Does only atrial fibrillation influence VEGF secretion?

To the Editor:

We read with great interest the article by Seko, et al. on serum vascular endothelial growth factor (VEGF) and transforming growth factor (TGF) -β1 levels in patients with atrial fibrillation. However, some aspects of their methodology and discussion seem questionable.

First, because of low serum VEGF levels, they eliminated 7 cases from an initial 20 patients with atrial fibrillation and thus only discussed the remaining 13 cases. It is reasonable to select the population on the basis of a factor which might influence the results. However, it is not reasonable from a validity standpoint to select the population on the basis of the results.

Secondly, they reported that the serum VEGF levels were undetectable in normal control subjects. On the contrary, their results indicated that the serum VEGF levels after defibrillation were still higher than those in control subjects, and they did not explain the reason. If the study subjects had other underlying heart diseases, they should have been discussed.

In addition, they stated that VEGF levels in patients with acute myocardial infarction returned rapidly to the normal range after reperfusion therapy. If atrial fibrillation was directly involved in VEGF secretion and the half life of VEGF was so short, then the serum VEGF levels might have returned rapidly to the normal range after defibrillation therapy. However, although the second blood sampling was done between 24 hours to 57 days after defibrillation, the serum VEGF levels were still higher than those in normal control subjects. Thus, we are obliged to question whether only atrial fibrillation really influenced the VEGF secretion. (Jpn Heart J 2000; 41: 681-682)

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Response:

We thank Drs. Amitani and Miyahara for their interest in our study. We think that while a fair question, it is not an easy one to answer. As we stated in our paper, because one of our previous studies clearly showed that pulsatile mechanical stretch significantly stimulates VEGF secretion from cardiac myocytes *in vitro*, this study was designed to investigate whether mechanical stress such as pulsatile stretch can influence serum VEGF levels *in vivo*. However, in general, there are several limitations in most of the clinical studies. For example, although all the patients studied had no apparent heart diseases other than atrial fibrillation as stated in the methods, we could not exclude the possibility that atrial fibrillation-induced mechanical overload caused the subclinical ischemic heart diseases because we did not perform coronary angiography in these patients. Therefore, we planned to evaluate only the influence of defibrillation on the serum VEGF level. Because serum VEGF levels in the 7 patients with atrial fibrillation remained low (undetectable) after defibrillation, we could not accurately evaluate the influence of defibrillation. We thought that elimination of such cases from the analysis was warranted. The fact that serum VEGF levels after defibrillation in the other 13 cases were still higher than those in the control subjects may indicate that some factors other than atrial fibrillation can influence serum VEGF levels. It would be interesting to determine what kind of factors other than ischemia (hypoxia) and mechanical stress can stimulate VEGF secretion from cardiac myocytes, and indeed further investigation into these is required.

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REFERENCES