Predictive value of echocardiographic markers of diastolic dysfunction for heart failure in overweight and obese patients in CAMELLIA-TIMI 61

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BACKGROUND

- Echocardiography guidelines have outlined several markers of diastolic dysfunction in patients with preserved left ventricular systolic function.
- However, evidence is limited for the prognostic value of these markers for hospitalization for heart failure (HHF) in overweight and obese patients.
- We sought to investigate the association between diastolic dysfunction parameters and HHF in a well-characterized population of obese and overweight patients with an LV EF ≥35%.

METHODS

- CAMELLIA-TIMI 61 was a randomized placebo-controlled trial of the weight loss agent, lorcaserin, in 12,000 pts with a BMI ≥27 with or at risk for CV disease, with median follow-up of 3.3 yrs.1
- Echocardiography with core lab interpretation was performed on a subset of patients. Diastolic dysfunction parameters included the ratio of the peak early-transmitral diastolic flow velocity over the early diastolic mitral annulus velocity (average E/e’), left atrium volume index (LAVi), and tricuspid regurgitation jet velocity (TRV).
- The primary outcome for this analysis, HHF, was adjudicated by reviewers blinded to echo data.
- Echo variables were analyzed 1) continuously, 2) according to standard (guideline) cutpoints of average E/e’>14, LAVi>34 mL/m², and TRV>2.8 m/s, and 3) with optimized cutpoints (identified via the Youden index method) for prediction of HHF.

RESULTS

- On a continuous scale, all 3 diastolic dysfunction parameters were univariate predictors of an increased risk of HHF (0.001 for all; Fig 1).
- In an analysis using standard (guideline) cutpoints, only E/e’>14 remained independent predictor after adjustment for all 3 echo parameters and clinical variables (Fig 2).
- In an analysis of optimal cutpoints in these overweight and obese patients, >13 was optimal for average E/e’, >2.5 m/s for TRV, and >58 mL/m² for LAVi.
- In a model with all 3 echo parameters, all remained significant predictors of HHF (data not shown). When also incorporating clinical variables, only E/e’ and LAVi remained independent predictors of HHF (Fig 2).

Figure 1. Unadjusted Association Between Diastolic Dysfunction Parameters and HHF

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Parameters</th>
<th>% Elevated</th>
<th>Adj MV HR* (95%CI)</th>
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</thead>
<tbody>
<tr>
<td>Standard Cutpoints</td>
<td></td>
<td></td>
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<tr>
<td>Average E/e’&gt;14</td>
<td>13%</td>
<td>(1.40,4.27)</td>
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<tr>
<td>Tricuspid Velocity&gt;2.8</td>
<td>6%</td>
<td>(0.48,10.66)</td>
</tr>
<tr>
<td>LA Volume Index&gt;34</td>
<td>87%</td>
<td>(0.61,3.72)</td>
</tr>
<tr>
<td>Alternate Cutpoints</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tricuspid Velocity&gt;2.5</td>
<td>25%</td>
<td>(0.73,3.26)</td>
</tr>
<tr>
<td>LA Volume Index&gt;58</td>
<td>37%</td>
<td>(1.33,4.36)</td>
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</tbody>
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*Adjusted for 3 echo parameters, age, BMI, diabetes and TIMI Risk Score for HF in DM variables (Prior HF, Atrial fibrillation, CAD, eGFR<60, INR>2.0).

- Using the alternative cutpoints for the independent predictors, 47% of patients had one or both abnormal parameters (E/e’>13 or LAVi>58 mL/m²; Fig 3).
- A significant gradient of risk for HHF was observed in patients with none, one, or both measures of diastolic dysfunction (Fig 3).

CONCLUSIONS

- Established echocardiographic markers of diastolic dysfunction used in current guidelines predict increased risk of HHF events in the prevalent but understudied overweight and obese population.
- Average E/e’ and LAVi (using a higher cutpoint of >58 mL/m²) remained independent predictors after adjustment for other measures of diastolic dysfunction and clinical variables.
- A higher number of abnormal measures of diastolic dysfunction predicts increased risk of HHF in this population of patients.


Figure 3. Rate of HHF in Patients with Stratified by Number of Abnormal Diastolic Dysfunction Parameters

- HR 2.31 (1.31, 4.09) for the independent predictors, 47% of patients had one or both abnormal parameters (E/e’>13 or LAVi>58 mL/m²; Fig 3).
- A significant gradient of risk for HHF was observed in patients with none, one, or both measures of diastolic dysfunction (Fig 3).