Letters to the Editor


Clinical outcome after coronary events in patients treated with HIV-protease inhibitors

The introduction of highly active antiretroviral therapy (HAART) in 1996 has resulted in dramatic improvements in the immune status of HIV-infected patients. As a result, the spectrum of the cardiac manifestations encountered has turned from pericardial and myocardial opportunistic infections occurring in about 5% of patients to miscellaneous cardiac side-effects of drugs among which acute coronary events related to the use of HIV-protease inhibitors are increasingly recognized.

In a cohort of 700 HIV-infected patients treated with a combination of two reverse transcriptase inhibitors and one protease inhibitor (HAART), nine (1.3%) suffered acute coronary events between February 1996 and September 1999. All were men (mean age: 40±7 years), infected with the HIV for several years (first positive HIV-test: 6±1.3 years previously) and four of them had experienced previous opportunistic infections before highly active antiretroviral therapy was begun. Their past history also included mild hypercholesterolaemia in one patient, hypertension in another and eight of them were smokers. At presentation for the coronary event, highly active antiretroviral therapy (ritonavir:4; indinavir:5, saquinavir:2) lasted for 17.8±6.6 months and resulted in a complete viral control of plasma lipid levels and discontinuation of smoking, which was obtained in almost all patients. This may be particularly valuable because the onset of symptoms, with inaugural acute myocardial infarction in the setting of a dramatic increase in lipid levels during the year following the initiation of highly active antiretroviral therapy, may suggest that rupture of a vulnerable, lipid-rich and rapidly growing plaque might be the substrate. Finally, this also leads to the reinforcement of primary prevention, including careful control of plasma lipid levels and discontinuation of smoking in all HIV patients treated with highly active antiretroviral therapy.

Eight patients presented with acute myocardial infarction, two of them after a short-period of unstable angina, and one had exertion angina. Primary PTCA (n=10) was performed in eight patients, followed by four stent implantations in four patients. Primary success was achieved in all dilated lesions. Coronary angiography also showed a single vessel stenosis in three patients, two vessels in four others and three vessels in one, involving the left anterior descending coronary artery in six patients, the left coronary artery in five and the right coronary artery in four patients.

During a 22.7 months subsequent follow-up, adverse events occurred in three patients. Recurrent angina followed by lethal ventricular tachycardia and fibrillation occurred in one patient 10 days after primary PTCA of the distal left anterior descending coronary artery. Another patient died from facial cellulitis 1 year after the initial myocardial infarction. One patient experienced recurrent acute myocardial infarction 100 days after PTCA and was successfully treated with repeat PTCA and stenting of the same lesion of the right coronary artery. Finally, seven patients remained coronary-symptoms free after the initial cardiac events.

Seven of eight patients ceased tobacco consumption. Follow-up cholesterol of eight patients peaked at 5.45±0.88 mmol.L−1 (HDL-C: 0.65±0.38, LDL-C: 2.9±1.1), and triglycerides at 2.36±1.02. This was obtained by combining diet with lipid lowering drugs and by switching patients to HIV-protease inhibitors, which would have fewer hyperlipidaemic effects. After a mean 22.7 months follow-up, the eight patients who survived the acute phase are free of recurrent angina. Only one suffers mild shortness of breath. Their mean ejection fraction is 61±5.1% with an ejection fraction ≥55% in seven patients and ≤50% in only one of them.

Seven patients were subsequently exercised during a treadmill stress test, which was negative in all (five after discontinuation of antischaeemic therapy).

No severe ventricular premature beats or ventricular tachycardia were seen on a 24-h Holter ECG recording. Medical therapy at follow-up included aspirin (8), beta-blockers (8), nitrates (2), molsidomine (4), calcium-annel blocks (2), angiotensin converting enzyme inhibitors (1), statins (5), fibrates (3), cholestyramine (1).

