa statistički značajnom razlikom u odnosu na kontrolnu grupu (35.5% prema 50.4%, p < 0.0004; 25.8% prema 48.7%, p < 0.0001 i 25.8% prema 45.6%, p < 0.0002, respektivno). Nivo TnI, 4 i 24 h posle nakon CPB, bio je statistički značajno viši u kontrolnoj grupi nego u PUFAs grupi (11.4 prema 6.6 ng/mL, p < 0.009 i 12.7 prema 5.9 ng/mL, p < 0.008). Nivo CK-MB, 4 h nakon CPB, bio je statistički značajno viši u kontrolnoj grupi nego u PUFAs grupi (61.9, prema 37.7 U/L, p < 0.008), dok je nivo CK-MB 24 h nakon CPB bio bez statistički značajne razlike između dve grupe bolesnika (58.9 prema 40.6 U/L, p < 0.051). Zaključak. Preoperativna primena omega-3 PUFAs pomaže u ranom metabolizam oporavku srca nakon revaskularizacije tako što štiti srčani mišić. Ovo istraživanje je pokazalo da omega-3 PUFAs nisu samo nutricioni dodatak već i klinički bezbedan i snažan kardioprotektor tokom CPB.

Ključne reči: masne kiseline, omega-3; miokard, reperfuzija; aortokoronarno premošćavanje; hirurgija, elektivna, procedure.

Introduction

Myocardial protection by using hypothermia and cardioplegia methods during ischemia and reperfusion remains one of the cornerstones of postoperative myocardial function. Coronary artery bypass grafting (CABG) performed with the aid of cardioplegia and cardiopulmonary bypass (CPB) requires a period of cardiac arrest. During this time, myocardial ischemia and necrosis may occur, which is an important determinant of surgical procedures, complete myocardial protection is provided with parallel groups. Study enrollment occurred with August 2010 and September 2011. The study protocol was approved by the Ethical Committee of the Military Medical Academy, Belgrade, and all the patients gave written informed consent.

Fifty patients scheduled to undergo their first on-pump CABG surgery were included in the study. To do so, the patients needed to be older than 18 years of age, in normal sinus rhythm, and in stable hemodynamic conditions before surgery. The patients were excluded in cases of emergency CABG, redo CABG, combined CAGB and any other cardiac procedure, Q-wave myocardial infarction in the last six weeks, un-

stable angina, or poor left ventricular function. All the patients were treated by the same surgical and anesthesiologist team.

Eligible patients were assigned to one of the two study arms according to a computer-generated randomization list: control (placebo) group (usual care), and usual care plus PUFAs.

The PUFAs infusion consisted of 100 mL of a lipid emulsion with a high content of omega-3 PUFAs (Omegaven® 10%, Fresenius Kabi, Bad Homburg, Germany). The same batch of Omegaven® was used throughout the study, and 100 mL of the lipid emulsion contained 1.25–2.82g EPA and 1.44–3.09 DHA. Infusion was given one day before surgery and repeated 4 h before starting CPB via the peripheral vein at single doses of 100 mL (25 mL/h). The patients of the control group received an equal volume of 0.9% saline.

Preoperative sedation with 5 mg of intramuscular midazolam was administered to the patients on call to the operating room. All the patients received prophylactic preoperative antibiotics (cefazolin, 2 g preincision and 2 g post-CPB; or if allergic to penicillin, vancomycin, 1 g preincision and 500 mg post-CPB). The same anesthesiologist administered standardized total intravenous anesthesia using sufentanil, midazolam, propofol and pancuronium.

Immediately before CPB, 300 IU/kg heparin was administered intravenously, followed by additional doses as necessary to maintain an activating clotting time exceeding 500 sec. Protamine was administered as 1 mg/100 IU of the heparin dose after complete separation from CPB.

