Anticoagulant therapy and atrial fibrillation

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Atrial fibrillation (AF) is one of the most common cardiac arrhythmias but the only one known to be associated with an increased risk of systemic embolism (SE).

In a review of several studies [10], Fisher found that the site of 43 to 82 percent of SE associated with AF was localized in the cerebral arteries; in a retrospective study [11], Harrisson and Marshall noted that emboli from the fibrillating atrium, probably because of their size, cause usually "long" transient ischemic attacks (TIAs) or completed strokes. In a review of cardiogenic brain embolism [6] Dyken and al found that about 50 percent of presumed cardiogenic embolic strokes resulted from valvular or non-valvular AF, and that stokes associated with AF were often large, functionally devastating and usually unheralded by warning TIAs. Therefore, an effective therapy obviously appears essential for the prevention of these severe complications.

However, the incidence of SE in AF varies with different predisposing factors associated with the dysrhythmia itself. Thus, the annual rate of SE ranges from below 1 percent in patients with lone AF and younger than 60 years [14] to about 17 percent in those with AF and a previous history of SE [19]. Added
to that, adverse effects are not uncommon in long term anticoagulant therapy. With conventional levels of anticoagulation, risk of brain haemorrhage is about 1 percent per year and risk of severe haemorrhage is 2 percent per year [6]. This risk is increased in patients over 65 years, with renal insufficiency, hypertension, history of previous stroke and with the intensity of anticoagulation [16]. Consequently, while an aggressive antithrombotic therapy is justified in patients with high risk of SE, in those at lower risk the expected benefit of therapy should always be balanced against haemorrhagic complications.

Furthermore, blood stasis by releasing the activation of the coagulation system and the generation of fibrin induces thrombus formation in the left atrial chamber (or in the atrial appendage) which constitute the main source of SE [22]. Visualisation by transesophageal echocardiography of spontaneous contrast echoes within the left atrium and the atrial appendage [5] and the increase of plasma D-dimer levels [15] in patients with AF seem to confirm this mechanism. However, the presence of AF does not necessarily mean that an ischemic event is or will be due to cardiogenic embolism [6]. In non-valvular AF and especially in elderly patients, concomittant cerebrovascular or atherosclerotic ascending aortic diseases must be sought [7]. Thus, the prevalence of carotid artery stenosis is two-fold higher in patients with non-valvular AF [25], and it seems likely that at least 20 to 30 percent of strokes in patients with non-valvular AF are not due to cardiogenic embolism [12]. Consequently, in some cases, the use of antiplatelet agents should be considered as an alternative therapy to anticoagulant medication.

It is acknowledged that the risk of SE in patients with AF varies with the underlying heart disease. Thus, there is a 17-fold increase in stroke associated with AF and rheumatic mitral valve disease [13], and the annual rate of SE is estimated to be about 6 percent in patients with AF and mitral stenosis [16]. Therefore, despite the lack of randomized placebo controlled trials, anticoagulant therapy at a dose sufficient to obtain an International Normalized Ratio (INR) 2.0 to 3.0 has been used in these patients for