Heartbeat: lower risk of dementia with a direct oral anticoagulant, compared to a vitamin K antagonist, for patients with atrial fibrillation

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Patients with atrial fibrillation (AF) have a higher risk of dementia and mild cognitive impairment, in addition to a fivefold higher risk of stroke, compared with patients in normal sinus rhythm. Potential mechanisms of cognitive impairment or dementia related to AF include recurrent micro emboli versus cerebral hypoperfusion in association with increased oxidative stress, inflammation and disruption of the blood-brain barrier. Using linked electronic health records from the Clinical Practice Research Datalink in the UK, Cadogan and colleagues compared the incidence of dementia or mild cognitive impairment in 39200 patients (median age 76 years, 45% women) with AF treated with either a vitamin-K antagonist (VKA) or a direct oral anticoagulant (DOAC). Incident dementia was diagnosed in 3.2% with a 16% lower risk of dementia in patients treated with a DOAC versus VKA (adjusted HR 0.84, 95% CI: 0.73 to 0.98). Mild cognitive impairment was diagnosed in 4.0% with a 26% lower risk in those treated with a DOAC versus VKA (adjusted HR 0.74, 95% CI: 0.65 to 0.84) (figure 1). For patients taking a VKA, greater time with anticoagulation in therapeutic range was associated with a lower risk of dementia.

In the accompanying editorial, Chua points out that ‘The exact mechanisms linking AF and dementia are likely to be complex and multifactorial, presenting a demanding challenge for researchers to tackle. Nevertheless, it is apparent that one of the most plausible risk factors for brain dysfunction is the presence of chronic and recurrent microemboli. Within this framework, cognitive decline and dementia manifest on a disease spectrum which includes transient ischaemic attacks and stroke. Therefore, intuitively, the use, timing and efficacies of oral anticoagulants play a role in modifying this risk.’ Although the study by Cadogan...
Heart and colleagues suggest that anticoagulant therapy in patients with STEMI. Kaplan-Meier survival curves depicting the association of admission hs-cTnT quartiles with probability of in-hospital (A) and overall (B) mortality in patients with STEMI. Kaplan-Meier survival curves displaying the association between 12-hour post-PCI hs-cTnT quartiles and in-hospital (C) as well as overall mortality (D). hs-cTnT, high-sensitivity cardiac troponin T; PPCI, primary percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

and colleagues suggest that anticoagulation is effective for prevention of cognitive decline, prospective studies still are needed. In addition, further attention should be directed toward the complex issues of adherence to and persistence with anticoagulant therapy in patients with atrial fibrillation.

Also in this issue of Heart, Dolgner and colleagues report that in a retrospective study of 346 adults with a secundum atrial septal defect (ASD), 10% presented with a history of stroke despite no known history of atrial arrhythmias. Risk factors for stroke in these patients with an uncorrected ASD were a body mass index over 25 kg/m² (OR: 18.2; 95% CI: 4.0 to 82.2; p < 0.001), smoking (OR: 9.5; 95% CI: 3.8 to 23.9; p < 0.001) and a prominent Eustachian valve (OR: 9.2; 95% CI: 3.4 to 25.2; p < 0.001) (figure 2). There was no significant difference in the size of the ASD between those with and without a stroke, with a median ASD diameter of 13 mm (range 11 to 20 mm), and most patients in both groups had right ventricular enlargement. Based on these findings, the authors suggest that paradoxical embolism across an uncorrected ASD may contribute to the risk of stroke, raising the question of whether ASD closure may be warranted even in the absence of current haemodynamic criteria.

Fraisse, Hascoet and Kempny discuss how these findings challenge our current paradigm that ‘the main indication for closing a secundum ASD is a significant left-to-right shunt’. Although the current study has some limitations, ‘Dolgner et al should be congratulated for providing additional evidence to support ASD closure for secondary and even primary stroke prophylaxis.’ However, as they conclude, ‘Further studies are urgently needed to better identify patients with ASD who should undergo closure of haemodynamically non-significant defects, to reduce the risk of first or recurrent stroke.’

In patients presenting with a possible ST-elevation myocardial infarction (STEMI) the diagnostic role of high-sensitivity cardiac troponin T (hs-cTnT) is well established. However, the prognostic value of hs-cTnT levels is less clear, particularly in the setting of primary percutaneous coronary intervention (PPCI). In a retrospective longitudinal study of 3113 consecutive STEMI patients treated with PPCI, Coelho-Lima and colleagues sought to determine the prognostic value of both pre- and post-reperfusion hs-cTnT levels. At a median follow-up of 4.4 years, an admission hs-cTnT in the highest quartile (>515 ng/L) was associated with both in-hospital (HR = 2.53 per highest to lower quartiles; 95% CI: 1.32 to 4.85; p = 0.005) and overall (HR = 1.27 per highest to lowest quartiles; 95% CI: 1.02 to 1.59; p = 0.029) mortality even after multivariable adjustment (figure 3). However, post-reperfusion hs-cTnT levels were not predictive of clinical outcome.

McLeod, Adamson and Coffey point out that ‘Despite significant advances in the treatment of ST elevation myocardial infarction (STEMI), there remains a significant short-term and long-term
increased mortality risk. Risk stratification to target those who may benefit from more intensive therapy post-revascularisation therefore remains an important goal.’ Current clinical risk scores are imperfect as many were developed in the thrombolytic era, or include few patients with STEMI undergoing PPCI. Potential mechanisms for the association between baseline hs-cTnT and mortality are discussed (figure 4), but it remains unclear what action would ensue after identifying patients at high risk. As they conclude: ‘Future research should focus on linking risk prediction with changes in management, and in the meantime all patients presenting with STEMI should be treated as high risk.’

The Education in Heart article 7 in this issue reviews the evidence and guideline recommendations for the use of hs-cTnT for early ‘rule-out’ pathways for myocardial infarction. Practical guidance is provided on implementation of an early rule-out strategy in clinical practice, along with a discussion of the strengths and limitations of different approaches and some difficult clinical situations.

In the Cardiology in Focus article in this issue, Steiner and Cooper* provides insight into building a career that combines both cardiology and palliative care. This multi-disciplinary career pathway is especially important both from a clinical point of view for optimising care of patients with chronic cardiac conditions, such as heart failure, and from a research point of view ‘to answer the many questions related to the application of palliative care principles to patients with heart disease.’

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