CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Natriuretic Peptide Testing for Pulmonary Arterial Hypertension: Clinical Effectiveness, Cost-Effectiveness, and Guidelines
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Funding: CADTH receives funding from Canada’s federal, provincial, and territorial governments, with the exception of Quebec.

Questions or requests for information about this report can be directed to requests@cadth.ca
Research Questions

1. What is the clinical utility of natriuretic peptide testing for prognosis or guiding therapy for pulmonary arterial hypertension?

2. What is the cost-effectiveness of natriuretic peptide testing for prognosis or guiding therapy for pulmonary arterial hypertension?

3. What are the guidelines for natriuretic peptide testing for pulmonary arterial hypertension?

Key Findings

One systematic review, five non-randomized studies, and three evidence-based guidelines were identified regarding natriuretic peptide testing for pulmonary arterial hypertension.

Methods

A limited literature search was conducted by an information specialist on key resources including PubMed, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine’s MeSH (Medical Subject Headings), and keywords. The main search concepts were natriuretic peptide testing and pulmonary arterial hypertension (PAH). Search filters were applied to limit retrieval of a broader search to health technology assessments, systematic reviews, meta-analyses, or network meta-analyses, randomized controlled trials or controlled clinical trials, economic studies, and guidelines. The search was also limited to English language documents published between January 1, 2014 and July 12, 2019. Internet links were provided, where available.

Selection Criteria

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

Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention</th>
<th>Comparator</th>
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<tbody>
<tr>
<td>Patients of all ages with pulmonary arterial hypertension</td>
<td>Natriuretic peptide testing (BNP/NT-proBNP blood tests) with or without additional diagnostic tests</td>
<td>Q1 &amp; Q2: No natriuretic peptide testing; Other prognostic testing (e.g., cardiac troponin T test, echocardiography) Q3: No comparator</td>
</tr>
</tbody>
</table>
Outcomes

Q1: Clinical utility (e.g., changes to therapy)
Q2: Cost-effectiveness
Q3: Evidence-based guidelines

Study Designs

Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations, evidence-based guidelines

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, economic evaluations, and evidence-based guidelines.

One systematic review, five non-randomized studies, and three evidence-based guidelines were identified regarding natriuretic peptide testing for pulmonary arterial hypertension. No relevant health technology assessments, randomized controlled trials, or economic evaluations were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

One systematic review\(^1\) and five non-randomized studies\(^2\)\(^-\)\(^6\) were identified regarding the clinical utility of natriuretic peptide testing for pulmonary arterial hypertension. Detailed study characteristics are provided in Table 2.

Overall, the majority of study authors found that natriuretic peptide levels have prognostic value for a variety of endpoints, including death, lung transplantation, heart failure, and development of late pulmonary hypertension.\(^1\)\(^-\)\(^4\)

There were mixed findings regarding the clinical utility of natriuretic peptide testing for diagnosis. The authors of one systematic review found it unsuitable in pediatric patients diagnosed with pulmonary hypertension by right heart catherization.\(^1\) However, the authors of one non-randomized study found a significant correlation between echocardiographic results and B-type natriuretic peptide levels in patients with systemic lupus erythematous.\(^5\)

The authors of one non-randomized study assessed the clinical utility of natriuretic peptide testing for screening and found significantly elevated levels in preterm infants diagnosed with pulmonary hypertension by echocardiography.\(^6\)

Three evidence-based guidelines were identified regarding natriuretic peptide testing for pulmonary arterial hypertension.\(^7\)\(^-\)\(^9\) The European Society of Cardiology and European Respiratory Society states in their joint guidelines that natriuretic peptide testing should be used for risk assessment in patients with pulmonary arterial hypertension.\(^7\) The American Heart Association and American Thoracic Society recommend that either B-type natriuretic peptide or N-terminal-pro-fragment B-type natriuretic peptide should be measured at diagnosis, and that these levels can be useful in screening for pulmonary hypertension in patients with sickle cell disease.\(^8\) The American Thoracic Society states that natriuretic
peptide testing should not be used for diagnosis but can be used as an alternative to echocardiography for risk assessment.⁹

