tives on epidemiological and pathophysiological links. *Int J Cardiol*. 2005; 105:319-321.
3. Psaty BM, Manolio TA, Kuller LH, et al. Incidence of and risk factors for atrial fibrillation in older adults. *Circulation*. 1997;96:2455-2461.
4. Benjamin EJ, Levy D, Vaziri SM, D'Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population-based cohort: the Framingham Heart Study. *JAMA*. 1994;271:840-844.
5. Movahed MR, Hashemzadeh M, Jamal MM. Diabetes mellitus is a strong, independent risk for atrial fibrillation and flutter in addition to other cardiovascular disease. *Int J Cardiol*. 2005;105:315-318.

Corticosteroids in Atrial Fibrillation: Friends or Foes?

I read with great interest the recent contribution by van der Hooft et al,[1] which provided epidemiological evidence for an association between high-dose corticosteroid exposure (oral or parenteral steroid at a daily dose of ≥7.5 mg of prednisone equivalents) and the development of AF. A direct arrhythmogenic effect of these agents was also speculated, and some potential triggering mechanisms were proposed.[1]

I consider that some relevant issues merit further clarification because inconsistent findings on this topic have been reported in the literature. The authors do not discuss the current evidence regarding the role of inflammation and oxidative stress in AF, and more importantly, some recent studies indicating favorable effects of corticosteroids are not mentioned.

Accumulating evidence suggests that inflammation and oxidative stress may have a significant impact on atrial remodeling, which favors AF development and perpetuation.[2,3] Corticosteroids represent major anti-inflammatory drugs with immunomodulatory and indirect antioxidant properties.[2,3] Dernellis and Panaretou[4] were the first to assess the efficacy of corticosteroid treatment in preventing recurrent AF as well as the variation of C-reactive protein (CRP) levels during this therapy. They randomized 104 patients with first-appeared persistent AF, who were successfully cardioverted and were given oral propafenone and then low-dose methylprednisolone (16 mg for 4 weeks tapered to 4 mg for 3 months) or placebo. Methylprednisolone significantly reduced recurrent AF as well as the development of permanent AF during the 30-month follow-up period. It also became evident that corticosteroid treatment significantly reduced CRP levels from the first month, and a strong relationship between increase in CRP level and the risk of AF recurrence was observed.[4] In another study, 88 patients were prospectively randomized to receive 1 g of methylprednisolone before bypass surgery and 4 mg of dexamethasone every 6 hours during the first postoperative day or placebo.[5] Notably, AF occurred in 21% of patients treated with corticosteroids compared with 51% of those in the placebo group.[5] Finally, in a recent experimental canine model, it was demonstrated that prednisone successfully suppressed the increase in duration of induced AF and the decrease in atrial effective refractory period and its rate adaptation, whereas other anti-inflammatory agents such as ibuprofen and cyclosporine A were ineffective.[6] In addition, prednisone decreased CRP levels and attenuated the increase in protein levels of left atrial endothelial nitric oxide synthase.[6]

Undoubtedly, further studies are needed to elucidate the exact role of corticosteroids in atrial remodeling and their clinical impact on AF.

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1. van der Hooft CS, Heeringa J, Brusselle GG, et al. Corticosteroids and the risk of atrial fibrillation. *Arch Intern Med*. 2006;166:1016-1020.
2. Boos CJ, Anderson RA, Lip GYH. Is atrial fibrillation an inflammatory disorder? *Eur Heart J*. 2006;27:136-149.
3. Korantzopoulos P, Kolettis TM, Galaris D, Goudevenos JA. The role of oxidative stress in the pathogenesis and perpetuation of atrial fibrillation [published online ahead of print June 9, 2006]. *Int J Cardiol*. doi:10.1016/j.ijcard.2006.04.026.
4. Dernellis J, Panaretou M. Relationship between C-reactive protein concentrations during glucocorticoid therapy and recurrent atrial fibrillation. *Eur Heart J*. 2004;25:1100-1107.
5. Prasongsukarn K, Abel JG, Jamieson WR, et al. The effects of steroids on the occurrence of postoperative atrial fibrillation after coronary artery bypass grafting surgery: a prospective randomized trial. *J Thorac Cardiovasc Surg*. 2005; 130:93-98.
6. Shiroshita-Takeshita A, Brundel BJ, Lavoie J, Nattel S. Prednisone prevents atrial fibrillation promotion by atrial tachycardia remodelling in dogs. *Cardiovasc Res*. 2006;69:865-875.

Corticosteroids and Atrial Fibrillation: Risks or Benefits?

We read with great interest the recent case-control study by van der Hooft et al,[1] which showed that high-dose corticosteroid therapy increased the risk of developing AF in a population-based cohort, and they also presented some potential mechanisms that may contribute to this association. However, Dernellis and Panaretou[2] demonstrated that low-dose glucocorticoid therapy following successful cardioversion of persistent AF could prevent recurrent AF, and this effect correlated with a significant reduction of C-reactive protein levels. Furthermore, another prospective randomized study[3] also showed that short-term corticosteroid administration in patients undergoing coronary artery bypass grafting significantly reduced postoperative AF. The protective effects of corticosteroid therapy on AF are possibly explained by anti-inflammatory mechanisms.[4,5]

How can we evaluate these divergent results? We think the risks or benefits of corticosteroids on AF are mainly dependent on the drug dosage and patient selection. High-dose corticosteroid administration may increase the risk of AF in the general population, whereas low-dose corticosteroid therapy may prevent AF in some specific clinical settings, such as in patients after successful cardioversion of persistent AF and coronary artery bypass grafting.

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