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Please note: Dr. Movahed has a pending patent for a coronary sinus catheter for contrast removal.

## REFERENCES

1. Cigarroa RG, Lange RA, Williams RH, Hillis LD. Dosing of contrast material to prevent contrast nephropathy in patients with renal disease. *Am J Med* 1989;86:649-52.
2. Rihal CS, Textor SC, Grill DE, et al. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. *Circulation* 2002;105:2259-64.
3. Boehm DH, Reichenspurner H, Gulbins H, et al. Early experience with robotic technology for coronary artery surgery. *Ann Thorac Surg* 1999;68:1542-6.
4. Molloi SY, Mistretta CA. Quantitation techniques for dual-energy cardiac imaging. *Med Phys* 1989;16:209-17.
5. Ersahin A, Molloi S, Qian Y. A digital filtration technique for Scatter-glare correction based on thickness estimation. *IEEE Trans Med Imaging* 1995;14:587-95.
6. Swindle MM. Swine as replacement for dogs in the surgical teaching and research laboratory. *Lab Anim Sci* 1984;34:383.
7. Crick SJ, Sheppard MN, Ho SY, Gebstein L, Anderson RH. Anatomy of the pig heart: comparisons with normal human cardiac structure. *J Anat* 1998;193:105-19.
8. Ansari A. Anatomy and clinical significance of ventricular thebesian veins. *Clin Anat* 2001;14:102-10.

## Letters to the Editor

### Effects of N-3 Fatty Acids on Postoperative Atrial Fibrillation Following Coronary Artery Bypass Surgery

We read with considerable interest the recent contribution by Calò et al. (1) about the reduced incidence of postoperative atrial fibrillation (AF) after administration of n-3 polyunsaturated fatty acids (PUFAs) in patients undergoing coronary artery bypass surgery (CABG). Even though the investigators discuss the potential role of inflammation in this setting we consider that some important issues merit further clarification.

First, 19 of the studied patients were subjected to off-pump surgery, a procedure considered to be associated with a lesser oxidative and inflammatory response (2). Bearing in mind the hypothesis that postoperative AF may be reduced by off-pump CABG (3), it would be meaningful to examine whether there was a difference in the incidence of postoperative AF in this subset of patients.

In addition, it has been observed that the peak incidence of AF on the second or third postoperative day coincides with the peak of inflammatory markers such as C-reactive protein (CRP) and complement-CRP complexes (4). Recently, Abdelhadi et al. (5) confirmed this association, demonstrating a more pronounced and

prolonged increase in white blood cell counts of patients who developed postoperative AF. Thus, to validate the anti-inflammatory effects of PUFAs someone could investigate the variation of simple inflammatory indexes in the postoperative period. If Calò et al. have some available data on this issue it would be of interest to perform comparisons between the two groups.

Of note, more than one-half the total study population was taking statins perioperatively (1). Even though there were no differences regarding statin administration between the studied groups, the investigators could mention some data on potential differences in the incidence of postoperative AF within each group. Statins may exert beneficial pleiotropic effects on atrial remodeling, reducing the burden of the arrhythmia. It has also been indicated that statin therapy reduces the incidence of arrhythmias after CABG, although no specific data on AF was reported (6). Recently, Auer et al. (7) demonstrated a reduced incidence of AF after cardiac operation in patients receiving statins, but 44.7% of these had been subjected to valve surgery.

Accumulating evidence suggests that inflammation augments oxidative stress and vice versa, whereas oxidative stress seems to play an important role in atrial remodeling (2,8). Specifically, it has been shown that oral vitamin C administration significantly reduces the incidence of postoperative AF in CABG patients (8). Taking into account that PUFAs can attenuate oxidative stress in humans (9), it is reasonable to assume that their antioxidant action may contribute to their favorable effect on postoperative AF.

