# Hemorrhage and thrombosis with different LVAD technologies: a matter of flow?

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**Background:** Much of the morbidity and mortality associated with ventricular assist devices (VADs) is due to haemorrhagic and thrombotic complications. To manage antithrombotic therapy, interactions between the patient and pump should be better understood.

**Methods:** We have compared the Jarvik 2000, an axial flow left ventricular assist device (LVAD), with the HeartWare ventricular assist device (HVAD) centrifugal pump, regarding conventional laboratory findings, thromboelastometric and aggregometric tests.

**Results:** Patients with the Jarvik 2000 experienced a significant reduction in platelet count following implantation, a phenomenon not seen with the HeartWare model. Conversely, we observed that levels of platelet activation, as assessed by a platelet function analyzer, and activation of the coagulation system, as assessed by thromboelastometry, were significantly greater in the HeartWare group.

**Conclusions:** It seems that axial flow pumps, being more destructive on blood cells, tend to reduce platelet numbers. On the other hand, centrifugal flow is associated with a hypercoagulable state, possibly resulting from the activation of the coagulation system in the absence of platelet destruction.

Keywords: Ventricular assist device (VAD); bleeding; thrombosis; axial flow; centrifugal flow



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#### Background

In recent years, ventricular assist devices (VADs) have been increasingly used in the treatment of end-stage congestive heart failure, both as bridge to transplantation (BTT) and, more recently, as destination therapy (1). Major limiting factors for their use have been hemorrhagic and thrombotic complications, which contribute significantly to the morbidity and mortality associated with VADs (1-3).

Thrombotic complications are attributed to nonphysiological flow patterns resulting in shear stress and platelet activation, as well as the interaction of blood with the artificial surfaces of the VAD system (2). Efforts to minimize these complications include life-long treatment with anticoagulant and antiplatelet therapies. Such therapies are vital for preventing catastrophic thrombotic complications. However, they may also lead to iatrogenic haemorrhage, which is seen in the early postoperative period and may continue for the duration of support (3). Balancing the risk of thrombosis and hemorrhage is a major challenge. The present authors believe that there are two key interactions that must be understood: the interaction between different VAD designs and the coagulation system, and individual patient responses to VADs and antithrombotic therapy.

### VAD designs and impact on the coagulation system

To date, there have been little comparative data published on the different VAD designs and their individual effects on hemorrhagic and thrombotic risks. With this in mind, the fifth INTERMACS annual report by Kirklin *et al.* (1) was an important paper as it compared the adverse event rate of pulsatile and continuous flow VAD technology. This demonstrated a significantly lower risk of bleeding and thrombotic events in patients treated with newer generation continuous flow VADs. This reduced risk of thrombotic and hemorrhagic events has been one of the primary drivers of increased use of continuous flow devices in recent times. However, continuous VADs are not a homogenous group of device designs, as they include both axial flow and centrifugal flow devices, which differ significantly in their characteristics and would be expected to have different effects on the coagulation and hematological systems.

In this context, we read with interest the recent paper by Birschmann et al. (4) comparing 10 patients who underwent implantation of HeartMate II (HMII, Thoratec Corp, Pleasanton, CA, USA) with 10 patients who underwent implantation of HeartWare HVAD (HeartWare International Inc, Framingham, MA, USA) from 2009 to 2010, in terms of their relative effects on the coagulation system and hemolysis. Indications for LVAD implantation were not reported. Most notably, these two systems differ in design as the HeartMate II is an axial flow device, which uses an impeller to drive blood, while the HeartWare employs a centrifugal pump with a magnetically suspended rotor. The study demonstrated that within the HeartMate II group, there was a higher mean lactate dehydrogenase (LDH) (469.8 vs. 249.8 U/L, P<0.001), while in the HeartWare group there was higher mean D-dimer level (0.9 vs. 2.0 mg/L, P=0.0068). However, it should be noted that the analyses were performed only once and not at the same time point for each patient. Other parameters such as hemoglobin, platelet counts, International Normalized Ratio (INR) and Activated Partial Thromboplastin Time (aPTT) did not differ significantly between the groups. As LDH is a marker of hemolysis, the authors have postulated that increased hemolysis may occur in the HeartMate II patients due to greater shear stresses generated by the axial nature of the flow produced by its pump.

These findings are consistent with our experience with axial and centrifugal flow LVADs at the Cardiac Surgery Unit of the University of Padua. In a preliminary study, we have compared the Jarvik 2000, an axial flow LVAD, with the HeartWare HVAD centrifugal pump. We observed that patients with the Jarvik 2000 experienced significant reductions in platelet counts following implantation, a phenomenon not seen with the HeartWare model. Conversely, we observed that levels of platelet activation, as assessed by platelet function analyser, and activation of the coagulation system, as assessed by maximal clot firmness on thromboelastometry, were significantly greater in the HeartWare group. We interpret this as a reflection of the nature of the flow generated with the axial flow device. The axial flow generated by the Jarvik 2000 is likely more destructive to platelets as it subjects them to greater shear stress, resulting in reduced platelet numbers. The resultant hypercoagulable state seen with the HeartWare device may represent activation of the coagulation system by the LVAD in the absence of a compensatory destruction of platelets. It is possible that in the study by Birschmann *et al.* (4) the higher D-dimer level, a fibrin degradation product, reflects a more activated coagulation system in the HeartWare group.

Beyond the theoretical interest in understanding the effects of various VAD designs on the coagulation and hematological systems, there is also significant potential for clinical application of this knowledge. If it is established that axial flow pumps do indeed cause a greater degree of platelet destruction, while centrifugal pumps are associated with greater risks of thrombosis likely mediated by platelets, it may be possible to initiate more rational antithrombotic therapies from the outset. For example, antiplatelet therapy is more likely to be indicated in patients with centrifugal flow devices than axial flow devices, which consume platelets.

Another important finding of Birschmann et al. (4) was the degree of incomplete platelet inhibition seen in patients with clopidogrel use. In their study, five out of nine patients demonstrated insufficient platelet inhibition using aggregometry testing. It must be noted, however, that an atypical dosing regimen was used with clopidogrel doses given only three times per week. Consequently, this may have contributed to the low level of platelet inhibition. Nonetheless, in the setting of VAD, this still demonstrates that response to antiplatelet therapy may be less predictable compared to the general population, potentially reflecting patient-specific interactions between platelets and the VAD. For this reason, we believe that the best way to reduce thromboembolic and haemorrhagic complications in these patients is to use the multi-monitoring system (aggregometry and thromboelasto-metry/graphy) to calibrate antithrombotic therapy using a multi-targeted approach (5).

#### Conclusions

Insights into the effect of specific VAD designs on the

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coagulation system could lead to the implementation of more rational antithrombotic regimens. Further studies are required to better understand individual responses to antiplatelet therapy in patients with VAD therapy.

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