Antiplatelet therapy following TAVI: time to randomise

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Published online: 8 January 2014

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Following the introduction of transcatheter aortic valve implantation (TAVI), it is now possible to treat elderly patients with severe aortic stenosis and a high surgical risk. This advancement in interventional cardiology has led to increased survival, health status and quality of life. However, as with many invasive interventional procedures, TAVI is associated with the risk of cerebral embolisation and consequent ischaemic cerebrovascular events with possible neurological impairment. The risk estimates of post-procedural stroke associated with TAVI vary from 1.5 to 10 % and have been reported both early and late after the procedure. In the PARTNER Cohort B study, the Canadian multicentre TAVI registry and the study by Nuis et al., about 50 % of the stroke events occurred more than 24 h post-procedure [1]. In addition to clinically overt stroke, asymptomatic silent cerebral infarcts have been frequently observed on MRI, with a prevalence ranging from 62 to 93 % [2]. Although asymptomatic, accumulating evidence implicates that these silent cerebral infarcts are related to risk of future stroke, cognitive decline, dementia, and depression. Whether stroke occurs due to incomplete endothelialisation of the valve or by new onset of silent atrial fibrillation is unknown. Early post-procedural stroke (<24 h) is more likely the result of embolisation during valve implantation.

Given this high incidence of cerebral events, adequate anticoagulation is probably required both during the procedure and in the following months. However, the exact regimen of anticoagulation involves a clinical dilemma with the therapeutic potential of reducing ischaemic complications at the expense of increasing the bleeding risk. The overall incidence of bleeding following TAVI has been reported in 41 % of the

patients in the meta-analysis conducted by Généreux et al., of which 16 % were life-threatening [3]. It is important to bear in mind that life-threatening bleeding is associated with a six- to nine-fold increase in 30-day mortality after procedure and acts as an independent predictor of 1-year mortality [4]. Therefore, for clinical decision-making on antithrombotic treatment, it is important to find a balance between prevention of ischaemic complications and avoidance of bleeding risk.

The recently published study by Nijenhuis et al. addresses this clinical dilemma regarding decision-making on anticoagulation treatment of elderly patients treated with TAVI [5]. As pointed out by the authors, the current European and American guidelines merely provide recommendations based on retrospective registries. The European Society of Cardiology guidelines recommend a combination of low aspirin and a thienopyridine early after TAVI, followed by aspirin or a thienopyridine alone. In those cases where there is an indication for treatment with vitamin K antagonists, such as in atrial fibrillation, a combined treatment of vitamin K antagonist and aspirin or a thienopyridine is in general installed. However, the guidelines do not provide any recommendations on the duration of dual antiplatelet therapy (DAPT).

As observed in the survey undertaken in the Netherlands, a wide heterogeneity in the duration of dual antiplatelet therapy (DAPT) and loading dose of clopidogrel was noted. In two-thirds of the centres ($n=9$) DAPT was prescribed for 3 months. In one centre, where only transapical TAVI is performed, no concomitant clopidogrel was prescribed at all. The duration of concomitant clopidogrel was dependent on the type of prosthesis in only two centres according to the recommendations of the respective manufactures, 6 months versus 3 months for supra-annular Core Valve[™] and intra-annular prostheses (e.g. SAPIEN[™], JenaValve), respectively. Whether the decision on the duration of concomitant clopidogrel and its loading dose indeed should be dependent on the valve type (SAPIEN[™] or Medtronic Core Valve[™]) or procedural approach

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(transfemoral or apical) has not been described in the literature. Moreover, clinical decision-making becomes more complex in circumstances where there is a high bleeding risk, PCI (<1 year) prior to TAVI, triple therapy pre-TAVI and new-onset atrial fibrillation. This is nicely illustrated in the survey of the participating centres showing different approaches to these scenarios.

In conclusion, the appropriate regimen of antiplatelet and anticoagulant therapy following TAVI is undefined and warrants the conduction of randomised controlled trials for clinical decision-making in this steadily growing patient population.

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