REPLY

We appreciate the interest of Dr. Karamanoukian and colleagues in our study about the relation between postoperative stroke in cardiac surgery and presence, location and extent of atherosclerosis in the ascending aorta (1). Our study showed a 3.5% incidence of stroke due to atherosclerosis of the ascending aorta as detected by epiaortic ultrasound (in 26% of the patients) despite minor surgical modifications. Furthermore, a multivariate analysis showed that the two best predictors for perioperative stroke were atherosclerosis of the ascending aorta and diabetes mellitus. Age is usually associated with atherosclerosis in the ascending aorta. Consequently, atherosclerosis of the ascending aorta (detected by intraoperative ultrasound) is a better predictor than age. Therefore, we recommended a more radical change in surgical strategy in the presence of atherosclerosis of the ascending aorta, and especially when the disease of the aortic wall is extended.

One interesting option in this situation is off-pump coronary artery bypass (OPCAB). Still, partial clamping of the ascending aorta is usually used in OPCAB. Clamping of the ascending aorta has been shown to generate cerebral emboli (2-5). Thus, with OPCAB cross-clamping can be avoided, but usually partial clamping is conducted, unless an anastomotic device is employed or the ascending aorta is totally avoided. A further possibility is the use of intraoperative intraaortic filters, if clamping is necessary (5).

We congratulate Dr. Karamanoukian and colleagues for their successful results with OPCAB in octogenarians. Notably, approximately 12% of their patient cohort had atherosclerosis of the ascending aorta, presumably detected by palpation. It is unclear how these patients were handled in terms of proximal anastomosis on the ascending aorta. Considering that their patients received only on average 1.8 grafts, we assume that their conclusion should be that OPCAB incomplete revascularization without touching the ascending aorta may be the preferred operative technique in high-risk patients (i.e., octogenarians).

Recently, we employed OPCAB to achieve complete revascularization in 20 patients with extensive disease of the ascending aorta according to intraoperative ultrasound and totally avoided the ascending aorta in the majority of the patients. None of the 20 patients suffered a perioperative stroke.

In conclusion, we believe that OPCAB techniques may have a justified place in high-risk patients (i.e., with extended atherosclerosis the ascending aorta according to epiaortic ultrasound) in order to prevent perioperative stroke. However, well-designed randomized studies have to be conducted to prove the superiority of OPCAB over conventional coronary surgery.

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REFERENCES


Cytokine Gene Polymorphisms and Development of CAD Associated with CP Infection

We read with great interest the study by Momiyama et al. (1) in a recent issue of the Journal. The study reports that cytokine gene polymorphisms, in particular interleukin-1 (IL-1) polymorphisms, play a role in the development of coronary artery disease (CAD) in patients with Chlamydia pneumoniae (CP) infection. Moreover, they found that CP seropositivity was not significantly different between patients with and without CAD. Momiyama et al. (1) suggested that “triggers” such as IL-1 gene polymorphisms could influence the effect of such infectious agents as CP on development of CAD.

Increasing evidence exists indicating that inflammation plays an important role in atherogenesis (2). The hypothesis of infectious agents that might play an important role in the atherogenesis is supported by results of several epidemiologic studies suggesting possible atherogenic potential not only from CP (3) but also from such pathogens as cytomegalovirus (4), herpes simplex virus (HSV) (5) and Helicobacter pylori (6).

However, existing epidemiologic data about the association of some of these pathogens and atherosclerosis are conflicting (7). We support the finding of Momiyama et al. (1) that CP seropositivity is not associated with CAD by data from 218 consecutive patients undergoing coronary angiography. Blood of all subjects was tested for serum IgG antibodies to CP and for seromarkers of five other pathogens (hepatitis A-virus, Helicobacter pylori, HSV, influenza type A and influenza type B). Of the 218 patients, 88 (40.4%) had anti-CP IgG antibodies. The CAD prevalence was 61.4% in CP-seropositive and 66.9% in CP-seronegative patients ($p = 0.49$). Moreover, seropositivity for each other pathogen (tested in our study) was not associated with CAD.

In contrast, the number of infectious pathogens to which an individual has been exposed (8) (“infectious burden”) correlates with prevalence of CAD. Four or more of the six seromarkers tested for particular infections were positive in 48.8% of patients with CAD and in 31.2% of patients in patients without CAD ($p = 0.02$). Therefore, our data support the results from Momiyama et al. (1) that seropositivity for a particular infectious agent, like CP, represents no predictor of risk for CAD. However, some “triggers,” such as cytokine gene polymorphisms or additional exposure to...
other pathogens, could influence the susceptibility to the atherogenic effect of infection with a particular pathogen like CP. Consequently, this finding suggests that "susceptibility" factors could make subjects more likely to develop CAD when infected with a particular pathogenic agent.

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REPLY

We greatly appreciate the comments of Dr. Auer and colleagues regarding our article recently published in the Journal of the American College of Cardiology (1).

Chlamydia pneumoniae (CP) was often reported to be associated with coronary artery disease (CAD) in seroepidemiologic studies, but the potential contribution of CP to CAD remains controversial. As shown in our article (1), Auer et al. also found no significant difference in the CAD prevalence between patients with and without CP seropositivity. However, CP organism was detected within atheroma by direct immunofluorescence and polymerase chain reaction (PCR), and CP infection was shown to accelerate atherosclerosis in a rabbit model. We agree with Dr. Auer and colleagues that some triggers like cytokine gene polymorphisms or additional exposure to other pathogens could influence susceptibility to the atherogenic effect of CP infection.

Regarding genetic factors for CAD associated with CP infection, we reported that two polymorphisms of interleukin (IL)-1 genes play a role in the development of CAD, especially myocardial infarction, in patients with CP infection (1). However, other cytokine gene polymorphisms, such as IL-6 and IL-10, were also reported to be associated with CAD as well as inflammatory diseases. In addition to the IL-1 gene polymorphisms, they may be contributing to the development of CAD associated with CP infection. We will continue to seek genetic factors influencing the susceptibility to CAD associated with CP or other infections.

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Patients With CHF and Depression
Have Greater Risk of Mortality and Morbidity Than Patients Without Depression

With great respect and interest, we read the recently published study by Vaccarino et al. (1) in the Journal. That study supports our previous findings, presented at the annual meetings of the American Psychiatric Association (2) and the American Heart Association (3) and was just published a day before in the Archives of Internal Medicine this month, that the short-term prognosis of patients with heart failure (HF) and comorbid depression is much worse than that of such patients without depression.

Vaccarino and colleagues assessed the level of depressive symptoms by means of the Geriatric Depression Scale (GDS) on 391 patients aged 50 or older who were hospitalized with HF. They followed the patients for six months and assessed mortality and functional capacity in activities of daily living (ADL). They found that mortality at six months was two to three times higher in patients with greater depressive symptoms than in those with lesser depressive symptoms or those considered to have normal mood. Patients with moderate to severe depressive symptoms also showed significant functional declines during follow-up. Apparently, the covariates of age, gender, race and education were not associated with the relationships of depression to mortality and functional decline; but when the statistical model was adjusted for other variables, such as prior infarction, diabetes, prior admission for HF, certain limiting factors of ADL and several baseline clinical features (systolic blood pressure, serum creatinine, pulse and left ventricular ejection fraction), in addition to these demographic characteristics, the adverse relation between depression and mor-