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Case report

# Acquired von Willebrand syndrome after exchange of the HeartMate XVE to the HeartMate II ventricular assist device

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**Abstract**

Instead of pulsatile ventricular assist devices an increasing number of nonpulsatile ventricular assist devices are introduced to clinical practice. The different flow characteristics of this new technique lead to alteration in shear stress on blood components, which may affect the coagulation system. Repeated von Willebrand factor analyses were performed in a patient who first was implanted with a pulsatile ventricular assist device (Thoratec HeartMate XVE), which had to be replaced after 405 days with an axial flow device (HeartMate II). During support with the pulsatile ventricular assist device there was no sign of any coagulation disorder. However, on the axial flow device acquired von Willebrand syndrome Type 2 developed. Inhibition of platelet function was also observed, which may be in part due to the von Willebrand syndrome. The HeartMate II axial flow device may induce von Willebrand syndrome, which was not observed in HeartMate XVE pulsatile ventricular assist device. Patients put on continuous flow devices should be screened for acquired von Willebrand syndrome.


*Keywords:* Platelets; Von Willebrand syndrome; Ventricular assist device

## 1. Introduction

Thromboembolic and bleeding events are still the most common serious adverse events after implantation of a left ventricular assist device (LVAD). There is no general consensus about anticoagulation strategies. In addition, the design of devices may itself change the coagulation system after implantation [1,2]. Better understanding of interaction between devices, the vasculature and blood stream components will be helpful not only for the therapeutic management after device implantation, but also for future developments of new LVAD. We describe a case of acquired von Willebrand syndrome (vWS) after exchange of a pulsatile LVAD (HeartMate XVE, Thoratec, USA) to a continuous flow rotary pump (HeartMate II, Thoratec).

## 2. Case report

A 55-year-old patient with end stage heart failure due to dilated cardiomyopathy was referred to our hospital for emergency treatment. The left ventricle was enlarged (LVEDD 75 mm) and ejection fraction was reduced to 10%. A low cardiac index of 1.4 l/min/$m^2$ despite catecholamine therapy and acute renal failure was present.

A Thoratec HeartMate XVE was implanted the same day. The implant procedure was uneventful via median sternotomy and use of extracorporeal circulation. The LVAD was implanted in a preperitoneal pocket and connected to the left ventricular apex and the ascending aorta.

The setting of this pulsatile volume displacement device in our patient was: pump rate 54/min, stroke volume 82 ml, pump flow 4.3 l/min.

The patient recovered from surgery and left the ICU after 1 week. We administered anti-platelet medication (aspirin 100 mg/d) and anticoagulation therapy with phenprocoumon (Marcumar®, Roche, Germany) was given in this case because of previous deep vein thrombosis (INR 2.5—3.0). The clinical course was uneventful apart from trivial epistaxis due to phenprocoumon overdose after 3 months.

On day 348 we performed analysis of von Willebrand factor (vWF) as part of a screening program. Von Willebrand factor antigen (vWF:AG) was increased to 216% (ELISA, normal range 50—160%). Collagen-binding activity (vWF:CB) was 212% (ELISA, normal range 50—250%). The ratio vWF:CB/vWF:AG was 0.98, also within the normal range (0.8—2.0). Gel electrophoresis displayed a normal distribution of vWF-multimers (U. Budde, Hamburg, Germany). The triplet structure of vWF-oligmers was normal. No qualitative or quantitative defect was detected [3].

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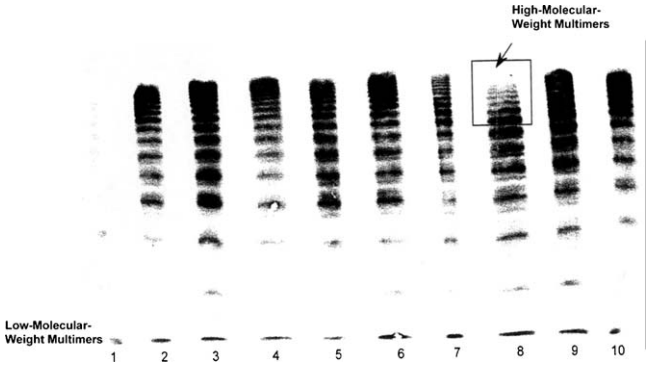


Fig. 1. Lack of highest-molecular-weight von Willebrand factor multimers in one patient (8) compared to control samples.

On day 388 the patient was hospitalized because of mechanical device malfunction, which emerged as a bearing failure. The electric driving mode of the HeartMate XVE had stopped. While the device worked on pneumatic driven mode, LVEDD increased from 62 mm to 70 mm and ejection fraction decreased from 40% to 20% over 2 weeks. Therefore on day 405 we exchanged the HeartMate XVE for an axial flow device (HeartMate II) via re-sternotomy.

