

Evaluation of the Molecular Testing for Factor V Leiden and Prothrombin 20210G>A Mutations: A Single Institute's Experience

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Background

Molecular testing for Factor V Leiden (FVL) and prothrombin 20210G>A (PTM) mutations has become the gold standard for the evaluation of hypercoagulation status as well as to guide patient management. Like all molecular tests applied to genetic disorders, the clinical sensitivity for FVL and PTM detection varies depending on the testing methodology and patient population. Therefore, technical standards and guidelines have been established by the American College of Medical Genetics¹. To maintain a high-quality performance as well as to follow the College of American Pathologists recommendation for genetic testing improvement in our laboratory, we reviewed our results for FVL and PTM testing and the corresponding clinical data.

Materials and Methods

Real-time PCR using Roche Diagnostics reagents and the LightCycler 1.2 was performed for Factor V Leiden and prothrombin 20210G>A mutation analyses^{2,3}. All the test results from November 2007 to May 2008 were analyzed. The clinical charts for all cases positive for mutation by our assay were reviewed.



Results

(1). 637 and 434 samples have been tested for FVL and PTM respectively in the six months. 43/637 (6.8%) were tested to be heterozygous for FVL and 16/434 (3.7%) were heterozygous for PTM. One case was compound heterozygous for both mutations. Two cases were shown to be prothrombin variants. No homozygote for either FVL or PTM was identified except for a CAP survey sample, which was not included in this study.

(2). Memorial Hermann Hospital is a major health care facility located in the Texas Medical Center and serving the Houston metropolitan area. Our molecular diagnostic laboratory serves as the central reference lab for all the community hospitals in the Memorial Health System, as well as its outreach clinics. The majority (>90%) of the samples were from internal medicine, neurology and emergency room services for patients presented with a possible thrombotic event. The molecular testing was mainly used as a confirmatory test for the diagnosis as well as a criterion for prognosis and determining treatment plan. Less than 10% of the samples were obtained from other various services to facilitate the diagnosis. Most of the patients in the latter setting were asymptomatic.

(3). Patient age at testing was from 2 to 76 years old for FVL and 1 week to 75 years old for PT, with medians of 42 and 52 years old, respectively. There were 18 males and 20 females positive for FVL. Among them, 84% were American Caucasian and 9.3% were Hispanic. Two were Asian and 1 was African-American. For PTM heterozygotes, 11 were males and 4 were females. 81% were American Caucasian. 13% were from Hispanic, 1 was African-American. Interestingly, both prothrombin variant cases were from African-American patients.

(4). Almost all the patients were suffering from another medical condition when the thrombotic events occurred. Trauma or operative procedure appeared to be the dominant accompanying risk factor.

(5). The majority of the patients with FVL presented with deep venous thrombosis (DVT), while more patients with PTM seemed to experience pulmonary embolism than DVT.

(6). Clinical sensitivity has been determined to be 85% and 79% on average for FVL and PTM, respectively. Based on the patient demographic characteristics of our hospitals, we believe that our data are representative and may reflect the clinical sensitivity in general laboratories using this FDA-approved system.

Conclusions

In our patient population, 6.8% and 3.7% of our patients were determined to be positive for FVL and PTM, respectively. These data are consistent with previous literature reports. Medical chart study revealed the importance of co-existing conditions for thrombogenesis. The clinical sensitivities of our assays were also determined, which facilitates the quality assessment in our laboratory.

References and Acknowledgements

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2. Roche Diagnostics. Factor V Leiden kit for use with the LightCycler 1.2 instrument. Apr. 2006.
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