Table 2: Characteristics of Included Literature

<table>
<thead>
<tr>
<th>First Author, Year</th>
<th>Study Characteristics</th>
<th>Interventions and Comparators</th>
<th>Outcomes</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systematic Reviews and Meta-analyses</strong></td>
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<tr>
<td>Ten Kate, 2015¹</td>
<td>• 14 studies included • Pediatric patients with PH diagnosed by RHC</td>
<td>Several, including: • NT-proBNP testing • RHC</td>
<td>• Prognostic value • Clinical utility as diagnostic marker</td>
<td>• NT-proBNP levels correlate with mortality and therefore have prognostic value • NT-proBNP testing is unsuitable for diagnosis but can be used to monitor patients</td>
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<tr>
<td><strong>Non-Randomized Studies</strong></td>
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<tr>
<td>Behere, 2019²</td>
<td>• Retrospective longitudinal study • Preterm infants with BPD • N = 37 • Follow-up ranged from 14 to 91 weeks</td>
<td>Serum BNP testing • Echocardiography</td>
<td>Prognostic value (endpoint of late PH)</td>
<td>• Infants who developed late PH had significantly elevated BNP at initial screening • BNP levels correlate with echocardiographic evaluation</td>
</tr>
<tr>
<td>Geenen, 2019³</td>
<td>• Prospective study • Patients with PH diagnosed by RHC • N = 106 • Median follow-up 24 months</td>
<td>Several biomarkers, including NT-proBNP • REVEAL risk score</td>
<td>Prognostic value (endpoints of death, lung transplantation, and or heart failure)</td>
<td>• Elevated NT-proBNP is significantly associated with endpoints • NT-proBNP does not yield prognostic value independent of REVEAL risk score</td>
</tr>
<tr>
<td>Stepnowska, 2018⁴</td>
<td>• Prospective study • Patients with PAH • N = 47</td>
<td>Several, including BNP testing</td>
<td>Prognostic value (endpoint of death)</td>
<td>• Elevated BNP is independent predictor of mortality</td>
</tr>
<tr>
<td>Ghofraniha, 2017⁵</td>
<td>• Cross-sectional study • Patients with SLE diagnosed with PAH by echocardiography • N = 50</td>
<td>Several, including: • Serum BNP testing • Echocardiography</td>
<td>Clinical utility as diagnostic marker</td>
<td>Significant correlation between echocardiographic results and BNP levels</td>
</tr>
<tr>
<td>Montgomery, 2016⁶</td>
<td>• Cross-sectional study • Preterm infants • N = 20</td>
<td>NT-proBNP testing • Echocardiography • Amino acid levels</td>
<td>Clinical utility as screening marker</td>
<td>• NT-proBNP levels are significantly elevated in patients diagnosed with PH by echocardiogram • Elevated NT-proBNP has significant correlation with low citrulline</td>
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</tbody>
</table>

⁶WMT = six-minute walk test; BNP = B-type natriuretic peptide; BPD = bronchopulmonary dysplasia; NT-proBNP = N-terminal-pro-fragment B-type natriuretic peptide; PAH = pulmonary arterial hypertension; PH = pulmonary hypertension; TnT = cardiac troponin T; RHC = right heart catheterization; SLE = systemic lupus erythematosus.
References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses


Randomized Controlled Trials

No literature identified.

Non-Randomized Studies


Economic Evaluations

No literature identified.
Guidelines and Recommendations

   See: Sections 5.1.9, 6.2.3, 6.2.4, and 7.1.1

   See: Sections 3 and 14

   See: Diagnosis of PH in SCD, page 729; Estimating Mortality Risk in SCD, page 732
Appendix — Further Information

Systematic Reviews and Meta-analyses – Unknown Comparator


Randomized Controlled Trials – Unknown Comparator


Non-Randomized Studies

Unknown Comparator


Alternative Population


Guidelines and Recommendations – Methodology Not Specified


Review Articles


Additional References

See: Section 6