Finally, we concur with the view of Calò et al. that administration of PUFAs merits further evaluation in other forms of AF, but, as suggested by a recent study that reported no association between PUFA consumption from fish and the risk of AF (10), careful selection of the studied population should be performed.

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## REFERENCES

1. Calò L, Bianconi L, Colivicchi F, et al. N-3 fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery. A randomized, controlled trial. *J Am Coll Cardiol* 2005;45:1723-8.
2. Matata BM, Sosnowski AW, Galinanes M. Off-pump bypass graft operation significantly reduces oxidative stress and inflammation. *Ann Thorac Surg* 2000;69:785-91.
3. Archbold RA, Curzen NP. Off-pump coronary artery bypass graft surgery: the incidence of postoperative atrial fibrillation. *Heart* 2003; 89:1134-7.
4. Bruins P, te Velthuis H, Yazdanbakhsh AP, et al. Activation of the complement system during and after cardiopulmonary bypass surgery: postsurgery activation involves C-reactive protein and is associated with postoperative arrhythmia. *Circulation* 1997;96:3542-8.
5. Abdelhadi RH, Gurm HS, Van Wagoner DR, Chung MK. Relation of an exaggerated rise in white blood cells after coronary bypass or cardiac valve surgery to development of atrial fibrillation postoperatively. *Am J Cardiol* 2004;93:1176-8.

6. Dotani MI, Elnicki M, Jain AC, Gibson CM. Effect of preoperative statin therapy and cardiac outcomes after coronary bypass grafting. *Am J Cardiol* 2000;86:1128–30.
7. Auer J, Weber T, Berent R, et al. Use of HMG-coenzyme-a-reductase inhibitors (statins) and risk reduction of atrial fibrillation after cardiac surgery: results of the SPAAF study—a randomised placebo-controlled study (abstr). *European Society of Cardiology Annual Congress, Munich 2004. Abstract book*, p. 353.
8. Carnes CA, Chung MK, Nakayama T, et al. Ascorbate attenuates atrial pacing-induced peroxynitrite formation and electrical remodeling and decreases the incidence of postoperative atrial fibrillation. *Circ Res* 2001;89:e32–8.
9. Mori TA, Woodman RJ, Burke V, et al. Effect of eicosapentaenoic acid and docosahexaenoic acid on oxidative stress and inflammatory markers in treated hypertensive type 2 diabetic patients. *Free Radic Biol Med* 2003;35:772–81.
10. Frost L, Vestergaard P. N-3 fatty acids consumed from fish and risk of atrial fibrillation or flutter: the Danish Diet, Cancer, and Health Study. *Am J Clin Nutr* 2005;81:50–4.

## REPLY

In our study (1) we observed a reduced incidence of atrial fibrillation (AF) following coronary artery bypass surgery in patients receiving polyunsaturated fatty acids (PUFAs). The way these compounds could have determined this result is, at present, only speculative. Indeed, PUFAs have been demonstrated to have a direct anti-arrhythmic effect in different laboratory models, but the importance of a concurrent (or prevalent) anti-inflammatory action cannot be excluded. In fact, PUFAs have anti-inflammatory properties (2), and inflammation, as correctly pointed out by Dr. Korantzopoulos and colleagues can play a fundamental role in postcardiac surgery AF. Actually, the efficacy of an anti-inflammatory therapy in this setting is still not clear owing to conflicting reports. Whereas a single postinduction steroid administration was shown to prevent postoperative AF (3), a similar protocol was found ineffective in other hands (4). The debate on this subject is thus still open, but unfortunately a further contribution cannot be obtained by our study, because C-reactive protein (CRP) levels or other inflammatory indexes were not routinely collected in our patients.

Concerning off-pump surgery that could carry a lower risk of AF due to a lesser oxidative and inflammatory response, aside from reports supporting this assumption (5) there are other studies that do not confirm this finding (6). In our study the incidence of AF was similar in patients receiving off-pump surgery (26.3% of 19 cases) and those submitted to on-pump surgery (24.1% of 141 cases). However, our population is too scarce to draw any conclusion on this subject.

