Factor XIII Deficiency

Indications for Ordering

Factor XIII Activity
- Preferred first-line test to diagnose inherited or acquired factor XIII (FXIII) deficiency
- Appropriate for evaluation of individuals with a bleeding disorder presenting with normal PT, PTT, and platelet count test results
- Monitor therapy in individuals being treated for FXIII deficiency
- To confirm abnormalities identified in the qualitative FXIII assay (clot solubility test)

Factor XIII, Qualitative, with Reflex to Factor XIII 1:1 Mix
- Most useful if severe FXIII deficiency is suspected (<1% of normal activity)
- To distinguish between FXIII deficiency and a FXIII inhibitor

Test Description

Factor XIII Activity
- Chromogenic assay
  - Consumption of NADPH is measured spectrophotometrically
    - Decrease in absorbance is directly proportional to FXIII activity
  - Can quantitate factor activity as low as 5% of normal

Factor XIII, Qualitative, with Reflex to Factor XIII 1:1 Mix
- Qualitative solubility test
  - If clot lysis occurs in the initial testing, factor XIII 1:1 mix added

Tests to Consider

Primary tests

Factor XIII Activity 2006182
- First-line test to diagnose FXIII deficiency
- More specific than qualitative assays for FXIII

Factor XIII, Qualitative, with Reflex to Factor XIII 1:1 Mix 2002819
- Most useful for acquired or severe FXIII deficiency testing
- Abnormal results should be confirmed with quantitative testing

Disease Overview

Incidence – ~1/1 million

Inherited – rare autosomal recessive FXIII deficiency

Symptoms
- FXIII deficiency
  - Suspect if coagulation screening tests are normal (eg, PT, PTT, platelet count, and thrombin time)
  - Two forms – inherited, acquired
    - Inherited
      - Delayed postsurgical or traumatic bleeding
      - Umbilical cord bleeding
      - Central nervous system hemorrhage
      - Poor wound healing
      - Recurrent miscarriages
    - Acquired
      - Often presents as severe deficiency
      - Caused by decreased production or increased consumption of FXIII
      - Associated with a number of medical conditions
        - Major surgery
        - Thrombosis
        - Inflammatory bowel disease
        - Liver cirrhosis
        - Sepsis
        - Disseminated intravascular coagulation
      - Associated with autoantibodies that form against FXIII
        - Autoimmune disease
        - Malignancy
        - Drugs
          - Isoniazid
          - Penicillin
          - Phenytoin
          - Idiopathic

Physiology
- FXIII is essential for normal hemostasis
- FXIII covalently crosslinks fibrin polymers to form a stable fibrin clot
- FXIII circulates in the plasma as tetramer of 2 catalytic A subunits and 2 carrier B subunits
- Activated by thrombin and calcium into FXIIla
  - Involved in wound repair, cytoskeletal remodeling, phagocytosis, placental attachment, and inflammatory processes
Test Interpretation

Results
- Activity test
  - Reference interval – FXIII activity, 69-143%
  - Severe bleeding usually does not occur until FXIII level <1-3%
  - Mild or moderate deficiencies may be associated with increased bleeding risk in some cases
- Qualitative reflex test
  - No lysis within 24 hours
    - Clot lysis only occurs in samples with <1% of normal activity

Limitations
- Activity test
  - A low FXIII level does not distinguish deficiency from a low value due to FXIII autoantibodies
  - False negative (artificially increased) results
    - Lipemic plasma
    - Elevated ammonia
    - Clot lysis only occurs in samples with <1% of normal activity
- Qualitative reflex test
  - Normal results do not exclude deficiency
  - Does not identify
    - Mild or moderate deficiency
    - Heterozygous carriers for FXIII deficiency
    - Treated, yet deficient, individuals
    - Individuals with weak FXIII inhibitors that do not decrease FXIII activity to <1% of normal