Routine clinical variables predicted mortality in patients with heart failure and systolic dysfunction


Clinical impact ratings GP/FP/Primary care ★★★★★★ IM/Ambulatory care ★★★★★★ Cardiology ★★★★★★ Internal medicine ★★★★★★

In patients with heart failure (HF) and depressed systolic function, can routine clinical variables be used to predict short term and long term mortality?

Methods

Design: derivation and validation of a multivariate statistical model to predict mortality using data from the Digitalis Investigation Group (DIG) trial.

Setting: 300 centres in North America.

Patients: 6422 patients with HF who had a left ventricular ejection fraction <45%, were in sinus rhythm, and were taking angiotensin converting enzyme (ACE) inhibitors. Exclusion criteria: age <21 years, serum creatinine concentration >3.0 mg/dl, unstable coronary syndromes, cor pulmonale, complex congenital heart disease, or recognizable non-cardiac causes of HF. The derivation and validation cohorts included 4277 and 2145 patients, respectively (mean age 63.9, 78% men).

Prediction guide: the modelling procedure included 11 variables. The final Cox proportional model included the 11 variables listed in the table.

Outcomes: mortality at 12 and 36 months.

Main Results

Total mortality in the derivation sample was 11% at 12 months and 30% at 36 months. Independent predictors are summarised in the table. In the lowest risk decile, 12 month predicted mortality was 4.0% compared with 3.8% observed mortality, and 36 month predicted mortality was 11.8% compared with 10.7%. In general, the models performed less well for the highest risk decile.

Prediction guide: mortality at 12 and 36 months.

Commentary

Brophy et al have contributed a model that predicts the likelihood of mortality at 12 and 36 months in patients with congestive heart failure (CHF). The authors used rigorous methods, including a Bayesian approach intended to minimise the risk of over-fitting and optimise prediction in future patients with similar characteristics. Indeed, the calibration curves by decile of risk suggest good performance in the validation dataset.

The model variables do not require sophisticated laboratory or imaging studies, but the equation requires 11 variables (table), including a composite variable of 7 clinical signs and symptoms. Although a computer-based tool may enable calculation of a risk score, it is unclear whether these variables can be easily or reliably obtained in routine clinical practice. Importantly, it is unclear how or why busy clinicians would use such a complex prognostic tool.

The authors suggest that risk models may be useful when selecting treatments for patients with CHF. Now that several mortality reducing treatment options are available, risk stratification may have a role in targeting more intense therapies to those most likely to benefit. This will only become clear when such models are used to stratify patients within clinical trials testing these therapies. The critical test is whether such stratification enables identification of patients at such low risk that they are unlikely to benefit from additional therapies to an extent that justifies the risks and costs of therapy. However, in this sample that included NYHA Class I–IV patients who were all receiving ACE inhibitors, the average 3-year mortality rate was 30%, and the mortality rate of even the lowest risk decile was about 10%. This suggests that even patients at low and moderate risk have considerable room for improvement beyond therapy with ACE inhibitors.

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Source of funding: not stated.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference group</th>
<th>Hazard ratio (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt;50 years</td>
<td>Mortality at 12 months: 1.20 (1.13 to 1.28)</td>
</tr>
<tr>
<td>Ejection fraction (per 10% decrease)</td>
<td></td>
<td>Mortality at 36 months: 1.34 (1.22 to 1.48)</td>
</tr>
<tr>
<td>NYHA class</td>
<td>Class I</td>
<td>1.44 (1.24 to 1.68)</td>
</tr>
<tr>
<td>Cardiorespiratory ratio &gt;50%</td>
<td></td>
<td>1.60 (1.29 to 1.97)</td>
</tr>
<tr>
<td>Clinical signs or symptoms</td>
<td>0–1 signs or symptoms</td>
<td>1.21 (1.06 to 1.38)</td>
</tr>
<tr>
<td>Serum creatinine (per mg/dl increase)</td>
<td></td>
<td>1.85 (1.49 to 2.38)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>&gt;29.7 kg/m²</td>
<td>1.18 (1.08 to 1.28)</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>&gt;80 mm Hg</td>
<td>1.17 (1.08 to 1.28)</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>&gt;139 mm Hg</td>
<td>Not significant</td>
</tr>
<tr>
<td>Nitrates</td>
<td></td>
<td>Not significant</td>
</tr>
<tr>
<td>Diabetes ischaemic aetiology</td>
<td></td>
<td>1.46 (1.19 to 1.79)</td>
</tr>
</tbody>
</table>

*BP = blood pressure. Hazard ratios are per 1 group increase for the following categorical variables: age, New York Heart Association (NYHA) class, clinical signs or symptoms, and per 1 group decrease for body mass index and blood pressure.
†Rales, increased jugular venous pressure, peripheral oedema, dyspnoea, limitation of activity, S3 gallop, or radiological evidence of pulmonary congestion.
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Evid Based Med 2004 9: 154
doi: 10.1136/ebm.9.5.154

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