All the patients had CABG with the use of CPB, which was conducted with a roller pump and a membrane oxygenator primed with a solution. During CPB, pump flow was set at 2.4 times the body surface area, and mean arterial pressure maintained between 50 and 60 mmHg. Temperature was set at 2.4 times the body surface area, and mean arterial pressure maintained between 50 and 60 mmHg. Temperature was allowed to drift with active rewarming at the end of CPB. Myocardial protection was afforded with cold potassium cardioplegia. A single-clamp technique was used, and cardioplegia was given in an anterograde fashion. In all the patients, the left internal mammary artery harvested and anastomosed to the left anterior descending artery. The rest of the grafts were constructed using the great saphenous vein.

After total release of the aortic cross-clamp, epicardial atrial or ventricular pacing wires were placed. Aortic and venous cannulas were removed after the appropriate test dose of protamine, and the surgery proceeded with closure of the pericardium and sternum.

After the surgery, the patients were followed up in the intensive care unit and were weaned off mechanical ventila-

### Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control group</th>
<th>PUFAs group</th>
<th>( \bar{x} \pm SD )</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), ( \bar{x} \pm SD )</td>
<td>62.4 ± 7</td>
<td>65.3 ± 8</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>Gender, male/female (n)</td>
<td>18/2</td>
<td>17/3</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Weight (kg), ( \bar{x} \pm SD )</td>
<td>89.8 ± 6</td>
<td>92.1 ± 5</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>Height (cm), ( \bar{x} \pm SD )</td>
<td>176.4 ± 4</td>
<td>178.5 ± 3</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>LVEF (%), ( \bar{x} \pm SD )</td>
<td>54 ± 6</td>
<td>53 ± 9</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>CPB (min), ( \bar{x} \pm SD )</td>
<td>101.4 ± 21</td>
<td>95.5 ± 17</td>
<td>0.29</td>
<td></td>
</tr>
<tr>
<td>Aortic cross-clamp time (min), ( \bar{x} \pm SD )</td>
<td>42.5 ± 9</td>
<td>38.9 ± 8</td>
<td>0.66</td>
<td></td>
</tr>
<tr>
<td>CABG (number), ( \bar{x} \pm SD )</td>
<td>2.9 ± 0.8</td>
<td>2.8 ± 0.7</td>
<td>0.65</td>
<td></td>
</tr>
</tbody>
</table>

PUFAs – polyunsaturated fatty acids; LVEF – left ventricular ejection fraction; CPB – cardiopulmonary bypass; CABG – coronary artery bypass grafting; \( \bar{x} \) – mean; SD – standard deviation.
operative characteristics (CPB, time of the aortic cross-clamp and CABG number).

*The influence of PUFAs on lactate and oxygen extraction in the patients with CPB*

Table 2 shows that the results of both studied parameters – lactate and oxygen extraction – were opposite in the two groups of patients. Namely, lactate uptake before ischemia in the patients the PUFAs treated patients was highly statistically significant at all the three observed times after CPB in relation to the control group (with p ranging from 0.0001 to 0.0004).

**Table 2**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Extraction (%)</th>
<th>Control group (n = 20)</th>
<th>PUFAs group (n = 20)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate before CPB</td>
<td>36.7 ± 18.3</td>
<td>23.9 ± 14</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Lactate 10 min after CPB</td>
<td>-19.6 ± 22.8</td>
<td>7.9 ± 20.5</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>Lactate 20 min after CPB</td>
<td>-19.9 ± 22.8</td>
<td>8.2 ± 27.1</td>
<td>0.0008</td>
<td></td>
</tr>
<tr>
<td>Lactate 30 min after CPB</td>
<td>6.9 ± 11.8</td>
<td>4.2 ± 21.9</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>Oxygen before CPB</td>
<td>22.9 ± 16.5</td>
<td>29.5 ± 18.6</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Oxygen 10 min after CPB</td>
<td>35.5 ± 8.5</td>
<td>50.4 ± 5.2</td>
<td>0.0004</td>
<td></td>
</tr>
<tr>
<td>Oxygen 20 min after CPB</td>
<td>25.8 ± 9.7</td>
<td>48.7 ± 8.2</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>Oxygen 30 min after CPB</td>
<td>25.8 ± 9.3</td>
<td>45.6 ± 8.7</td>
<td>0.0002</td>
<td></td>
</tr>
</tbody>
</table>

