Coagulation Activity Is Increased in the Left Atrium of Patients With Mitral Stenosis—I

I read the study by Yamamoto et al. (1) with immense interest. However, their conclusion of activation of the coagulation system in the left atrium even during anticoagulation may be incorrect. We do not know the severity of pulmonary hypertension in the patients studied. Although the authors found no correlation of elevated fibrinopeptide A (FPA) levels with either chronic atrial fibrillation or severity of mitral stenosis, no attempt at correlation with severity of pulmonary hypertension was made. There is evidence to suggest activation of the coagulation system in pulmonary hypertension, both in primary (2) and secondary pulmonary hypertension (3), although controversy also exists (4). To my knowledge, no studies have been done to date on FPA or thrombin anti-thrombin III (TAT) activity and pulmonary hypertension secondary to mitral stenosis. The coagulation activation in the present study suggests an activation in the pulmonary circuit rather than the left atrium, contrary to the suggestion by the authors. If this hypothesis is correct, particularly if the FPA levels decrease after correction of mitral stenosis, pulmonary hypertension with mitral stenosis may itself be a risk factor for coagulation. Hence, there is an argument for early definitive therapy for mitral stenosis to better control or correct the coagulation abnormality.

The TAT levels in the present study were not significantly elevated in the left atrium, although they correlated with the FPA levels. This difference could have resulted from the influence of different blood sampling techniques. Significantly lower TAT levels are measured in blood samples taken from central catheters than those with blood samples obtained from direct venipunctures (5). The TAT levels measured in the left atrium in the present study may thus be artificially low, when the TAT levels are in fact significantly elevated in patients with mitral stenosis. Congratulations for the wonderful study.

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Coagulation Activity Is Increased in the Left Atrium of Patients With Mitral Stenosis—II

We read with interest the report by Yamamoto et al. (1) on coagulation activity in patients with mitral stenosis. In this interesting study, various coagulation markers in 12 patients were compared with those of 15 normal subjects. Eleven of the 12 patients were in atrial fibrillation, but the heart rhythm of the normal control subjects was not stated (we assume that they were in sinus rhythm) (1). However, patients with atrial fibrillation who are not receiving any antithrombotic therapy are known to demonstrate abnormalities in coagulation factors, consistent with a prothrombotic or hypercoagulable state, that may contribute to the high risk of stroke and thromboembolism in such patients. For example, patients with atrial fibrillation who are not receiving any antithrombotic therapy demonstrate an elevation in plasma levels of fibrinogen, fibrin D-dimer, von Willebrand factor antigen and beta-thromboglobulin compared with control subjects in sinus rhythm, and this finding is independent of any underlying structural heart disease (2-4). There was also no relation to left atrial size or ventricular function (3).

In addition, all patients in the study by Yamamoto et al. (1) had received warfarin therapy for 3 months. The introduction of warfarin therapy normalizes certain markers of thrombogenesis, such as fibrin D-dimer and beta-thromboglobulin; although other markers, such as von Willebrand factor antigen and fibrinogen, remain unchanged (3,4). It is therefore not surprising that Yamamoto et al. (1) found no significant differences in levels of D-dimer and beta-thromboglobulin between their patients (taking warfarin) and control subjects and that von Willebrand factor antigen levels remained significantly elevated. A better assessment of hypercoagulable state in mitral stenosis would have been to compare patients with mitral stenosis in sinus rhythm (and not on any antithrombotic therapy) and matched healthy control subjects in sinus rhythm (who are also not receiving any therapy). However, whether such a study is feasible remains debatable because most patients with significant mitral stenosis should be started on antithrombotic therapy, in view of the risk of developing atrial fibrillation and thromboembolism.

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References

Reply

We very much appreciate the interest of Siddiqui in our recent study on coagulation activity in the left atrium of patients with mitral stenosis (1). Siddiqui raises two issues with regard to our study. The first is the possibility of increased coagulability in the pulmonary circuit rather than in the left atrium of patients with mitral stenosis. We therefore evaluated the correlation of elevated fibrinopeptide A (FPA) and thrombin-antithrombin III complex (TAT) levels in the left atrium of the patients in relation to the severity of pulmonary hypertension. However, the levels of these biochemical markers did not correlate well with the mean pulmonary artery pressure (FPA: r = 0.47, p = 0.15; TAT: r = 0.41, p = 0.19). As pointed out by