INAHTA Brief

Issue 2016/023

Title Factor V Leiden and Prothrombin Mutation Testing in Patients Presenting With a First Unprovoked Venous Thromboembolic Episode

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Reference Canadian Agency for Drugs and Technologies in Health. Effectiveness of factor V Leiden and prothrombin mutation testing in patients presenting with a first unprovoked venous thromboembolic episode: a systematic review and economic analysis [Internet]. Ottawa: The Agency; 2015 Mar. (CADTH Optimal Use Report vol.4, no.1a). [cited yyyy mmm dd]. Available from: http://www.cadth.ca/media/pdf/OP0517_Thrombophilia_Science_Report.pdf

Aim

To assist decision-makers considering implementation or reassessment of testing practices for factor V Leiden (FVL) or prothrombin gene (PG) mutations in patients with unprovoked venous thromboembolism (VTE) by systematically reviewing the clinical evidence on the association of a positive FVL or PG test with a first, unprovoked VTE (suspected thrombophilia), and the risks and benefits resulting from test use. The cost implications of FVL and PG testing in Canada were also assessed.

Conclusions and results

Despite a significant association between FVL and PG mutations and first unprovoked VTE, there was limited evidence to determine whether FVL or PG mutations increase the risk of future VTE recurrence. Evidence regarding whether FVL or PG testing influences patient management or clinical outcomes was sparse and of insufficient methodological quality to make a meaningful assessment of clinical utility. Available clinical practice guidelines suggest that there is insufficient evidence to warrant differential treatment based on FVL or PG mutation status, and the available data on physician practice outside of Canada indicated that treatment modification based on mutation status may occur relatively infrequently. Given this lack of evidence, it appears that routine testing for FVL and PG mutations in patients with unprovoked first VTE may have limited clinical effectiveness.

The results of the cost analysis indicate that, given the lack of clinical utility associated with FVL and PG mutation testing in patients with an initial unprovoked VTE episode, stopping funding of these tests in jurisdictions that are currently doing so would lead to cost savings. The results were robust to changes in assumptions, as epidemiologic data indicate that the probability that results of tests would affect medical management is low. Testing would be cost-saving for payers only when negative test results lead to a reduction in treatment. If further information becomes available that suggests different clinical outcomes for patients, the current analysis may need to be revised.

Recommendations

Patients with a first unprovoked VTE should not routinely be tested for FVL and PG mutations.

Methods

A peer-reviewed literature search was conducted using MEDLINE, EMBASE, and PubMed. Grey literature was identified by searching relevant sections of the CADTH Grey Matters checklist. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic studies, and guidelines. The search was limited to English-language documents published between January 1, 2004 and April 28, 2014. Two reviewers independently screened citations for randomized controlled trials and non-randomized studies with a no-testing control group, involving the administration of FVL or PG mutation assay available in Canada to patients with a first, unprovoked VTE. VTE was considered unprovoked if patients had not recently (within four weeks) undergone surgery or trauma, were not receiving exogenous estrogen, did not have active malignancy, and had not been immobilized for more than three days. Studies conducted on pregnant women were also excluded. Data were extracted and study quality was assessed independently by two reviewers. A narrative synthesis of results of included studies was conducted.

Further research/reviews required

There is currently a paucity of evidence regarding the clinical outcomes associated with FVL and PG mutation testing. More research is required in this area.

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