Clinical utility of echocardiographic left-ventricular ejection fraction monitoring for cardiotoxicity risk assessment in patients with HER2+ early breast cancer undergoing trastuzumab-based therapy.

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Topic(s):
Cardio-Oncology

Citation:
Background: Monitoring left-ventricular ejection fraction (LVEF) is a routinely-practiced strategy to survey patients with breast cancer (BC) towards cardiotoxic treatment effects. However, whether the LVEF as a single measurement or as a trajectory over time is truly sufficient to identify patients at high risk for cardiotoxicity is currently debated. Purpose: To quantify the prognostic impact of LVEF and its change over time for predicting cardiotoxicity in women with HER2+ early BC. Methods: We analyzed 1,136 echocardiography reports from 185 HER2+ early BC patients treated with trastuzumab ± chemoimmunoendocrine therapy in the neoadjuvant/adjuvant setting (Table 1). Cardiotoxicity was defined as a 10% decline in LVEF below 50%. Results: Median baseline LVEF was 64% (25th-75th percentile: 60-69). Nineteen patients (10%) experienced cardiotoxicity (asymptomatic n=12, symptomatic n=7, during treatment n=19, treatment modification/termination n=14), Median time to cardiotoxicity was 6.7 months, and median LVEF decline in patients with cardiotoxicity was 18%. One-year cardiotoxicity risk was 7.6% in the 35 patients with a baseline LVEF=60% and 24.5% in the 150 patients with a baseline LVEF<60% (Hazard Ratio (HR)=3.45, 95%CI:1.35-8.75, Figure 1). During treatment, LVEF declined significantly faster in patients who developed cardiotoxicity than in patients without cardiotoxicity (1.3%/month vs. 0.1%/month, p<0.0001). A higher rate of LVEF decrease predicted for higher cardiotoxicity risk (HR per 0.1%/month higher LVEF decrease/month=2.50, 95%CI: 1.31-4.76, p=0.005), and cardiotoxicity risk increased by a factor of 1.7 per 5% absolute LVEF decline from baseline to first follow-up (HR=1.70, 95%CI: 1.30-2.38, p<0.0001). Thirty-six patients (19%) developed an LVEF decline of at least 5% from baseline to first follow-up ("early LVEF decline"). One-year cardiotoxicity risk was 6.8% in those without early LVEF decline and a baseline LVEF=60% (n=117), 15.7% in those without an early LVEF decline and a baseline LVEF<60% (n=65), and 66.7% in those with an early LVEF decline and a baseline LVEF<60% (n=3), respectively (log-rank p=0.0001). Conclusion: Both a single LVEF measurement and the rate of LVEF decrease strongly predict cardiotoxicity in early BC patients undergoing HER2-targeted therapy. Routine LVEF monitoring identifies individuals at high risk of cardiotoxicity that may benefit from more sensitive screening techniques such as strain imaging.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years, median [IQR])</td>
<td>55 [49-65]</td>
</tr>
<tr>
<td>Estrogen receptor positive (n, %)</td>
<td>124 (67%)</td>
</tr>
<tr>
<td>Neoadjuvant setting (n, %)</td>
<td>103 (56%)</td>
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</tbody>
</table>
Abstract: P6237
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