Von Willebrand disease and von Willebrand factor: an old story, a new perspective

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Stellingen
behorende bij het proefschrift

Von Willebrand disease and von Willebrand factor:
an old story, a new perspective

1. Hemostasis is a physiological balance that prevents spontaneous bleeding and thrombosis. Von Willebrand factor is involved in both pathways (this thesis).

2. Von Willebrand factor levels are not constant throughout life, but increase with age in the general population and in mild von Willebrand disease (this thesis).

3. Gastro-intestinal bleeding in congenital and acquired von Willebrand disease is a severe rare condition, with the potential of new effective treatments (this thesis).

4. The availability of automated assays to determine von Willebrand factor levels was the first step to collect large data (this thesis).

5. The plasma level of von Willebrand factor in normal individuals varies over a six-fold range, from 0.40–2.40 iu/ml, and VWF levels are approximately 25% lower in blood group O individuals than in non-O. *Laffan MA et al. The diagnosis and management of von Willebrand disease: a United Kingdom Haemophilia Centre Doctors Organization guideline approved by the British Committee for Standards in Haematology. Br J Haematol 2014;167: 453-65.* The wide range of von Willebrand factor in the normal population poses a challenge to von Willebrand disease diagnosis.

6. The most controversial decision made in the von Willebrand disease guideline documents is to reclassify individuals with a bleeding phenotype and von Willebrand factor activity levels of 0.30-0.50 IU/mL as having von Willebrand disease. *Makris M and Hermans C. The 2021 von Willebrand disease guidelines: Clarity and controversy. Haemophilia 2022; 28: 1-3.* Our findings support the dilemma of classifying individuals with low levels of von Willebrand factor as patients, since the levels of von Willebrand factor increase with age and may fully normalize.

7. Increased levels of coagulation factors are associated with an increased risk of venous thrombosis, with factor VIII and von Willebrand factor levels as the strongest identified risk factors. *Rietveld IM et al. High levels of coagulation factors and venous thrombosis risk: strongest association for factor VIII and von Willebrand factor. J Thromb Haemost 2019; 17: 99-109.* This emphasizes the role of von Willebrand factor in bleeding and thrombosis.

8. The personalized approach in the treatment of both bleeding or thrombotic disorders can be improved by use of global assays such as thrombin generation assays. *Valke LLFG et al. Thrombin generation assays to personalize treatment in bleeding and thrombotic diseases. Front Cardiovasc Med 2022; 9:1033416.* The goal and challenge of modern medicine is to find a personalized treatment for patients, especially when the therapy is associated with relevant side-effects.

9. Our categorical imperative, as clinicians who treat rare diseases, is to collect and publish all available data (through case reports, case series and registry data), to improve patients clinical care.

10. It is never too late for clinicians to study epidemiology.