Bridging therapy and risk of major bleeding and thrombosis in continuous-flow left ventricular assist device patients: a quasi-experimental study


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Background: Bridging with low molecular weight heparin (LMWH) on top of vitamin K antagonist treatment is recommended in continuous-flow left ventricular assist device (CF-LVAD) patients during subtherapeutic anticoagulation. However, the consequence of bridging on the risk of bleeding and thrombosis are unknown.

Aim: To assess the risk of major bleeding and thrombosis associated with bridging in CF-LVAD patients, through a regression discontinuity (RD) design, a quasi-experimental design.

Methods: We included CF-LVAD patients implanted at our university medical center between 2010-2021. Outcomes were major bleeding (INTERMACS type 3, 4, 5) and thromboembolic events (pump thrombosis, arterial non-central nervous system and venous thromboembolism). We estimated incidence rates and hazard ratios (HR) with 95% confidence intervals (95%CI) by time-dependent Cox regression. Using an RD design, a quasi-experimental design, we compared patients using LMWH due to a subtherapeutic international normalized ratio (INR) to patients with no LMWH and an INR just in target range. As LMWH treatment is initiated based on an INR threshold (i.e., when INR is below the lower target range) and INR is subject to random variability, patients just below and in the INR target range are comparable, mimicking a randomized trial. Analyses were performed five times including INRs ±0.1, ±0.2, ±0.3, ±0.4 and ±0.5 around the INR threshold.

Results: 77 patients were included, with a median age at implantation of 69 years, 60 (78%) were male, 45 (58%) had ischemic heart failure and 35 (45%) had INTERMACS classification 3. We included 35,466 INRs during 91 patient-years of follow-up. Bridging was associated with increased major bleeding rates compared to no-bridging in all analyses (Figure 1). In particular, the risk of major bleeding was 6.9-fold increased (95%CI 1.2-38.9) during bridging compared to no-bridging considering INR+0.1, and 3.4-fold (95%CI 1.4-8.2) considering INR±0.5 (Figure 2A). While thrombotic events were infrequent, the risk of thrombosis was around unity during bridging compared to no-bridging considering INR±0.5 (HR 1.1, 95%CI 0.1-9.9, Figure 2B).

Conclusions: During bridging with LMWH, CF-LVAD patients had a 6.9-fold increased risk of major bleeding, while the risk of thrombosis was around unity compared to no-bridging.
Incidence rates
Hazard ratios

A  INR                  Major bleeding (HR, log scale)  Hazard Ratio (95% CI)

Threshold ± 0.1 6.9 (1.2 - 38.9)
Threshold ± 0.2 4.2 (1.2 - 15.1)
Threshold ± 0.3 2.3 (0.8 - 6.5)
Threshold ± 0.4 3.5 (1.2 - 9.7)
Threshold ± 0.5 3.4 (1.4 - 8.2)

B  INR                  Thromboembolic events (HR, log scale)  Hazard Ratio (95% CI)

Threshold ± 0.1 *  *
Threshold ± 0.2 *  *
Threshold ± 0.3 2.9 (0.3 - 32.1)
Threshold ± 0.4 2.3 (0.2 - 22.0)
Threshold ± 0.5 1.1 (0.1 - 9.9)