The impact of the Oncotype Dx® Breast Cancer Assay in clinical practice: systematic review and meta-analysis

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INTRODUCTION

• The Oncotype Dx® Breast Cancer Assay (ODX) is a gene expression test of 21 genes.
• It has been shown to provide prognostic and predictive information for ER positive, lymph node negative early-stage breast cancer patients in retrospective studies of clinical trials.
• The test’s purported benefits—in improved patient selection for chemotherapy use, improved clinical outcomes, and decreased costs, may be muted if patients and physicians do not follow the treatment course suggested by the test or if the test performs poorly in actual practice.
• Many studies have evaluated ODX and its impact on adjuvant chemotherapy (ACT) treatment decisions.
• However, it can be difficult for clinicians and other stakeholders to interpret the findings of these studies, as they were conducted in diverse settings and have limited sample sizes.

METHODS

• Two reviewers performed a systematic review using PubMed, Embase, ASCO, and San Antonio Breast Cancer Symposium databases.
• Candidate studies were identified with the search terms: oncotype, 21-gene, breast, and chemotherapy
• Included studies investigated ER+, node -, early stage breast cancer, reported use of ODX to inform actual ACT decisions, reported outcomes of interest, and were published in English
• Pooled outcomes included:
  1. Distribution of ODX recurrence scores (RS)
  2. Impact of ODX on ACT recommendations
  3. Impact of ODX on ACT use
  4. Proportion of patients following treatment suggested by ODX RS

• Fixed and random effects models were evaluated for each outcome
• Studies were weighted by sample size in pooled analyses
• Publication bias was assessed using funnel plots

RESULTS

• A total of 22 studies met inclusion criteria and contributed to pooled analyses
• The pooled distribution of RS categories was 48.8% low, 39.0% intermediate, and 12.2% high (21 studies, 4,156 patients)
• ODX changed the clinical-pathological ACT recommendation in 33.4% of patients (9 studies, 1,437 patients)
• In patients receiving ODX testing, pooled receipt of ACT was 28.2% overall, 5.8% low, 37.4% intermediate, and 83.4% high.
• Low RS patients were significantly more likely to follow the treatment suggested by ODX vs. high RS patients RR: 1.07 (1.01–1.14)
• There was little evidence of publication bias in the pooled analysis of treatment adherence in High RS vs. Low RS patients as indicated by symmetrical distribution of results around the pooled RR

CONCLUSIONS

• The pooled results for the impact of ODX on ACT recommendations are consistent with most individual studies to date.
• However, the proportion of intermediate RS results is nearly 2-fold higher than reported in the ODX development studies by Paik et al., which may have implications for the clinical utility and cost impacts of testing.
• Also, low RS vs. high RS patients were more likely to follow the ODX results, suggesting a tendency toward less aggressive treatment despite a high ODX RS.
• Finally, there was a lack of studies on the impact of ODX on ACT use vs. standard approaches, suggesting additional studies are warranted.

REFERENCES

Table 1: Included studies and pooled proportion

<table>
<thead>
<tr>
<th>Study</th>
<th>Proportion of High RS</th>
<th>Proportion of Intermediate RS</th>
<th>Proportion of Low RS</th>
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<tbody>
<tr>
<td>Study 1</td>
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<td>0.60</td>
<td>0.05</td>
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<tr>
<td>Study 2</td>
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<td>0.55</td>
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<tr>
<td>Study 3</td>
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<td>0.50</td>
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Table 2: Proportion of physicians changing chemotherapy recommendation after ODX testing

<table>
<thead>
<tr>
<th>Study</th>
<th>Weighted Proportion Changing ACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>0.25</td>
</tr>
<tr>
<td>Study 2</td>
<td>0.30</td>
</tr>
<tr>
<td>Study 3</td>
<td>0.40</td>
</tr>
</tbody>
</table>

RESULTS

Figure 1: Adherence to treatment by recurrence score classification. Figure 1 shows the overall proportion of patients who adhered to the chemotherapy recommendation after ODX testing. The high recurrence score group is assumed to be indicated to receive ACT. The low recurrence score group is assumed to not be indicated for ACT.