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Pearls in Anticoagulation Management for Patients With Left Ventricular Assist Devices

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Introduction

Patients with left ventricular assist devices (LVADs) are at a high risk of both bleeding and thrombotic complications. Patients must be on therapeutic anticoagulation to prevent pump thrombosis, but many develop acquired von Willebrand disease from the shear stress.[1] Careful management of anticoagulation is essential for these patients.

Current Recommendations

The manufacturer of the HeartMate 3 LVAD (Abbott Vascular) recommends bridging with heparin, with gradual titration to therapeutic levels. In addition to warfarin, 81 to 100 mg aspirin is recommended, with a target international normalized ratio (INR) of 2 to 3 as long-term therapy.[2]

Warfarin inhibits vitamin K epoxide reductase, which is required to activate factors II, VII, IX, and X. It helps prevent the production of new clotting factors, but existing clotting factors need time to break down based on their half-lives. Warfarin is monitored using prothrombin time/INR, which is a measure of the extrinsic pathway and mainly reflects factor VII. Factor VII has the shortest half-life, however, so a change in the INR at the beginning of therapy may not reflect the amount of residual factor activity remaining. As a result, warfarin may take 3 to 5 days to take full effect, and rapid uptitration of warfarin at the beginning of therapy is not recommended. Starting doses of 2.5 to 7.5 mg warfarin are recommended, depending on the patient's age, baseline INR, drug-drug and disease-state interactions, and genetic factors. An increase in INR of 0.3 to 0.5 is ideal after 2 days of the same regimen.[3]

Recent Developments

The MOMENTUM 3 trial studied the HeartMate 3 vs the HeartMate 2 LVADs. Patients in the HeartMate 3 group had fewer pump thrombosis, stroke, and bleeding events.[4] This finding posed the question of whether more conservative anticoagulation strategies would benefit these patients. The current recommendation of bridging to warfarin with heparin stemmed from an increased rate of pump thrombosis seen in patients with the HeartMate 2 LVAD who were not bridged. A retrospective chart review from the Netherlands found fewer bleeding/tamponade events as well as shorter duration of hospital stay in patients with a HeartMate 3 LVAD whose condition was managed using a conservative anticoagulation strategy postoperatively, with no bridging and slow initiation of warfarin to a goal INR of 1.8 to 2.5. No difference in thromboembolic events was found.[5] Because of the retrospective nature of this study and its small sample size, additional research in this area into patients with a HeartMate 3 LVAD would be beneficial.

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A meta-analysis of 5 studies found that time in therapeutic range for warfarin was only 46% in patients with LVADs. Because maintenance of INR within a therapeutic range correlates with clinical outcomes, additional methods of anticoagulating these complex patients are of interest.[1] Guidelines provide a class III recommendation against the use of direct oral anticoagulants, citing the RE-ALIGN trial and the Andreas et al trial.[6,7] Both these studies showed an increase in thromboembolic events with the use of dabigatran. Newer case series have been publishing looking at apixaban and rivaroxaban. Parikh et al[8] described 7 cases of rivaroxaban and apixaban use in patients with a HeartMate 2 LVAD or HeartWare Ventricular Assist Device system (Medtronic). No patients developed thrombotic events after a mean 208 days. Schulte et al[9] examined 48 patients on apixaban, mostly with a HeartWare system, and reported no pump thrombosis events. Whitehouse et al[10] examined the use of apixaban (n = 15) vs warfarin (n = 20) in patients with a HeartMate 3 LVAD. No differences in outcomes were seen between the groups at a median duration of treatment with apixaban of 148 days. Based on these small studies, rivaroxaban and apixaban may be considered alternatives in patients with "warfarin failure"; however, large, randomized studies must be conducted to make definitive therapy recommendations.

In patients requiring anticoagulation reversal, vitamin K should be the primary agent used in patients on warfarin. Because of warfarin's slower onset of effect, however, prothrombin complex concentrates have been of interest in urgent cases. Several small, retrospective, single-center studies have been conducted to examine prothrombin complex concentrate use in patients with LVADs, with the majority being intracranial hemorrhage cases. Studies found shorter time to reversal, with no increase in thromboembolic events. There were no differences in outcomes, however, in terms of bleeding expansion and mortality. Based on this limited amount of data, the use of prothrombin complex concentrates in patients with LVADs appears to be safe, but clinicians should consider using a low-dose strategy and limiting use to patients with intracranial hemorrhage.[11]

Future Directions

Considering that patients with an LVAD are at high risk for bleeding, more conservative anticoagulation regimens should be studied in patients with a HeartMate 3 device because of the lower thrombotic risks seen in the MOMENTUM study. Ongoing studies are examining the use of direct oral anticoagulants in patients with a HeartMate 3 device to determine whether they could become a therapeutic option for these patients in the future.

Abbreviations and Acronyms

INR	international normalized ratio
LVAD	left ventricular assist device

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