CPB – cardiopulmonary bypass; \( \mu \) – mean; SD – standard deviation.

in the control group was statistically significantly higher compared with the PUFAs group (36.7% vs 23.9%; \( p < 0.01 \)). The level of lactate extraction 10 and 20 min after aortic declamping had negative value in the control group compared with positive value in the PUFAs group with statistically significant differences (-19.6% vs 7.9%; \( p < 0.0001 \) and -19.9% vs 8.2%; \( p < 0.0008 \), respectively). A negative value 10 and 20 min after aortic declamping indicated lactate excretion in the control group compared with the positive value in the PUFAs group which indicated lactate uptake. The level of lactate extraction 30 min after aortic declamping was not statistically different between the groups (6.9% vs 4.2%; \( p = 0.54 \)) (Table 2). In contrast to this, the level of oxygen extraction increased in both groups of patients. Their peak values ranged from 22.9 ± 16.5% in the control group before CPB to 35.5 ± 8.5% 10 min after aortic declamping and from 29.5 ± 18.6% in the PUFAs group before CPB to 50.4 ± 5.2% 10 min after aortic declamping. The extraction of oxygen in values before CPB marked as 100% and the percentage of their respective values at all the three observed time intervals after aortic declamping are presented in Figure 2, and show the time-course of their relative values.

It is self-evident from the results presented in this way that in the case of lactate extraction 10 min and 20 min after aortic declamping they diverge (plate A), and in those of oxygen extraction 10 min after aortic declamping converge, equalizing at 30 min after aortic declamping in the case of lactate, but not in the case of oxygen extraction (plate B).

*The influence of PUFAs on the serum level of TnT and CK-MB*

Figure 2 shows that the levels of TnT (plate A) and CK-MB (plate B) in both groups of patients were markedly higher at 4 h (\( p < 0.009 \) and \( p < 0.007 \)). The level of troponin I, 24 h after CPB, was significantly higher in the control

group as compared with the PUFAs group with statistically significant differences (12.7 versus 5.9 ng/mL \( p < 0.008 \)) (Figure 2A). The level of CK-MB, 24 h after CPB was not statistically different between the groups (58.9 vs 40.6 U/L \( p < 0.051 \)) (Figure 2B).

Concerning the relationship between the two groups, the serum level of TnT (plate A) was statistically significantly lower in the PUFAs treated patients in relation to the control group at both observed times, being 72% (11.4 ng/mL: 6.67 ng/mL, \( p < 0.009 \)) and 115% (12.7 ng/mL: 5.9 ng/mL, \( p < 0.008 \)) lower at 4 hrs and 24 hrs after CPB, respectively. At the same time, the serum level of CK-MB (plate B) was also lower in the PUFAs treated patients at both observed time intervals of 4 h and 24 h after CPB, being 65% (61.9 U/L: 37.7 U/L, \( p < 0.007 \)) and 45% (58.9 U/L : 40.6 U/L \( p < 0.051 \)), respectively, in relation to the control group of patients.

**Coefficient of correlation (r) values**

Reliability of described trends of the single values of all four parameters in both groups of patients were additionally confirmed by the coefficient of correlation. Its calculation was based on the values of parameters at all the observed time intervals (i.e. 10 to 30 min after aortic declamping in the case of lactate and oxygen extraction or 4 and 24 h after CPB in the case of TnT and CK-MB level) in relation to their initial (basal) values found before CPB.

In this respect, Figure 3 shows that the drop of lactate extraction (plate A) was uniform in both studied groups, but it was less pronounced in the the PUFAs group of patients.

Regarding oxygen (plate B), its level of extraction in the control group did not change from the baseline values in relation to the observed time intervals from 10 to 30 min after aortic declamping. In contrast to this, its level in the PUFAs group of patients steadily increased during that time.