Unlike myocardial and pericardial opportunistic infections, which have been reported to dramatically shorten the survival of HIV-infected patients[1–2,6–7], acute coronary events occurring in HIV-infected patients treated with highly active antiretroviral therapy, have a better prognosis. The relationship between acute coronary events and protease inhibitor therapy is still debated, since no case-control study has been performed until now. In our series, the largest published and the only one for which follow-up data are now available, the overall prognosis of patients is favourable, most of them being free of cardiac symptoms and recurrent coronary events. This has possibly been achieved by careful management of HIV-protease inhibitor-related lipid disorders, using a combined approach in which diet and lipid lowering drugs, plus discontinuation of the protease inhibitors, induced marked hyperlipaemia for other antiviral regimens with fewer metabolic effects[8].

Another important goal of secondary prevention focuses on smoking cessation, which was obtained in almost all patients. This may be particularly valuable because the onset of symptoms, with inaugural acute myocardial infarction in the setting of a dramatic increase in lipid levels during the year following the initiation of highly active antiretroviral therapy, may suggest that rupture of a vulnerable, lipid-rich and rapidly growing plaque might be the substrate. Finally, this also leads to the reinforcement of primary prevention, including careful control of plasma lipid levels and discontinuation of smoking in all HIV patients treated with highly active antiretroviral therapy.

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Cavotricuspid isthmus ablation and atrial fibrillation

I read with great interest the study by Reithmann and colleagues [1] concerning the efficacy of cavotricuspid isthmus ablation on the elimination of paroxysmal atrial fibrillation, as well as the editorial by Geelan and Brugada [2]. I do concur with the conclusions of the original study and the thoughtful comments of the editorial authors.

It is, however, rather disappointing to see that the earliest study to point out the possibility of treating atrial fibrillation by flutter ablation, published as early as in 1996 [3], has escaped the attention of the authors.

We have shown that patients without structural heart disease and a history suggestive of paroxysmal atrial fibrillation may have evidence of common atrial flutter triggering fibrillation episodes [3]. Should this be the case, this patient group may benefit by ablation of the flutter circuit. These patients usually present with episodes of both regular and irregular arrhythmias, suggesting supraventricular tachycardia and paroxysmal atrial fibrillation. Ambulatory electrocardiographic monitoring may reveal that atrial fibrillation is preceded by a narrow QRS complex tachycardia with characteristics of typical atrial flutter. At electrophysiology study, typical atrial flutter is inducible in all patients but is noted to spontaneously degenerate into flutter/fibrillation, with recording of flutter waves from the right atrium and typical fibrillation from the left atrium. Catheter ablation of the cavitricuspid isthmus eliminates the paroxysms of atrial fibrillation, particularly if the arrhythmia is not inducible following ablation [3-4].

The mechanism of prevention of atrial fibrillation by this ablation approach is not clear. Konings et al. [5] have identified a subgroup of patients with atrial fibrillation in the context of normal atria, who demonstrated broad uniform fronts propagating in the right atrium, probably as part of a large circuit. We do not know whether ablation of the cavitricuspid isthmus area modified the background of atrial fibrillation itself or simply eliminates an important stimulus for the induction of atrial fibrillation in such patients groups. Apart from patients with flutter-fibrillation, patients with flutter-like organized activity around the tricuspid valve during atrial fibrillation may also benefit from such an approach [6]. It seems that interruption of the isthmus may be beneficial in broader patient groups with atrial fibrillation, and preliminary results suggest that the lesion does not appear to be proarrhythmic [7].

Atrial fibrillation, particularly in its paroxysmal form, is not a single entity; it comprises a variety of arrhythmographic disorders which might be amenable to catheter ablation therapy. Our observations as well as others’ underline the importance of full electrophysiological assessment of patients presenting with the clinical syndrome of paroxysmal atrial fibrillation.

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References


Clinical trials for conversion of recent onset atrial fibrillation must consider the role of digoxin

Clinical trials comparing the efficacy of amiodarone vs placebo in the conversion of recent onset atrial fibrillation have controversial results. While some series showed no difference between amiodarone and placebo [1-3], others, with higher doses of amiodarone or a longer period