

Letters to the Editor

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Mitral valve prolapse: *The Merchant of Venice* or *The Tales of Hoffman*?

I enjoyed reading the hotline editorial on mitral valve prolapse (MVP),

especially its title^[1]. Whether MVP claimed the life of Shylock in the *Merchant of Venice* who claimed the heart of Portia's lover^[1] or Antonia in the *Tales of Hoffman* who sang herself to death^[2], there is no question that, though generally a benign condition^[3], MVP may be a deadly disease at times^[4]. Up to 1989, 106 cases of sudden death have been reported as a complication of MVP^[5]. Whether increased plasma catecholamines related to stress ('Dr Miracle sings: 'Nineteen. Glorious springtime of life. And now, let me take your pulse . . . Sh! Quiet while I count . . . Her pulse — very uneven and fast (inegal

et vif). A dangerous symptom! Now sing! Now sing!^[2]. In Robert Lawrence's analysis^[6], '... the slimy Dr Miracle who . . . induces Antonia to sing herself to death while accompanying her on a macabre violin^[2] or present as an associated state of autonomic dysfunction/imbalance may predispose subjects to ventricular ectopy or catastrophic tachyarrhythmias, or both, is not known, but has been suggested^[5,7]. Increased QT dispersion with or without QT prolongation in MVP has also been recently postulated as an arrhythmogenic mechanism and shown to be a marker for sudden cardiac death^[8].

MVP may either be primary or secondary. In coronary artery disease, MVP may be the result of papillary muscle dysfunction^[9,10]. On the other hand, MVP may induce coronary artery spasm^[3]. Then, MVP and coronary artery disease, both being common diseases, may coexist^[3].

MVP is not only the most frequently diagnosed valve disorder in the United States but also a universal disease, having been described in nearly every country in the world^[11]. The reported prevalence has varied from less than 1% to as high as 38%, depending on whether the diagnosis is based on clinical or echocardiographic examination (Table 1)^[11]. When the diagnosis is based on echocardiographic examination, the view employed is also important, because the non-planar, hyperbolic-paraboloid or saddle-shaped mitral anulus allows mitral leaflets that are on the left ventricular side of the mitral anulus in the long axis view to appear to 'prolapse' into the left atrium in the apical four-chamber view^[12,13]. As Stefanadis and Toutouzas^[1] concluded, 'prudence in diagnosis, based on rigorous criteria and robust epidemiologic data, will define the true prevalence' of this ubiquitous disorder. By knowing the true prevalence of MVP, one can then better assess the risks of the disease^[14].

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Table 1 Prevalence of mitral valve prolapse around the world

Country	Male	Female	Overall
Australia*	4%	4%	4%
Brazil	—	—	4%
Britain*	—	2%	—
Britain	—	—	5%
Britain†	3.9%	5.2%	4.5%
Canada*	—	—	22%
China (Hans in Sichuan)*	2.2%	6.3%	4.3%
China (Kazaks in Xinjiang)	2.8%	7.7%	5.3%
China (school children in Guangdong)	—	—	1.9%
Denmark*	—	—	7%
Ethiopia*	15.4%	9.1%	13.3%
France	—	—	6%
Germany*	6.89%	13.84%	9.8%
Hong Kong (Chinese)	7.2%*	8%	7.7%*
	5.4%†	6.4%†	5.8%†
India (outpatient)	—	2.7%	—
India*	—	16%	—
Israel	—	—	5%
Italy	0.7%	3.3%	1.8%
Italy (blacks)	—	—	1.4%
Italy (athletes)	—	—	10%
Japan (school children)	0.78%	1.26%	1%
Japan†	1 × ‡	4 × ‡	7.5%
Japan*	11%	8%	11%
Korea	3.3%	10%	6.7%
Libya*	—	—	16.9%
Poland	—	—	4%
Russia*	—	—	2.64%
Russia (high altitudes)*	—	—	1.7%–10.9%
Saudia Arabia*	7.4%	12%	—
Spain	1 × ‡	2 × ‡	4.3%
South Africa	—	—	14.3%
South Africa (blacks)	—	—	17.9%
Sweden*	7%	8%	7.4%
Turkey*	—	—	7.6%
U.S.A.	3%	6.2%–17%	—
U.S.A. (blacks)*	9%	24%	17%
U.S.A. (health survey)	—	15.4%	—
U.S.A. (non-care-seeking adolescents)	2.25%	6.16%	4.18%
U.S.A. (children)*	31%	38%	35%
Yugoslavia (school children)	1.9%*	12.8%*	7.8%*
	—	—	18.1%

*Echocardiographic studies.

†Autopsy studies.

‡Expressed as a ratio.

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The role of tissue plasminogen activator on the progression of the coronary disease

We read with great interest the paper by Smith *et al.*^[1], which demonstrated the association between high levels of plasmatic tissue plasminogen activator (tPA) and increased risk of cardiovascular events in patients with angina pectoris. They performed a prospective study of the relationship between haemostatic and rheological factors

and cardiovascular events in subjects with angina pectoris. The authors conclude that the association of tPA and cardiovascular events is independent of the cardiovascular risk factors. We studied prospectively 55 survivors of a first acute low-risk myocardial infarction, and followed them up for 4 years. We measured tPA, its inhibitor (PAI-1), fibrinogen, von Willebrand factor, tissue factor and factor VII activity. For the classic cardiovascular risk factors, only low levels of high-density lipoprotein were associated with cardiovascular events. For the haemostatic parameters only tPA concentration was associated with an unfavourable evolution (new non-fatal acute myocardial infarct, unstable angina or death), with a relative risk of 1.4 (1.0–1.8, *P* 0.04) (using logistic regression). The predictive value of tPA was independent of the classic cardiovascular risk factors.

The role of antigenic tPA in cardiovascular disease is difficult to explain^[2]. An increase in tPA antigen concentration does not necessarily indicate stimulation of fibrinolytic activity. When we measure tPA antigen, we determine free tPA and tPA-PAI complexes^[3,4], therefore levels of tPA antigen are not similar to tPA activity^[5]. In the recent literature, enhanced levels of plasmatic haemostatic factors in arteriosclerosis are not considered to increase the propensity to thrombosis or fibrinolysis, but as an expression of the severity of vascular risk factors or vascular lesions^[6]. In this way and in agreement with Grant^[2] and Cushman^[6], the increase in antigenic levels of tPA may be related to plaque instability, since tPA may be important in destabilizing the fibrous caps of atheromatous plaques^[7], and in initiating a proteolytic cascade of matrix degradation of the plaque^[8].

Another explanation accepted by many authors, is the relationship between tPA plasmatic levels and the insulin resistance syndrome. Markers of impaired fibrinolysis, reflected by elevated tPA antigen and PAI-1 antigen levels, were significantly associated with hyperinsulinemia^[9], this situation belongs to a metabolic disorder called the insulin resistance syndrome. In the ECAT study^[10], the predictive value of tPA antigen was affected after adjustment by insulin resistance parameters and inflammation and endothelial cell damage markers, suggesting that tPA concentration may be influenced by a combi-

nation of pathological pathways. Contrarily Smith *et al.*^[1] conclude that tPA antigen may be an important risk factor in the development of atherothrombotic events, which is independent of the insulin resistance syndrome factors. It remains unclear whether tPA has a direct effect on thrombotic risk or if acts as a inflammation or endothelial damage marker.

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