TITLE: Thrombophilia Testing for Early Pregnancy Loss: Clinical Effectiveness and Guidelines

DATE: 24 March 2015

RESEARCH QUESTIONS

1. What is the clinical effectiveness of thrombophilia testing in women with early pregnancy loss?

2. What are the evidence-based guidelines for thrombophilia testing in women with early pregnancy loss?

KEY FINDINGS

One systematic review, one non-randomized study, and five evidence-based guidelines were identified regarding the clinical effectiveness of thrombophilia testing for women who have had early pregnancy loss.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 8), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2009 and August 7, 2014. Internet links were provided, where available.

The list of articles for this report was selected by one author and summarized by a second author.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

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SELECTION CRITERIA

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

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<tr>
<th>Table 1: Selection Criteria</th>
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<td><strong>Population</strong></td>
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<td><strong>Intervention</strong></td>
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<td><strong>Comparator</strong></td>
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<td><strong>Outcomes</strong></td>
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<td><strong>Study Designs</strong></td>
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RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and evidence-based guidelines.

One systematic review, one non-randomized study, and five evidence-based guidelines were identified regarding the clinical effectiveness of thrombophilia testing for women who have had early pregnancy loss. No relevant health technology assessments.

Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

One systematic review\(^1\), one non-randomized study\(^2\), and five evidence-based guidelines\(^3-7\) were identified regarding the clinical effectiveness of thrombophilia testing for women who have had early pregnancy loss.

A systematic review\(^1\) on Factor V Leiden and prothrombin G20210A testing in women with recurrent pregnancy loss examined their test performance, effect sizes, and treatment effectiveness. The authors reported statistically significant increased odds for the association of recurrent pregnancy loss with F5 in case-control and in cohort studies and noted that results for F2 testing were similar. The evidence for clinical utility indicated that anticoagulation treatments were not effective and could lead to net harms.\(^1\)

The non-randomized study\(^2\) evaluated testing for hereditary thrombophilia alone or in combination with uterine artery Doppler (UAD) for predicting recurrent complications in patients with previous preeclampsia, placental abruption, or stillbirth. The authors did not find thrombophilia testing to be useful in improving the accuracy of UAD alone in predicting complications.\(^2\)
Five evidence-based guidelines³-⁷ were identified regarding the clinical effectiveness of thrombophilia testing for women who have had early pregnancy loss. Detailed recommendations are provided in Table 2.

<table>
<thead>
<tr>
<th>Author</th>
<th>Recommendations</th>
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<tr>
<td>ACOG (2013)³</td>
<td>“There is insufficient evidence to either screen for or treat women with inherited thrombophilias and obstetric histories that include complications such as fetal growth restriction or preeclampsia.” Major Recommendations</td>
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<td>ACMG (2013)⁴</td>
<td>“5,10-methylenetetrahydrofolate reductase (MTHFR) polymorphism genotyping should not be ordered as part of the clinical evaluation for thrombophilia or recurrent pregnancy loss.” Major Recommendations</td>
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<td>RCOG (2011)⁵</td>
<td>“Women with second-trimester miscarriage should be screened for inherited thrombophilias including factor V Leiden, factor II (prothrombin) gene mutation and protein S” page 8.</td>
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<td>Baglin et al. (2010)⁶</td>
<td>“Testing for heritable thrombophilias in selected patients, such as those with a strong family history of unprovoked recurrent thrombosis, may influence decisions regarding duration of anticoagulation (C). It is not possible to give a validated recommendation as to how such patients should be selected.” page 210</td>
</tr>
<tr>
<td>SISET (2009)</td>
<td>Specific guidance not reported.</td>
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ACMG = American College of Genetics and Genomics; ACOG = American College of Obstetricians and Gynecologists; RCOG = Royal College of Obstetricians and Gynecologists; SISET = Italian Society for Haemostasis and Thrombosis.

* Verbatim recommendations.
REFERENCES SUMMARIZED

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses


Randomized Controlled Trials
No literature identified.

Non-Randomized Studies


Guidelines and Recommendations


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APPENDIX – FURTHER INFORMATION:

Non-Randomized Studies

Statistical Model


Decision Analysis


Guidelines and Recommendations

Methodology Unclear


See: Pregnant Patients, pages 9-13

See: Page 2

Review Articles


