This study shows that combined antiplatelet and anticoagulant therapy is effective in patients with mitral stenosis, but that patients with a history of prior embolism might benefit from increased anticoagulation therapy.

Claire Braybrook

Original article Pérez-Gómez F *et al.* (2005) Effect of antithrombotic therapy in patients with mitral stenosis and atrial fibrillation: a sub-analysis of NASPEAF randomized trial. *Eur Heart J* [doi: 10.1093/eurheartj/ehi667]

Is patent foramen ovale associated with an elevated risk of stroke?

Data supporting a link between patent foramen ovale (PFO) and stroke have generated controversy, partly because studies have not accounted for age or comorbidity and inappropriate controls have been used. Following the Stroke Prevention Assessment of Risk in a Community (SPARC) study, Meissner *et al*. have assessed whether PFO is an independent risk factor for stroke and atrial septal aneurysm (ASA) in the general population.

A total of 585 individuals aged at least 45 years were randomly selected from the SPARC study cohort. Participants were screened with transesophageal echocardiography for PFO and ASA. The incidence of cerebrovascular-related deaths, ischemic stroke and transient ischemic attacks was recorded over a median follow-up of 5.1 years.

PFO was detected in 140 (24.3%) of 577 individuals, confirming that this heart defect is common in the general population. ASA was found in 11 (1.9%) individuals, and 6 (4.3%) people with PFO also had ASA. At follow-up, a cerebrovascular event had occurred in 12 individuals with PFO, and in 41 study participants in total. By use of Kaplan–Meier analysis, the investigators ascertained that the incidence of cerebrovascular events over 5 years was similar in individuals with or without PFO, indicating that PFO is not linked with an elevated risk of stroke in the general population. Although there was a trend toward increased risk of stroke for people with ASA, the authors note that larger studies are required to confirm this potential association.

Claire Braybrook

Original article Meissner I *et al.* (2005) Patent foramen ovale: innocent or guilty? Evidence from a prospective population-based study. *J Am Coll Cardiol* **47:** 440–445

Should muraglitazar be approved by the FDA for the treatment of type 2 diabetes?

An FDA advisory committee recently recommended approval of muraglitazar, an agonist for both peroxisome proliferative-activated receptors α and γ, as monotherapy for type 2 diabetes and as combination therapy in patients with blood glucose inadequately controlled by metformin. Nissen *et al*. reanalyzed the data presented to the advisory committee, obtained from publicly disclosed FDA documents. The authors sought to determine the risk of cardiovascular events in patients treated with muraglitazar, compared with controls.

Overall, 2,374 muraglitazar-treated patients and 1,351 controls (823 taking the comparator drug pioglitazone and 528 placebo) with type 2 diabetes were included, from one phase II and four phase III trials. Patients treated with muraglitazar doses ≥10 mg were excluded, as approval for these doses was not sought. Cardiovascular death, congestive heart failure, transient ischemic attack, nonfatal myocardial infarction or nonfatal stroke occurred in 2.11% of patients taking muraglitazar versus 0.81% of controls (relative risk = 2.62; $P = 0.004$).

The analysis by Nissen *et al.* was limited to data available through the FDA website and could not, therefore, allow a more complex statistical analysis; however, considering the number of adverse events in the short period (24–104 weeks) of these trials, the authors recommended that FDA approval for muraglitazar be postponed. The FDA subsequently stated that muraglitazar would not be approved without further long-term cardiovascular safety data (SE Nissen, personal communication).

Rebecca Doherty

Original article Nissen SE *et al.* (2005) Effect of muraglitazar on death and major adverse cardiovascular events in patients with type 2 diabetes mellitus. *JAMA* **294:** 2581–2586