myocardial infarction, or stroke. Furthermore, in comparison with heparin, fondaparinux significantly reduced major bleeding (2.2% versus 3.7% reduction, respectively) and fatal bleeding events (24 versus 40). Similar benefits were observed in patients who underwent invasive and conservative treatment strategies. The authors' results indicate that administration of fondaparinux, instead of heparin, to patients with a broad range of acute coronary syndromes could prevent 10 major bleeding events, 3 myocardial infarctions or strokes, and save 5 lives for every 1,000 patients treated.

Original article Mehta SR *et al.* (2008) Antithrombotic therapy with fondaparinux in relation to interventional management strategy in patients with ST- and non-ST-segment elevation acute coronary syndromes: an individual patient-level combined analysis of the Fifth and Sixth Organization to Assess Strategies in Ischemic Syndromes (OASIS 5 and 6) randomized trials. *Circulation* **118:** 2038–2046

Atrial fibrillation: oral anticoagulation therapy or antiplatelet therapy?

The efficacy of oral anticoagulation therapy for atrial fibrillation depends on preservation of the international normalized ratio within the established therapeutic range (2.0–3.0). Wide variation in the mean time in therapeutic range (TTR) of oral anticoagulation therapy has been reported, and a low TTR is associated with an increase in adverse events. In a multicenter, multinational study, Connolly *et al.* evaluated the benefit of oral anticoagulation versus clopidogrel plus aspirin according to the achieved TTR, and determined the minimum TTR required to confer a clinical benefit.

Data from ACTIVE (Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events) W were used to calculate the TTR of oral anticoagulation compared with that of clopidogrel plus aspirin therapy. The mean TTR for all patients was 63.4% (median 65%); the mean TTR for patients in individual countries ranged from 46% to 78%. Each study centre was assessed in terms of mean TTR and likelihood of a positive response to oral anticoagulation. Patients in centers with a mean TTR >65% benefited from oral anticoagulation therapy, whereas counterparts in centers with a mean TTR <65% experienced no such benefit. Connolly and colleagues suggest that medical centers unable to achieve a TTR >65% should consider treating patients with atrial fibrillation with therapies other than oral anticoagulation, such as antiplatelet therapy.

Original article Connolly SJ *et al.* (2008) Benefit of oral anticoagulant over antiplatelet therapy in atrial fibrillation depends on the quality of international normalized ratio control achieved by centers and countries as measured by time in therapeutic range. *Circluation* **118:** 2029–2037

Low-density lipoprotein receptor gene mutations diagnose familial hypercholesterolemia

Familial combined hyperlipidemia is difficult to diagnose definitively, as the inherited abnormality shares clinical characteristics with familial hypercholesterolemia. The low-density lipoprotein receptor (*LDLR*) and apolipoprotein B (*APOB*) genes are defective in familial hypercholesterolemia, but not in familial combined hyperlipidemia. Civeira and colleagues, therefore, investigated the frequency of *LDLR* and *APOB* gene mutations in patients diagnosed with familial combined hyperlipidemia, to correctly identify those with familial hypercholesterolemia.

The team recruited 143 patients with a diagnosis of familial combined hyperlipidemia (aged 51 ± 11 years, 93 men) from two lipid clinics in Spain. Patients underwent screening by Lipochip® (Progenika, Derio, Spain), a microarray that can identify mutations in *LDLR* and *APOB* genes.

Genetic defects (22 different mutations) were found in the *LDLR* gene of 28 patients; no *APOB* defects were identified. Compared with patients showing no *LDLR* mutations, patients with *LDLR* defects had higher serum levels of apolipoprotein B, LDL cholesterol, non-HDL cholesterol, and total cholesterol, lower triglyceride levels, and no cases of diabetes mellitus (versus 26 cases in patients without *LDLR* defects). Patients with *LDLR* mutations were more likely to have total cholesterol levels >335 mg/dl or apolipoprotein B levels >185 mg/dl, which the authors suggest indicates a diagnosis of familial hypercholesterolemia, rather than familial combined hyperlipidemia. Civeira *et al.* recommend, therefore, that patients with a clinical diagnosis of familial combined hyperlipidemia be screened for