Determination of the VWF activity with the ristocetin independent gain of function Glycoprotein 1b Innovance von Willebrand Activity Assay.

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OBJECTIVES

Von Willebrand disease (vWD) is a bleeding disorder caused by abnormalities in Willebrand factor (vWF) concentration and/or function. The prevalence is 1: 100, but only 1: 10.000 cases have a clinical significant bleeding tendency. VWD can be divided in three different subclasses.

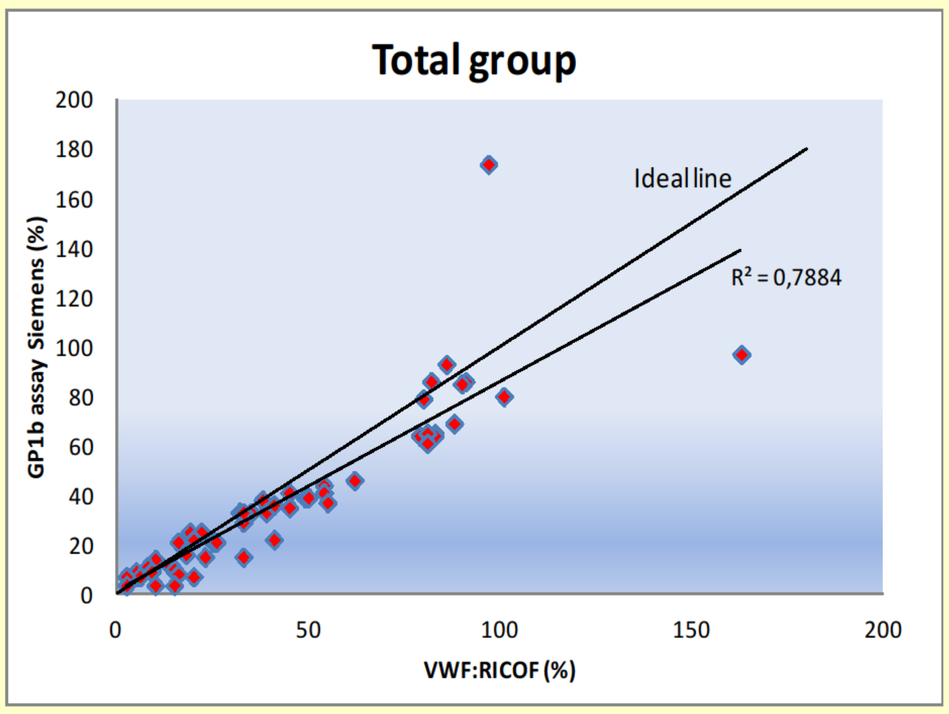
The vWF ristocetin assay (VWF:RICOF) is a cumbersome assay and affected by polymorphisms present in the ristocetin binding site of vWF resulting in *in vitro* decreased vWF activity (Flood et al, Blood, 2010).

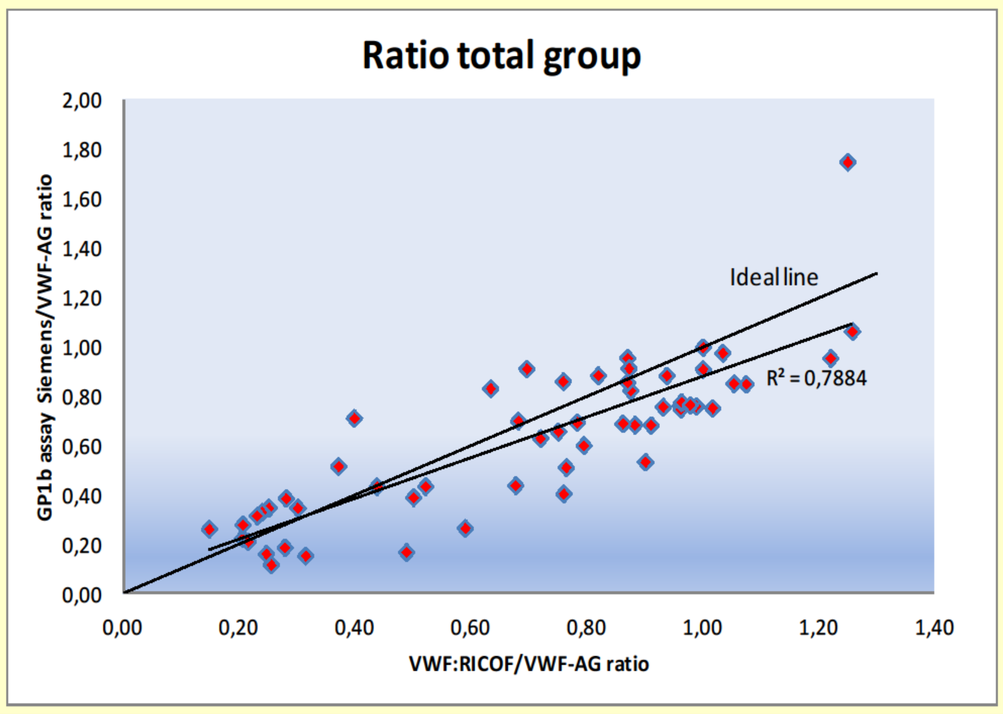
The gain of function Glycoprotein 1b (GP1b) assay is an automated assay that does not require ristocetin. In this study we compared both assays in a phenotypic and genotypic well defined patient cohort.

METHODS

The basis of the GP1b assay is the binding of VWF to its platelet receptor GPIb. The assay uses polystyrene particles coated with an antibody directed against the platelet receptor GPIb. After addition of plasma the two gain-of-function mutation containing recombinant GP1b, is added and binds to the antibody as well as to the VWF of the sample. Due to the gain-of-function mutation, vWF binding to GPIb does not require ristocetin. vWF binding induces GP1b-based particle agglutination which can be measured as an turbidimetric increase in extinction.

44 VWD patients (genotypically confirmed Type 1: N=9, type 2A: N=9, type 2B: N=6, 2M: N=9, type 2N: N=6, type 1/2N: N=4, type 3: N=1, acquired VWD: N=1) and 12 non VWD patients were analyzed with the GPIb assay and the VWF:RICOF assay.





RESULTS

In general no significant differences were observed between the two assays. The overall slope was 0,947 (0,862 – 1,032).

The positive predictable value (PPV) of the VWF:RICOF and the GPIb assay for type 1 and 2N patients (cut off ratio ≥0.7) is 85% and 94% respectively with a sensitivity of 90% and 79%. For type 2 patients (cut off ratio <0.7) the PPV is 91% and 85% respectively with a sensitivity of 87% and 96%.
The negative predictable value (NPV) of the VWF:RICOF and the GPIb assay for type 1 and 2N patients is 91% and 85% respectively with a specificity of 87% and 96%. For type 2 patients the NPV is 85% and 94% respectively with a specificity of 90% and 79%.
In the VWD 2N population there are patients who, besides their 2N mutation, have a type 1 mutation. The multiple mutations causes different phenotypes . If these patients are removed from the data the results are even better.

CONCLUSIONS

The GP1b assay distinguishes the different types of VWD as good or even slightly better than the VWF:RICOF assay. The assay seems to be a good alternative for the Von Willebrand ristocetin cofactor activity assay.

References

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