Figure 4 shows the increment tendencies of TnT (plate A) and CK-MB values (plate B) in both groups of patients. However, they were less pronounced in both cases in the PUFAs group of patients.

**Peri- and postoperative complications**

Postoperative complications were similar in both groups of patients. In the control group, one patient died of cardiac failure on the second postoperative day, two patients...
had perioperative infarction, three patients needed inotropic support. In the PUFAs group, one patient underwent reexploration for bleeding, one had a respiratory failure and two patients needed inotropic support. Due to the low number of the observed complications, no statistical comparison was performed.

Discussion

The results of our prospective, randomized placebo-controlled study in the two groups of adult patients subjected to CPB showed that the extraction of oxygen and the uptake of lactate were markedly increased in the PUFAs pretreated patients compared to the control group, with the subsequent decrease of serum TnT and CK-MB levels in the PUFAs group, pointing thus to their important cardioprotective effect.

Due to the two separate groups of results dealing with oxygen extraction and lactate uptake from one, to the serum levels of TnT and CK-MB to the other side, discussion is divided in two parts: the influence of PUFAs on oxygen extraction and lactate uptake, and their influence on TnT and CK-MB serum levels.

The influence of PUFAs on oxygen extraction and lactate uptake

Evaluation of myocardial metabolism during cardiac surgery allows the investigator to quantify the degree of physiologic impairment. Direct cannulation of the coronary sinus for coronary sinus blood sampling to measure metabolites or specific biochemical markers of myocardial damage has been shown to be a valid tool to define the degree of such impairment. One of the most sensitive markers of inadequate preservation of the myocardium is the development of myocardial tissue acidosis and lactate production.

We demonstrated in this study that omega-3 PUFAs intravenous pretreatment prepared the heart metabolically for ischemia and led to an earlier shift to aerobic metabolism during reperfusion, as indicated by earlier lactate uptake. In this respect, the level of lactate extraction 10 and 20 min after aortic declamping had negative values in the control group compared to the positive values in the PUFAs group indicating lactate uptake. The extraction of oxygen in the PUFAs treated patients was highly statistically significant at all three observed times after CPB in relation to the control group, increasing thus metabolic activity enabled by an increased supply of extracted lactate. Early lactate uptake in the PUFAs group is an index of more rapid recovery of aerobic metabolism, pointing to the improved cardioprotection in our patients. Otherwise, a persistent lactate release during reperfusion in the control group suggests a delayed recovery of aerobic metabolism and may be related to intraoperative inadequate myocardial protection. In contrast to this, a significant evidence shows that preserving or enhancing aerobic metabolism, or both, is a key in maintaining cardiac function after ischemia.

The influence of PUFAs on TnT and CK-MB serum levels

Intraoperative release of TnT and CK-MB has functional significance because it is closely related to ischemia time and reflects a delayed recovery of left ventricular function and oxidative metabolism. Therefore, their measurement can be used as an indicator of myocardial injury sustained during CABG.

This study demonstrated that the intravenous administration of omega-3 PUFAs before CPB statistically significantly decreased the level of TnT in the PUFAs treated patients in relation to the control group at both observed times, being 58.5% and 46.4% lower at 4 h and 24 h after CPB, respectively. (Figure 2 A and B). At the same time, the serum level of CK-MB was also reduced in the PUFAs treated patients at both observed time intervals of 4 h and 24 h after CPB amounting 60.9% and 68.9 %, respectively, in relation to the control group of patients.

