

clear. The levels of both TNF-alpha and IL-6 at the baseline are higher than the levels previously reported, which could be partially explained by the fact that the study is performed in a subgroup of high-risk patients with remarkable left ventricular dysfunction; however, the mean levels of the baseline TNF-alpha are approximately 10-fold higher than the baseline values of previous reports (2, 3). Also, the levels of both TNF-alpha and IL-6 show a decrease, though insignificant, following cardiopulmonary bypass, which has never been shown in previous studies that measured these levels immediately after surgery and later (2, 4). The explanation for this rather unexpected finding is not provided. The level of inflammatory cytokines is expected to rise when measured immediately after surgery and in subsequent time intervals, and the rise is expected to be lower in patients receiving pentoxifylline. In conclusion, though the paper aims to address the potential benefits of oral pentoxifylline in a high-risk subgroup of patients undergoing CABG, some clarifications needs to be made before drawing a conclusion.

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Author's Reply

To the Editor,

We appreciate you and the author(s) who accurately read and criticized our article entitled "Preoperative oral pentoxifylline in case of coronary artery bypass grafting with left ventricular dysfunction (ejection fraction equal to/less than 30%)" published in *Anatol J Cardiol* 2014 Dec 31 (1). The gold standard of clinical research is a randomized controlled trial (2). We considered all rules and laws of

allocation sequences in randomized trials. The levels of cytokines have been evaluated by laboratory-trained personnel using the same type of laboratory kit.

As you noticed, the study sample, a group of high-risk patients, may be one of the reasons for the higher level of cytokines before surgery. Also, we mentioned in our article that some novel results have been obtained that should be confirmed in further studies (1).

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Atrial fibrillation after cardiac surgery

To the Editor,

Postoperative atrial fibrillation (POAF) is mostly seen rhythm disturbance after coronary bypass surgery. POAF prolongs hospital care and increases hospital cost. It is a good indicator of a patient's morbidity and mortality. Studies aiming to investigate the pathogenesis of POAF show that inflammatory reactions and oxidative stress are the most important factors for the development of POAF. Inflammation changes the atrial transmission pathway, activates reentry mechanisms, and precipitates the development of POAF (1, 2). We read with great interest the article by Aydin et al. (3) entitled "Efficiency of postoperative statin treatment for preventing new-onset postoperative atrial fibrillation in patients undergoing isolated coronary artery bypass grafting: A prospective randomized study" published in *Anatol J Cardiol* 2015; 15: 491-5. The authors concluded that postoperative statin therapy seemed to reduce AF development after coronary bypass surgery. They also stated that CRP levels significantly decreased in patients undergoing coronary bypass surgery with early postoperative statin therapy.

In the results of this study, CRP levels showed no significant differences between the statin and non-statin groups on postoperative days 1 and 7. However, there was significant difference between the AF and non-AF groups. On postoperative day 14, the CRP levels showed significant differences between the statin and non-statin groups. There was also a significant difference between the AF and non-AF groups (Table 4). Due to high inflammation during the intraoperative period (extracorporeal circulation, cardiac ischemia-reperfusion injury, and oxidative stress) and postoperative period (pulmonary infections and cardiac deficiency), the inflammatory activity and CRP levels reach its

highest value in the first postoperative week. Therefore, we mostly detect atrial fibrillation in this early postoperative period (4). After 1 week, surgery induced inflammatory activity decreases, and postoperative risk factors gradually disappear. We think that statin shows its effect in this early postoperative time interval or we need to see the effect of statin in this period. According to the results of this study, we can say that early postoperative statin therapy is not effective in reducing inflammatory activity and CRP levels on postoperative days 1 and 7. We can also say that CRP levels are significantly lower in the non-AF group than in the AF group on postoperative days 1, 7, and 14 and that CRP is an effective indicator for predicting AF.

