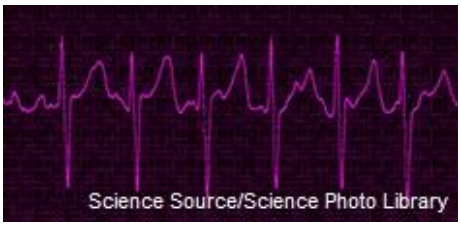
Perioperative anticoagulation for people with atrial fibrillation

A US randomised controlled trial found that not using 'bridging' heparin in people with atrial fibrillation who stopped taking warfarin before elective surgery or an invasive procedure had no adverse effect on the risk of thromboembolism or bleeding.

Overview:

- A randomised controlled trial in the USA and Canada studied people with atrial fibrillation who stopped taking warfarin before elective surgery or an invasive procedure.
- People who did not receive 'bridging' heparin had a lower risk of bleeding and no higher risk of thromboembolism than those who did receive heparin.
- This study is applicable to people with atrial fibrillation in the UK, although the dose of bridging heparin used was around twice that used in the UK.



Background: People with atrial fibrillation are at increased risk of developing blood clots that can block blood flow to a tissue (thromboembolism) such as the brain (Benjamin et al. 1998). Many people with atrial fibrillation regularly take anticoagulation drugs, such as warfarin, to reduce this risk of blood clots and stroke.

Surgery and invasive procedures are associated with a risk of bleeding, which may be increased by anticoagulation therapy in people with atrial fibrillation (Gallego et al. 2012). Warfarin is typically stopped several days before a procedure in people with atrial fibrillation and resumed afterwards (Baron et al. 2013). However, stopping anticoagulation therapy may temporarily increase the risk of thromboembolism, although the size of the risk is not known.

During the interruption of warfarin treatment, 'bridging' anticoagulation therapy, such as with low-molecular-weight heparin, can be used to minimise the time that people with atrial fibrillation do not have anticoagulation. However, the efficacy of this approach is unknown, and it may be associated with a higher risk of bleeding and adverse events (Steinberg et al. 2015).

Current advice: The NICE guideline on atrial fibrillation recommends assessing the risk of stroke using the CHA_2DS_2-VASc score in people with:

- symptomatic or asymptomatic paroxysmal, persistent or permanent atrial fibrillation

- atrial flutter
- a continuing risk of arrhythmia recurrence after cardioversion back to sinus rhythm.

Anticoagulation should be offered to men with a CHA_2DS_2-VASc score of 1, and men or women with a CHA_2DS_2-VASc score of 2 or more. The risk of bleeding should be taken into account.

The recommended options for anticoagulation are apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist. The options for anticoagulation should be discussed with the person, and the choice of drug based on their clinical features and preferences.

The NICE pathway on atrial fibrillation brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.

New evidence: Douketis et al. (2015) investigated whether using bridging anticoagulation therapy was necessary in people with atrial fibrillation who were undergoing an operation or other invasive procedure.

This randomised controlled trial enrolled adults with atrial fibrillation or flutter from 108 sites in the USA and Canada. Participants had to have been receiving warfarin therapy for at least 3 months and be scheduled to undergo an elective operation or invasive procedure that merited stopping warfarin therapy.

A total of 1884 people were assigned to bridging anticoagulation therapy with low-molecular-weight heparin (dalteparin sodium; n=934), or a matching placebo (n=950). Participants stopped warfarin 5 days before their procedure. They then received the assigned study drug at 3 days before the procedure until approximately 24 hours before the procedure, and for 5–10 days after the procedure.

At 30 days, the incidence of arterial thromboembolism (such as stroke or transient ischaemic attack) was 0.4% (4/918 participants) in the no bridging group and 0.3% (3/895 participants) in the bridging group (mean between-group difference=0.1 percentage points, 95% confidence interval [CI] −0.6 to 0.8 percentage points). The event rates indicated that in terms of thromboembolism risk, not using bridging anticoagulation was not inferior to using bridging anticoagulation (p=0.01 for non-inferiority).

Major bleeding occurred in 1.3% (12 participants) of the no bridging group and 3.2% (29 participants) of the bridging group. The risk of major bleeding was significantly lower in the no bridging group than in the bridging group (relative risk=0.41, 95% CI 0.20 to 0.78, p=0.005).

Limitations of this study include that the majority of participants (73.4%) were men and most were at low risk of stroke (mean $CHADS_2$ score=2.3), so the findings may not be generalisable to women or higher risk populations. In addition, the sample size was smaller than planned because of lower than expected rates of thromboembolism.

Commentary by Prof Beverley Hunt, Professor of Thrombosis & Haemostasis at Kings College London and Consultant at Guy's & St Thomas' NHS Foundation Trust:

"Warfarin has been the mainstay of oral anticoagulation for people with atrial fibrillation at risk of ischaemic stroke for the last 60 years. Management is not easy, however, because of warfarin's slow onset and offset of action and unpredictable pharmacokinetics. Due to the long period of time taken for the anticoagulation effect of warfarin to diminish, it is normal practice to stop warfarin 5 days before an operation in people with atrial fibrillation. To mitigate the perceived risk of the person having an arterial thromboembolic event while warfarin levels are falling, it has been normal practice to offer 'bridging' anticoagulation therapy with a short acting low-molecular-weight heparin such as dalteparin sodium, enoxaparin, or tinzaparin sodium.

"This study is the first to look at the utility of bridging anticoagulation therapy in people on long-term warfarin for atrial fibrillation. It found that there was no increased risk of arterial thromboembolism without heparin bridging, a very important finding with enormous practical implications. Moreover, from the safety perspective there was also a statistically lower rate of

major and minor bleeding in those who did not receive heparin bridging.

"However, the doses of heparin used in this US-based study were based on weight and were considerably greater than those used in the UK, where bridging is usually a fixed dose. So for example, a 70 kg man in this study would have received 7,000 IU dalteparin twice daily. In the UK, he would have received 5,000 IU once daily. Therefore the dose would have been more than double the UK dose, so the increased bleeding rate seen in this study cannot be applied to UK-based practice.

"There is an international drive to improve the care of people on warfarin that has paradoxically coincided with the emergence of more efficacious and safer alternatives, such as the direct oral anticoagulants apixaban, dabigatran etexilate, rivaroxaban and edoxaban. These drugs are being used increasingly in preference to warfarin for the prevention of stroke in atrial fibrillation. Managing bridging anticoagulation in people receiving direct oral anticoagulants is much easier, because of their short onset and offset of action. Therefore this study has no applicability to patients with atrial fibrillation on direct oral anticoagulants."

Study sponsorship: US National Heart, Lung, and Blood Institute.

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