The study demonstrated for the first time that acute intravenous administration of omega-3 emulsion, which is normally used as a part of parenteral nutrition regimens, was associated with a significant reduction in myocardial ischemic-reperfusion injury. At least a part of this effect could be ascribed to the findings that the ischemic preconditioning actually increases the content of the omega-3 fatty acid DHA in the myocardial membrane in advance of a further injury, reduces myocardial oxygen demand, and attenuates acidosis and lactate accumulation in the ischemic heart.
At molecular level, a special attention in PUFAs cardioprotective effect should be devoted to their high ROS scavenger potential. Namely, the susceptibility of fatty acids to oxidation is thought to be directly dependent on their degree of saturation. Fatty acid micelles scavenge superoxide in an unsaturation dependent manner, up to EPA, which is the most effective fatty acid. From a mechanistic viewpoint, NAD(P)H oxidase is one of the major contributors to endothelial free radical production: its inhibition by DHA and (presumably) other PUFAs, might greatly explain the observed effects on ROS production. DHA-mediated inhibition of IL-1-induced ROS production would also contribute to the anti-inflammatory actions of omega-3 fatty acids at the endothelial level. One additional mechanism of PUFAs action would be that they act as a “sink” to trap free radicals, hence becoming oxidized themselves.

Myocardial reperfusion injury is a complex process with inadequately understood mechanisms and multiple initiating factors. Therefore, instead targeting some specific disturbances, many different pharmacological compounds have been tested not on a genuine, but rather on a screening basis.

All together, the results of such treatments may be divided in two groups: with no or modest outcome and positive findings which deserve further study.

The first group concerns adenosine, Ca\(^{2+}\)-channel antagonists, corticosteroids, NAC, diazoxide, L-arginine, cariporide, isoflurane, sevoflurane and nicorandil. So for example, adenosine reduced the levels of TnT, IL-6 and IL-8 release, but was without an effect on the CK-MB level. Corticosteroids had no beneficial effect on mortality and cardiac and pulmonary complications; NAC appears to be promising, but increases post-surgical cardiac complications, while the levels of TnT and CK-MB were higher in isoflurane compared to sevoflurane group of patients. Glucose-insulin-potassium improved hemodynamic parameters, but no significant effect on plasma TnT levels was demonstrated, and may cause severe disturbances in glucose homeostasis, which in case of hyperglycemia may enhance oxidative stress and exacerbate myocardial infarction during reperfusion.

In the second studied group, encouraging results were reported with the use of pexelizumab, which in the CPB patients decreased the level of CK-MB and protected against myocardial injury, and coenzyme Q10, which increased protection of mitochondria and myofilaments against oxidative stress, with a consequent maintenance of energy production and improved contractile recovery of pectinate trabeculae isolated from patients receiving coenzyme Q10 after reoxygenation stress in vitro.

According to these results and taking into account the favorable cardioprotective effects of PUFAs in CPB in our patients, it seems appropriate to consider their combination with coenzyme Q10. Coenzyme Q10 is a physiological constituent, declining in synthesis with age. It is an antioxidant and cofactor for mitochondrial ATP generation, basic source of energy in all cells, including myocardial ones. At least, such a combination could fulfill two fundamental requirements for myocardial membrane and cell function after cardioplegia and reperfusion oxygenation in CPB patients: protection by dramatic increase in the omega-3 content of myocardial membrane phospholipids, scavenging ROS, and accompanied by direct effects on ion channels modulating the protein kinase C activity by PUFAs, and by improving mitochondrial efficiency with coenzyme Q10.

Although we found significantly different results between the PUFAs group and the control group of patients in terms of myocardial injury in the favor of the first, there are still a few limitations of this study: our investigation was performed in a small size sample and with a limited number of clinical events; because of our research fund shortage, we did not use pulmonary artery catheter for monitoring hemodynamics; therefore, we were limited in recording changes between the two groups in myocardial function, and sampling method from coronary sinus does not represent global changes in heart metabolism.

### Conclusion

PUFAs therapy administered before CPB promotes early metabolic recovery of the heart during elective CABG and leads to better myocardial protection. This study shows that an omega-3 PUFAs emulsion should not be considered only as a nutritional supplement but also as a potentially clinically safe cardioprotective agent. This strategy warrants further investigation with optimization and shortening of pretreatment regimens to be more clinically applicable. It would be of interest to perform a larger randomized study with a design similar to the present study.

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### Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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