As a result, oxidative stress after cardiac surgery and other problems in the postoperative period, such as pulmonary infections and cardiac deficiency, induce inflammatory reactions and increase inflammatory capacity. A high inflammatory capacity is related to a higher risk of POAF. Early postoperative statin therapy may be late or inadequate to detect the effect of statins on POAF. We think that further studies are needed that investigate a reduction in inflammation in the intraoperative and postoperative periods to prevent atrial fibrillation.

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Author's Reply

To the Editor,

We thank the authors for their comments on our article entitled "Efficiency of postoperative statin treatment for preventing new onset postoperative atrial fibrillation in patients undergoing isolated coronary artery bypass grafting: a prospective randomized study" published in *Anatol J Cardiol* 2015; 15: 491-5 (1). Our prospective and randomized study with a statin therapy regimen in the early postoperative period showed a

statistically significant decrease in postoperative new-onset AF and a significant decrease in CRP levels in patients undergoing isolated CABG (1).

Preoperative statin therapy is also shown to reduce the incidence of postoperative AF (2, 3). ARMYDA-3 was the first randomized, controlled trial to evaluate the impact of preoperative statin therapy on postoperative AF. In that study, the peak CRP levels were not different between the placebo and atorvastatin groups, but preoperative atorvastatin reduced the risk of postoperative AF (2).

Recent studies have shown that statins reduce the CRP level in 2 weeks (4). Sakamoto et al. (3) started statin therapy in the preoperative period and showed that statins reduce the CRP level in the 7th postoperative day. The largest study is a systematic review of 91491 patients who showed a reduction in postoperative AF with preoperative statin therapy. In conclusion, preoperative statin therapy in patients undergoing elective cardiac surgery is associated with reduced levels of inflammatory markers postoperatively (5).

Sakamoto et al. (3) detected a delay of approximately 2 days in the occurrence of AF in patients with preoperative statin therapy compared with those without statin therapy. This fact is meaningful for postoperative care as it indicates that preoperative statin therapy can avoid AF development in unstable hemodynamics immediately after surgery.

Recently, CABG is frequently performed on the day after coronary angiography; therefore, preoperative statin therapy cannot be administered in most patients. The patients did not have preoperative statin therapy in our study, and we did not detect any difference in the occurrence day of the first postoperative AF. Therefore, we suggest that statin therapy should be preoperatively started if available (1).

Moreover, other mechanisms might contribute to the clinical benefit of statins such as antioxidant effects, direct antiarrhythmic effects by cell membrane ion channel stabilization, improvement of coronary flow velocity reserve by vasodilation of coronary microvessels, rapid (<12 h after a single dose of atorvastatin) improvement of endothelial function, or direct protection of the myocardium and might also play a role in extracellular matrix modulation (3, 4). These effects might contribute to the prevention of atrial fibrillation of statins.

In light of our study results, we suggest that if preoperative statin therapy is not administered to patients, statin therapy should be started in a short time postoperatively to obtain the beneficial effects of statins.

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Cardiac problem and MERS

To the Editor,

The Middle East respiratory syndrome (MERS) is an important emerging infection in the present day. Since its first origin in Saudi Arabia in 2012, this disease has already spread to several countries worldwide. The outbreak in Asia in 2015 is a present concern (1, 2). The big epidemic in Korea is a big challenge. In addition, other Asian countries including China and Thailand also have the problem of MERS. In this severe respiratory problem, a high mortality is reported. In cardiology, the effect of MERS is an interesting topic. First, there is no doubt that cardiac patients can get the infection and that this might lead to a difficulty in diagnosis. In a report from Saudi Arabia, 28% of MERS cases have underlying cardiac disease (3). The latest case in Thailand is an Omani patient with underlying heart disease and visited a private

hospital in Thailand to seek a cardiologist. Of interest, this case was delayed diagnosed to have MERS. Second, patients with underlying heart disease can be more severe than general cases without underlying diseases (2). There is no doubt that special medical concern should be given to patients with underlying disease. Finally, the important question is whether MERS virus can cause direct cardiac pathology or not. A recent animal model study clearly stated that viral RNA could be seen in cardiac tissue, implying direct cardiac pathology (4).

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