Statins have been reported to prevent AF both after cardiac surgery (7) and after electrical cardioversion (8), possibly by their pleiotropic anti-inflammatory action. In our examination we did not observe any difference in AF incidence between patients on statins (24.2% of 91 patients) and those not on statins (24.6% of 61 patients). This could be due to the fact that the mean dose of statins in our patients was low ( $15.3 \pm 9.2$  mg/day simvastatin and  $13.2 \pm 7.5$  mg/day atorvastatin) and the anti-inflammatory and thus, possibly, anti-arrhythmic effect of statins seems to be related to the dose. In fact, a recent study reported a significant decrease of CPR (–36.4%) with atorvastatin 80 mg but not with pravastatin 40 mg (–5.2%) (9).

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## REFERENCES

1. Calò L, Bianconi L, Colivicchi F, et al. N-3 fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery. A randomized, controlled trial. *J Am Coll Cardiol* 2005;45:1723–8.
2. Mori TA, Beilin LJ. Omega-3 fatty acids and inflammation. *Curr Atheroscler Rep* 2004;6:4161–7.
3. Yared JP, Starr NJ, Torres FK, et al. Effects of single-dose, postinduction dexamethasone on recovery after cardiac surgery. *Ann Thorac Surg* 2000;69:1420–4.
4. Halvorsen P, Reader J, White PF, et al. The effect of dexamethasone on side effects after coronary revascularization procedures. *Anesth Analg* 2003;96:1578–83.
5. Matata BM, Sosnowski AW, Galinanes M. Off-pump bypass graft operation significantly reduces oxidative stress and inflammation. *Ann Thorac Surg* 2000;69:785–91.
6. Enc Y, Ketenci B, Ozsoy D, et al. Atrial fibrillation after surgical revascularization: is there any difference between on-pump and off-pump? *Eur J Cardiothorac Surg* 2004;26:1129–33.
7. Dotani MI, Elnicki M, Jain AC, Gibson CM. Effect of preoperative statin therapy and cardiac outcomes after coronary bypass grafting. *Am J Cardiol* 2000;86:1128–30.
8. Siu CW, Lau CP, Tse HF. Prevention of atrial fibrillation recurrence by statin therapy in patients with lone atrial fibrillation after successful cardioversion. *Am J Cardiol* 2003;92:1343–5.
9. Nissen SE, Tuzcu EM, Schoenhagen P, et al. Effect of intensive compared with moderate lipid-lowering therapy on progression of coronary atherosclerosis: a randomized controlled trial. *JAMA* 2004;291:1071–80.

## Serum Erythropoietin Levels and Infarct Size

With great interest we read the recent study by Namiuchi et al. (1) showing an association between high serum erythropoietin levels and smaller infarct size in patients with acute myocardial infarction (MI) undergoing primary angioplasty.

Although originally considered a hematopoietic hormone, erythropoietin (EPO) has been shown to act as a pleiotropic survival and growth factor (2). There is accumulating evidence for a protective role of EPO in the heart. We and others have demonstrated that *exogenous* EPO administration in rodent ischemia-reperfusion models leads to reduced infarct size and inhibition of apoptosis (3,4).

Namiuchi et al. (1) suggested that *endogenous* EPO might also be protective against ischemia-reperfusion injury in humans. However, elevated EPO levels could also be a direct reflection of the disease severity. Serum EPO is elevated in chronic heart failure (CHF) patients, and this increase is related to the progression of the disease (5). Our group has shown that, in these patients, elevated plasma EPO levels are associated with an impaired prognosis, independent of hemoglobin levels and other established markers of CHF severity (6). Of note, in the study by Namiuchi et al. (1), MI patients with higher EPO levels were found to have significantly higher serum levels of B-type natriuretic peptide (BNP), a sign of hemodynamic impair-