This continuous flow device was set to a pump speed of 10,000 rpm, and a pump flow of 6.3 l/min.

The early postoperative course was complicated by bleeding from extensive adhesions requiring surgical re-exploration. Weaning from the respirator and right heart insufficiency prolonged the ICU stay.

One week after device exchange analysis of vWF was repeated. An increase of vWF:AG (432%) was found and attributed to the early postoperative inflammation. Collagen-binding activity (vWF:CB) was 468%, the ratio vWF:CB/vWF:AG was 1.08. However, electrophoresis revealed a complete loss of largest vWF multimers verifying acquired vWS (Fig. 1). Quantitative analysis of multimers was not done. Normal triplet structure of individual oligomers proved an unhindered interaction of vWF with receptors and screened out a qualitative defect.

Platelet function test (PFA-100) using platelet aggregation to collagen/epinephrine and collagen/adenosine diphosphate revealed prolonged closure times (>300 s) [4], indicating severe impairment of primary hemostasis. When the patient was discharged after 7 weeks, phenprocoumon was given again (INR 2.5–3.0). Aspirin dosage was reduced to 3 × 100 mg/week. When epistaxis reoccurred, we decided to discontinue anti-platelet therapy. The control platelet function test was unchanged with prolonged closure times (>300 s).

Twenty-three months after device exchange the patient was still on LVAD support. vWF-AG was increased (366%) while collagen-binding activity (vWF:CB) was relatively reduced (133%) reflecting impaired function, the ratio vWF:CB/vWF:AG was 0.36. Quantitative analysis of multimers revealed an increased fraction of small (<6) multimers (53.3% vs 33.7% in control plasma), a normal percentage of medium size (6–10) multimers (39.3% vs 36.9%) and a reduction of large (>10) multimers (7.1% vs 29.4%) with complete loss of largest multimers in gel electrophoresis. The triplet structure of individual oligomers was normal.

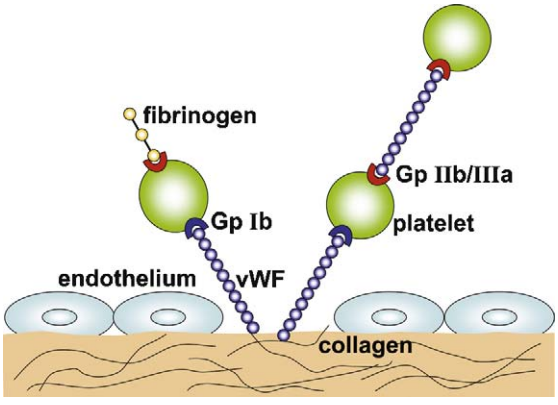


Fig. 2. VWF in primary hemostasis (modified after: Schneppenheim, R. and Budde, U.: von Willebrand-Syndrom und von Willebrand-Faktor – Aktuelle Aspekte der Diagnostik und Therapie, UNI-MED Verlag 2006).

## 3. Discussion

High molecular weight multimers of vWF mediate platelet adhesion and platelet aggregation (Fig. 2). Acquired vWS, characterized by loss of the large multimer fraction due to proteolysis, is a frequent finding in cardiovascular disorders exposing blood flow to high shear stress, like in aortic stenosis [5] or ventricular septal defects. The complex tertiary structure of molecules could change [6] and they may be exposed to proteolytic enzymes to a greater extent [7]. Also increased binding of the most active large molecules to active platelets in the area of turbulent flow is a hypothesis [8]. Other possible causes of acquired vWS, such as thrombocytosis or uremia, could be ruled out in our case.

Our hypothesis is that the design of the new device inducing high shear stress or the continuous flow itself is the most likely cause for our findings. During support with the pulsatile HeartMate XVE, no defect of vWF was detectable in our case. However acquired vWS has been described in patients with a biventricular pulsatile device (BiVAD) [9], but systems may not be comparable regarding inner surface and flow properties. The acquired vWS induces severe platelet inhibition.

From our findings it cannot be excluded that additional factors contribute to the impaired platelet function, since platelets may also be affected directly by an axial flow device.

As primary hemostasis is impaired in patients with acquired vWS, we suggest a reduction or even a discontinuation of anti-platelet therapy individually.

Since severe bleeding episodes may be life threatening and minor bleeding may be associated with an impaired quality of life all different types of LVAD should be screened for acquired vWS. Future design of rotary blood pumps should not only focus on mechanical stability and hemolysis, but also on other blood components like vWF and platelets.

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