von Willebrand Panel with Reflex to von Willebrand Multimeric Analysis

FOR DIAGNOSIS AND SUBTYPING OF VON WILLEBRAND DISEASE

Test Highlights

- The new panel includes the three first-line tests for von Willebrand disease (vWD) recommended by the National Heart, Lung, and Blood Institute (NHLBI) guidelines published in 2008:
  - von Willebrand factor (vWF) antigen
  - vWF activity
  - Factor VIII activity
- If any of the initial tests are abnormal, or if the ratio of vWF activity to vWF antigen is abnormal (less than 0.7), von Willebrand multimeric analysis is performed.
- The advantage of this panel is that multimeric analysis is only performed on samples that demonstrate an abnormality in the initial panel.

Clinical Background

- vWF is a multimeric plasma protein that functions to mediate adherence of platelets to areas of vascular injury and serves as a carrier for plasma coagulation factor VIII.
- vWD is a common inherited bleeding disorder that affects up to 1 percent of individuals and results from either quantitative or qualitative abnormalities of vWF.
- vWD is characterized by mucocutaneous bleeding (platelet-type bleeding) such as easy bruising, epistaxis, menorrhagia, and excessive bleeding with surgery or dental extractions.
- There are both quantitative (types 1 and 3) and qualitative (type 2) subtypes of vWD. Accurate subtyping is important since appropriate treatment is dictated by subtype and clinical presentation.
  - Type 1 is the most common subtype (75 percent of patients) and typically represents a partial quantitative vWF deficiency with mild bleeding symptoms.
  - Type 2 subtypes (2A, 2B, 2M, and 2N) are associated with dysfunctional vWF (qualitative disorder) and with moderate bleeding symptoms.
  - Type 3 is rare and is associated with severe bleeding due to absence of vWF.
- Certain subtypes (such as 2A and 2B) are associated with multimeric abnormalities.

Indications for Ordering

- vWD testing is appropriate in patients with a suspected bleeding disorder associated with mucocutaneous bleeding.
- Initial vWD testing should include vWF antigen, vWF activity, and factor VIII activity.
- Multimeric analysis is not considered a first-line test since it is qualitative. Multimeric pattern alone does not definitively diagnose vWD subtypes.
- Multimeric analysis is recommended to assist with diagnosis and subtyping if the initial tests are abnormal, or if the ratio of vWF activity to vWF antigen is abnormal (less than 0.7), since an abnormal ratio may indicate that a multimeric abnormality is present.
  - Multimeric analysis may also be appropriate if the clinical presentation suggests that a multimeric abnormality may be present.
- This panel includes the recommended first-line vWD tests and reflexes to multimeric analysis only when indicated by the initial test results. This approach avoids multimeric analysis in cases where it is not necessary and ensures that multimeric analysis is performed on the same sample in cases where it is indicated.

Interpretation

- vWF antigen, vWF activity, and factor VIII activity are quantitative tests.
  - Normal results to do not rule out vWD since values fluctuate over time and vWF and factor VIII are acute phase reactants.
  - Only vWF values below 20–30 percent of normal are considered diagnostic for vWD; mildly decreased values may represent vWD but are not diagnostic.
- Multimeric analysis is a qualitative test where the sizes and banding pattern of vWF multimers are evaluated. This test is interpreted by a pathologist.
- If the initial tests reflex to multimeric analysis, the interpretive comment will integrate the panel results and multimeric findings. Depending on the abnormalities identified, possible diagnoses will be suggested and/or additional testing will be recommended.
- Additional specialized testing may be necessary for diagnosis and/or subtyping in some patients.

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Limitations

- vWF values fluctuate over time, and both vWF and factor VIII are acute phase reactants. Acute phase reactions can mask deficiencies in mildly affected patients.
- Cold storage of the citrated whole blood prior to processing should be avoided because it can reduce vWF and factor VIII values, as well as induce multimeric abnormalities.

Methodology

- Microlatex particle-mediated immunoassay (vWF antigen).
- Platelet agglutination (vWF activity: ristocetin cofactor activity).
- Clotting (factor VIII activity).
- Electrophoresis/Western blot (multimeric analysis).

Related Tests

- von Willebrand Panel (0030125): includes the three first-line quantitative tests
- von Willebrand Multimeric Panel (0030002): includes the three first-line quantitative tests and multimeric analysis on every sample (no reflex)
- von Willebrand Factor Multimers (0092281): multimeric analysis alone

References

1. Nichols WL, et al. Von Willebrand disease (vWD): evidence-based diagnosis and management guidelines, the National Heart, Lung, and Blood Institute (NHLBI) Expert Panel report (USA). *Haemophilia* 2008;14(2):171–232.
2. Nichols WL, et al. Clinical and laboratory diagnosis of von Willebrand disease: A synopsis of the 2008 NHLBI/NIH guidelines. *Am J Hematol* 2009;84:366–70.
3. Torres R, Fedoriw Y. Laboratory testing for von Willebrand disease: toward a mechanism-based classification. *Clin Lab Med* 2009;29:193–228.
4. Budde U. Diagnosis of von Willebrand disease subtypes: implications for treatment. *Haemophilia* 2008;14 Suppl 5:27–38.

Test Information

2003387 von Willebrand Panel with Reflex to von Willebrand Multimeric Analysis

For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.