Peri-procedural antithrombotic bridging and the assessment of the associated risk of major bleeding

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Haemostasis refers to the continuous process of balancing the (sometimes iatrogenic) pro- and anti-thrombotic forces. The delicacy of this balance is exemplified by conditions, such as atrial fibrillation (AF), which cause a chronic prothrombotic distortion, but the consequent use of antithrombotic therapy increases the risk of major bleeding, especially intracranial haemorrhage (which is the most devastating complication of anticoagulation therapy). Therefore, the everyday antithrombotic management of anticoagulated patients is challenging as the benefits and risks need to be carefully judged for each and every patient.

In AF, updated and new risk stratification tools for stroke (CHA2DS2-VASC) (1) and major bleeding (HAS-BLED) (2) improve the guidance on long-term antithrombotic management of AF patients. However, similar degree of guidance regarding bleeding risk assessment in a clinically important ‘temporary’ aspect of antithrombotic therapy management remains lacking, that is, peri-procedural antithrombotic management (3).

In this issue of *Thrombosis and Haemostasis*, Omran and co-workers (4) present a German, multi-centre prospective cohort study among 1,000 anticoagulated patients undergoing a planned intervention and aimed to study the impact of an antithrombotic therapy bridging regimen on the short term (30 day) risk of thromboembolic events and major bleeding, as well as the clinical predictors of the latter. Their cohort was predominantly male (65%) and had AF (81%), and coronary angiography was the most common reason for bridging (66%). In 6.1% of patients, no bridging therapy was given. Apart from two patients receiving unfractionated heparin (UFH) the remaining patients were treated with weight-adjusted low-molecular-weight heparin (LMWH) (72.7%), fully therapeutic LMWH (18.8%) or a prophylactic LMWH dose (2.2%). Thromboembolic events occurred in four patients and clinically relevant bleeding events in 36. Their novel finding was that a high (>3) HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalised ratio, Elderly (>65 years) score was an independent predictor of major bleeding during antithrombotic therapy bridging, as well as a previous history of mechanical valve replacement (MVR).

The patients of the cohort presented by Omran et al. (4) were included because of a variety of reasons to discontinue anticoagulation (3). As the pro-thrombotic mechanisms – and thereby risks – associated with these procedures are likely to differ, perhaps a first question is whether interruption of anticoagulation is always necessary?

Jamula et al. performed a systematic review which included eight studies comparing two strategies for perioperative anticoagulation management in patients undergoing pacemaker or implantable cardiac defibrillator (ICD) implantation: interruption of a vitamin K antagonist (VKA) and use of bridging anticoagulation or perioperative continuation of VKA (5). The incidence of pocket haematoma was much higher in the group receiving bridging therapy compared to the group who continued the oral anticoagulation (12–20% vs. 1.9–6.6%). Looking at thromboembolic events, the incidence was only 0.1% irrespective of the used strategy (5). Similar evidence exists that for patients undergoing catheter ablation for AF (6) and elective coronary angiography (7), whereby uninterrupted VKA is safe with respect to bleeding events and may even help prevent peri-procedural (silent) strokes.

Thus, peri-procedural continuation of anticoagulation can be safe and even associated with less bleeding events compared to antithrombotic bridging, and it appears to be rightful for clinicians to firstly question the necessity to switch from warfarin to some form of antithrombotic bridging based on the type of procedure. Of note, recent consensus recommendations from Europe and North American do not advocate bridging therapy in patients undergoing coronary angiography, which should be performed whilst the International Normalised Ratio on warfarin is within the therapeutic range (8–10).

Secondly, given the relative benefit of continuing oral anticoagulation under the circumstances described above and in light of the upcoming new oral anticoagulants (dabigatran, rivaroxaban and apixaban) it is also important to know whether these convenient drugs could convince even more physicians to continue the oral anticoagulants. Unfortunately, the available data are extremely scarce. One study by Lakkireddy et al. analysed patients undergoing ablation and compared patients who continued warfarin periprocedurally with patients on dabigatran who only stopped dabigatran the morning of the procedure and resumed the dabigatran within 3 hours after haemostasis. The dabigatran group showed a significantly increased risk of bleeding or thromboembolic complications compared to the patients with uninterrupted warfarin therapy (11). This is
in contrast to a smaller single-centre cohort, which found that appropriate post- 
ablation management with dabigatran (with drug cessation dependant upon renal 
function and bridging, where necessary) was associated with a low risk of embolic or 
bleeding complications (12).

Thirdly, when discussing (the performance of) bleeding risk assessment tools the 
definitions used to characterise bleeding events are important. Beside the classic dis- 
crimination between minor and major bleeding, more and more attention is being 
paid to so-called non-major clinically relevant bleeding. In their paper, Omran et al. 
have chosen to combine the latter type with the classic ‘major bleeding’ definition into 
the endpoint of ‘clinically relevant bleeding’: bleeding requiring acute treatment/ 
re-surgery, medical evaluation, or transfusion with less than two units of blood, or 
need for prolonged hospitalisation (4).

Finally, regarding the actual bleeding risk and assessment of peri-procedural 
antithrombotic bridging, Omran et al. found – for the first time – that the HAS- 
BLED score was the strongest independent predictor of clinically relevant bleeding 
events in (AF and non-AF) patients undergoing bridging therapy. Although their novel 
findings need to be confirmed in other studies, the observation that the user- 
friendly HAS-BLED score is a reliable tool to predict major bleeding during peri- 
procedural bridging perhaps does not come as a surprise given the recent confirmation of 
its true bleeding risk predictive nature in AF populations (13, 14). Indeed, the HAS- 
BLED score is recommended in the European and Canadian guidelines on atrial fi- 
brillation, to assess potential bleeding risk; however, a high HAS-BLED score per se is 
not a reason to stop anticoagulation but to ‘flag up’ the patients that need extra review 
and follow-up, as well as attention to cor- 
rectable risk factors for bleeding (e.g. un- 
controlled blood pressure (the ‘H’ in HAS- 
BLED) and labile INRs if on warfarin (the 
‘L’ in HAS-BLED)). Also, the HAS-BLED 
score has been shown to outperform other 
bleeding risk assessment schemes (includ- 
ing the new ATRIA score) in its predictive 
value for serious bleeding events (15).

What are the clinical implications of the 
study by Omran et al.? Similar to its intend-