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Editorial

Decreased International Normalized Ratio on Left Ventricular Assist Device Support: To Bridge or Not to Bridge?

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Despite a growing level of comfort in managing patients on long-term left ventricular assist device (LVAD) support, certain areas remain poorly studied. One of them is managing anticoagulation when the international normalized ratio (INR) becomes subtherapeutic. A few studies addressed this issue in patients undergoing invasive procedures or surgeries when the routine maintenance anticoagulation with warfarin needs to be interrupted.[1] But when the INR becomes subtherapeutic as a result of multiple factors such as missed doses, administration of antibiotics for a concomitant infection, or change in the diet, each individual program has to establish their own protocol as no guidelines provide clear-cut directions.

This problem is not unique for the LVAD field. Patients who are on chronic anticoagulation for other conditions encounter similar challenges. In cases of surgery or procedure, no bridging is currently recommended for those who take warfarin for atrial fibrillation, because the bridging increases the rate of bleeding events without reducing thromboembolism.[2, 3] However, some patients with mechanical prosthetic valves and additional risk factors for thromboembolic events require bridging. One of the factors creating a higher risk for thromboembolic events in patients with mechanical prosthetic aortic valves is a low left ventricular ejection fraction, which is seen in patients on LVAD support. And yet, even detailed valvular guidelines do not give any specific directions for bridging in cases where the INR drifts to subtherapeutic

level without intentional interruption of anticoagulation.[4, 5] Therefore, studies filling this gap in knowledge are of certain interest.

In volume 6, issue 2 of *The VAD Journal*, we published a paper by Rainess et al.[6] who reported their experience with managing subtherapeutic INRs, mostly in patients with HeartMate II (HM II) (Thoratec, Pleasanton, CA). Although, the cohort did include some HeartMate 3-supported patients. In their program (Wake Forest University), pharmacists manage anticoagulation according to the institutional protocol, which allows bridging with low molecular weight heparin when INR decreases to less than 1.8. The study is unique because the patients did NOT require interruption of anticoagulation for any purpose. In all instances, the INR decreased because of dietary variations, recent dose changes, skipped doses, medication interactions, etc. Almost half of their patients had a history of hemolysis or pump thrombosis. After analyzing 155 bridging episodes, the authors reported systemic bleeding events in 9% of the patients and localized bleeding in 10%. Importantly, no event resulted in hospitalization or blood transfusion; this rate seems to be excessive considering a relatively minor deviation of INR from the therapeutic range, and it raises a question about an appropriate threshold for bridging initiation.

Several studies regarding reduced anticoagulation in LVAD patients provide some insights. Reversal of anticoagulation for procedures in patients on LVAD appear to be safe in terms of thromboembolic risks.[7, 8] After anticoagulation reversal with vitamin K or Factor VII, there was only one thromboembolism in 25 patients who experienced a total of 38 anticoagulation reversal events.[7] Another prospective study analyzed data on 14 patients whose anticoagulation, or both anticoagulation and antiplatelet therapy, was discontinued for more than 30 days due to gastrointestinal bleeding.[9] The mean duration off warfarin was 392 days (range, 31 - 1,980 days), with the total cumulative time off warfarin being 15 patient-years. Five (35.7%) patients remained off warfarin for at least 1 year. One patient had a pump thrombus due to device malpositioning that required a device exchange after being off warfarin for 1.3 years.[9]

Some authors also reported smaller groups of patients with anticoagulation interruption for bleeding and without bridging. Thus, per John et al.,[10] seven patients safely discontinued warfarin for a total duration of 39.1 patient-months.

In the study by Bhatia et al.,[1] which is referenced by Reiness, et al.,[6] there was a fourfold increase in major bleeding events during the bridged period in the enoxaparin group, although they initiated bridging at a lower INR (1.46) than Rainess et al. (1.62).

Several years ago, we reviewed our data on utilizing bridging with low molecular weight heparin in patients with HMII devices undergoing surgeries or invasive procedures.[8] We found that in patients who were bridged, the rate

of bleeding episodes was significantly higher than in those who continued warfarin throughout the surgery or who temporarily discontinued warfarin with no bridging (Figure 1).

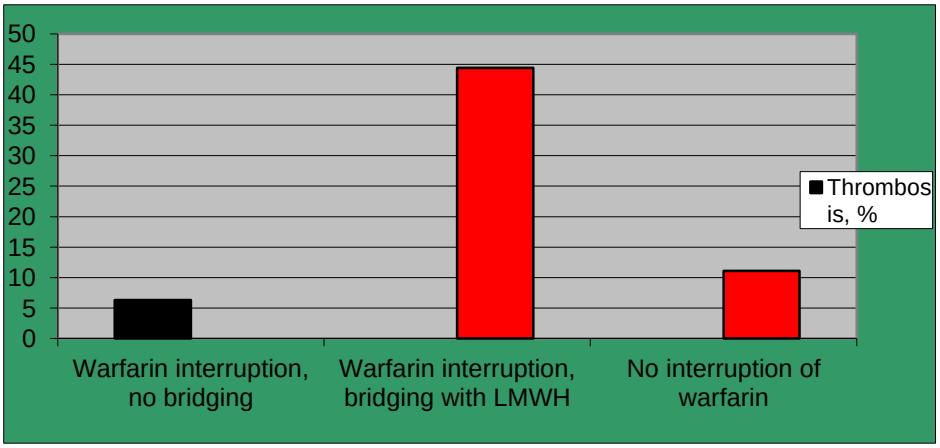

Figure 1. *Rate of thromboembolic events in patients on HeartMate II support depending on the strategy of anticoagulation management during elective surgery/procedure.*[8]

In summary, studies such as Rainess et al.[6] fill an important knowledge gap. From our standpoint, a 20% risk in bleeding, which includes a 9% risk of systemic bleeding, is a too high price to pay for such a minor decrease in INR. Perhaps tolerating a subtherapeutic INR for a few days would be a safer approach. A specific cutoff of the INR value triggering bridging should be a subject of a randomized study, but setting the bar at 1.8 may represent an excessively aggressive strategy.

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