Letters to the Editor


Aortic stiffness and calcification
The article by Stefanadis et al[1] and the accompanying editorial[2] highlight the potential use of aortic stiffness measurement as a predictor of acute coronary events in patients with coronary artery disease. It is interesting to note that one of the main factors leading to aortic stiffness may be the presence of vascular calcification in the form of hydroxyapatite crystals within the atherosclerotic intima and also within the media. In fact, aortic pulse wave velocity — a non-invasive measure of arterial wall stiffness — has been shown to independently correlate with aortic calcification in man[3]. Furthermore, the induction of vascular calcification in rats by vitamin D and nicotine results in a significant increase in aortic stiffness[4].

If the increased aortic stiffness measured by Stefanadis et al[1] is due to the presence of vascular calcification, then it would be consistent with a number of studies that have demonstrated increased coronary risk with increasing amounts of coronary artery calcium as measured by electron beam CT[5].

It would therefore be interesting to know if aortic stiffness, as measured by Stefanadis et al., correlates with aortic calcification. This may give some indication of the contribution of vascular calcification, as opposed to other factors such as medial fibrosis, to the pathogenesis of increased aortic stiffness. Furthermore, it may indicate if the increased coronary event rate observed with aortic stiffness is independent of the increased atherosclerotic plaque load associated with calcification, for example by causing a decrease in diastolic coronary perfusion due to loss of aortic elastic recoil.

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References

Lipoprotein (a) and thrombogenesis in left ventricular dysfunction
I read with interest the recent editorial by Rehnqvist[1] which implies that lipoprotein (a) may be involved in the pathogenesis of thrombosis, myocardial infarction and sudden death, with microthrombi present at autopsy. Indeed, lipoprotein (a) has long been associated with thrombogenesis and atherogenesis, although the data are mainly from case-controlled studies[2,3].

One particularly high risk group for sudden death and thrombus-related complications are patients with left ventricular dysfunction. Indeed, heart failure is recognized to be associated with a prothrombotic or hypercoagu- lable state[4]; nevertheless, the relationship with lipoprotein (a) levels, which are highly genetically determined and distributed in a greatly skewed fashion in the general population, is less certain.

In a prospective case-controlled study of 101 outpatients (81 male; mean age 57 years ± SD9) with coronary artery disease undergoing cardiac catheterization, we measured levels of serum lipoprotein (a) (immuno-turbidometric assay (INCASTAR Corp, Stillwater, Minnesota, U.S.A.)) and plasma fibrin D-dimer (ELISA-AGEN, Parsippany, NJ, U.S.A.), an established marker of thrombogenesis[5]. 29 patients had normal left ventricular function (Group 1); 30 patients had left ventricular dysfunction but no aneurysm formation (Group 2); 23 patients had left ventricular aneurysms and were not on warfarin (Group 3a); and 19 patients had left ventricular aneurysms and were taking warfarin therapy (Group 3b). In all patients, left ventricular function was initially assessed by reviewing the dynamic single-plane left ventriculogram (performed at cardiac catheterization). Patients with possible wall motion abnormalities were then further assessed by echocardiography and by a radionuclide ventriculogram, using a low energy general purpose collimator following in vivo red cell labelling with 99m-technetium pertechnetate. Lipoprotein (a) and fibrin D-dimer results were compared to 22 healthy volunteers of similar age and sex as a control group.

There were no significant differences in serum lipoprotein (a) levels between patients with left ventricular aneurysm or left ventricular dysfunction when compared with patients having normal left ventricular function and with healthy controls (Kruskal–Wallis test, P=0.842). There was also no difference between lipoprotein (a) levels in patients with left ventricular aneurysm on warfarin therapy (Group 3b) when compared with those not taking warfarin (Group 3a) (Mann–Whitney test, P=0.3732). By contrast, plasma fibrin D-dimer levels were highest in Group 3a (P<0.001), and were significantly reduced in Group 3b (vs Group 3a, Mann–Whitney test, P=0.0001 (Table 1).

No significant differences in serum cholesterol (P=0.167) or triglycerides (P=0.085) were demonstrable between the groups. There were no significant correlations between lipoprotein (a) with corresponding levels of fibrin D-dimer in any of the groups (Spearman correlations, all P=ns). There were also no significant correlations with left dimensions and left ventricular function (as measured by fractional shortening) (data not shown).

Whilst lipoprotein (a) is associated with atherogenesis and thrombogenesis, there has been little information on whether or not it is increased in conditions of high thromboembolic risk, such as severe heart failure. Despite the association with increased thrombosis, there was no significant relationship of lipoprotein (a) to fibrin D-dimer levels, nor a decrease of lipoprotein (a) levels in the patients established on warfarin therapy. It is conceivable that the ‘strong’ genetic influence upon lipoprotein (a) levels[6,7] may partly explain these results.
Furthermore, perhaps some lipoprotein (a) phenotypes do not contribute to thrombogenesis and as a result, some patients with high lipoprotein (a) levels may not be at ‘high risk’ for thrombogenesis: some evidence for such a dissociation has already been provided by population comparisons. For example, Afro-Caribbean have higher lipoprotein (a) levels than white caucasians, despite having lower rates of coronary artery disease[6].

Thus, our group has been unable to show significant interactions between lipoprotein (a) and thrombogenesis in patients with left ventricular dysfunction, despite this patient group being at high risk for sudden death and thrombus-related complications. If any relationship does exist, it may be weak and masked by the strong genetic influence on lipoprotein (a) levels and phenotypes.

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References


Stress-induced ST-segment elevation on Q leads after myocardial infarction

We read with great interest the paper by Mezlis et al.[1] which relates stress (exercise and dobutamine)-induced ST-segment elevation on Q-leads shortly after myocardial infarction to myocardial viability. According to previous works[2], it is suggested that this finding is a good predictor of myocardial viability and late improvement in the infarcted area. Some points should be clarified before accepting this conclusion:

No mention is made in the paper of the recent controversy on the significance of this electrocardiographic sign. The authors seem to think that current literature links exercise-induced ST-segment elevation on Q-leads with myocardial viability; obviously it is not the case[3].

As in a previous report[4] with similar results, the study group of Mezlis et al. is composed of patients with small infarctions (score index 1.31–1.68) and a high probability of viable myocardium (all patients were referred to revascularization by the cardiologist; 82% of cases had a positive exercise test; contractile reserve or remote ischaemia was observed in 98% of patients). Data about baseline ST segments are not reported; in the work of Margonato et al.[2], patients with baseline ST-segment elevation (in general, those with more severe systolic dysfunction and less viability[4–7]) were excluded. Taking into account the lack of patients with severe dysfunctions (those in whom a viability study is indicated) and the highly selected study group (patients referred to revascularization by the cardiologist in charge, probably because of evidence of either ischaemic or viable myocardium) the relationship between stress-induced ST-segment elevation and myocardial viability, suggested by the authors, could not be generalized to all post-infarction patients.

We recently analysed the same issue in 51 consecutive patients shortly after myocardial infarction[3]. Regional wall motion, contractile reserve, left ventricular volumes and late improvement were quantitatively determined. Patients with baseline ST-segment elevation (n = 36) were not excluded. As in previous works, exercise-induced ST-segment elevation was not a predictor of contractile reserve[4–6], moreover, patients without ST-segment elevation had a greater response to dobutamine. Nevertheless it was not related to late improvement or remodelling. Cases without baseline ST-segment elevation but with exercise-induced ST-segment elevation had the greatest improvement with