
**Reply**

We appreciate the opportunity to reply to questions raised by Dr. Nakazawa and colleagues. Please note that the coronary arteries distal to the stented segment but not the stented lesion were examined for the endothelial vasomotor function in our study (1). As described in our study (1), myocardial ischemia-reperfusion induces endothelial injury in the coronary trees for their entirety distal to the occluded segment in the infarct-related coronary artery. Thus, the healing process of the coronary arteries distal to the stented segment but not the stented lesion affected our data. Our previous reports (2–5) agreed that the atherosclerotic burden strongly affects coronary endothelial vasomotor functions. However, our study (1) showed that the frequencies of the atherosclerotic risk factors were comparable between the drug-eluting stent (DES) and bare-metal stent (BMS) groups. In addition, the 2 groups had no difference in cardiac medications, lesion, and procedural variables of percutaneous coronary intervention except for stent selection, and acute myocardial infarction (AMI)-related variables that potentially influence the coronary endothelial vascular function, as described in our study (1). Thus, the implanted stents were only the discriminate factor for the difference in the coronary endothelial vasomotor responses to acetylcholine between the patients treated with BMS and DES.

A number of previous reports (6,7) demonstrated that the vascular endothelial growth factor (VEGF) expression is increased in cardiomyocytes as well as vascular endothelial cells in ischemic or injured hearts and that sirolimus is capable of inhibiting VEGF production and the VEGF-mediated cellular signaling pathway in various types of cells. Our study (1) also showed that VEGF levels in the anterior interventricular vein (AIV), reflecting VEGF levels released from the ischemic myocardium, were increased in AMI patients treated with BMS compared with control subjects. As we described in our study (1), sirolimus levels in AIV in our study were 10- to 500-fold lower than the levels to exert its biological effects in vitro experiments (8,9). Considering the fact that sirolimus is eluted into coronary circulation over a period of 4 weeks, these exposure times were much longer as compared with the in vitro experiments. Moreover, the chronic exposure to the circulating sirolimus might cause a local accumulation of considerable amounts of this drug in the myocardium and the entire vascular bed distal to sirolimus-eluting stent (SES) in the infarct-related coronary artery. Thus, there is a possibility that SES could induce a decrease in VEGF release from myocardium and endothelium of large and resistance vessels, which may play a possible role in the mechanisms for endothelial vasomotor dysfunction in the infarct-related coronary arteries treated with SES.

**Correspondence**

Jyun-ii Obata, MD, PhD
Kiyotaka Kugiyama, MD, PhD

D Department of Internal Medicine II
Interdisciplinary Graduate School of Medicine and Engineering
University of Yamanashi
1110 Shimokato
Chuo City, Yamanashi Prefecture, 409-3898
Japan
e-mail: kugiyama@yamanashi.ac.jp

doi:10.1016/j.jacc.2007.12.007

**REFERENCES**


**Early Detection of Rheumatic Heart Disease and Prevention of Heart Failure in Sub-Saharan Africa**

In a recent issue of the *Journal*, Damasceno et al. (1) highlighted the need for action to reduce the prevalence of heart failure in sub-Saharan Africa, where this pathology is an important cause of mortality as well as a serious economic burden. Rheumatic heart disease is the most frequent cause of heart failure in this region of the world and is responsible for at least one-third of cases. In this context, the authors are prudent to insist on the need for a strategy of prevention with regards to risk factors for heart failure. Nevertheless, we would like to underline important new findings that should be considered when attempting to reduce the incidence of this life-threatening pathology.
Recently, an echocardiographic approach demonstrated that the prevalence of rheumatic heart disease in sub-Saharan Africa was 10-fold higher than previously reported (2). In other words, 9 out of 10 children have only minor infra-clinical rheumatic valve lesions and would not have been detected by the clinical criteria used in previous surveys. Secondary prophylaxis measures, based on monthly penicillin injections in children after a first episode of acute rheumatic fever and continued until the third decade, have been shown to be inexpensive and efficient. This therapeutic strategy is best delivered as part of a register-based control program, providing education and enabling better clinical follow-up. This approach has been recommended by the World Health Organization and the World Heart Federation since the 1980s.

Comprehensive echocardiographic screening programs could also enhance effective prevention strategies for rheumatic heart disease. Early detection of “subclinical” rheumatic valve disease is vital, as it presents an opportunity for case detection at a time when prophylactic penicillin can prevent progression to clinical valve disease and heart failure in young adult life.

*Eloi Marijon, MD
Xavier Jouven, MD, PhD
*Université Paris-Descartes
Hôpital Européen Georges Pompidou
Département de Cardiologie
20 rue Leblanc
75908 Paris Cedex 15
France
E-mail: eloi_marijon@yahoo.fr

doi:10.1016/j.jacc.2007.11.056

REFERENCES

Reply

We agree with Drs. Marijon and Jouven that the time has come for the adoption of echocardiographic screening as part of a strategy for the early detection of rheumatic heart disease in endemic regions of the world such as Africa, Southeast Asia, and the Asia-Pacific region. The Pan African Society of Cardiology (PASCAR) has called for the implementation of the Awareness-Surveillance-Advocacy-Prevention (A.S.A.P.) Programme for the prevention of rheumatic fever and rheumatic heart disease in Africa, which embraces echocardiographic screening as part of an effort to rid the continent of the scourge of rheumatic heart disease “in our own lifetime” (1,2).

Although we agree with the overall thrust of the comment by Drs. Marijon and Jouven, the statement that “rheumatic heart disease is the most frequent cause of heart failure in this region of the world” may only apply to children and young adults. A pooling study of 12 hospital-based case series involving 4,548 patients from 8 countries (Cameroon, Ghana, Kenya, Nigeria, Senegal, South Africa, Uganda, and Zimbabwe) has shown that hypertension (23%) is the leading cause of heart failure in sub-Saharan Africa, followed closely by rheumatic heart disease (22%), and cardiomyopathy (20%) (3).

Finally, the natural history of patients with “subclinical” (i.e., no history of rheumatic fever, no symptoms, no signs, no mitral stenosis) echocardiographic features suggestive of rheumatic heart disease that were detected in the study by Marijon et al. (4) is unknown. Studies are needed to examine the appropriate management of these cases with borderline abnormalities that are likely to be found in large numbers in through echocardiographic screening for rheumatic heart disease.

*Albertino Damasceno, MD, PhD
Gad Cotter, MD
Anastase Dzudie, MD
Karen Sliwa, MD, PhD
Bongani M. Mayosi, MBChB, DPhil
*Departamento de Medicina
Faculdade de Medicina
Universidade Eduardo Mondlane
Ave. M ao Tse Tung 836
Maputo, Moçambique
E-mail: tino_7117@yahoo.com.br


REFERENCES