Validation of a Prediction Rule for Adverse Cardiovascular Events from Drug Overdose

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In accordance with our prior work, we define overdose-related adverse cardiovascular events (ACVE) as follows:  

- Myocardial injury (troponin elevated)  
- Shock (hypotension requiring vasopressors)  
- Ventricular dysrhythmias (VT/VF/TdP)  
- Cardiac arrest (loss of pulse requiring CPR).  

ACVE complicate up to 16.9% of hospitalizations for acute drug overdose.  

We previously derived a risk prediction rule for ACVE in acute drug overdose patients with 97.1% negative predictive value:  

- Cardiac disease, metabolic acidosis, prolonged QTc  

Objective: Our aim was to internally validate the ACVE rule test characteristics at our own institutions.

Results

ED acute drug overdose (N=1,457)

Excluded (N=552)

Included (N=905)
Mean age, 41 years
Female, 44%
Suicidal, 40%

ACVE (N=65, 7.2%, CI 5.6-9.1)
Myocardial injury, 44
Shock, 31
Dysrhythmia, 16
Cardiac arrests, 17
Deaths, 16

<table>
<thead>
<tr>
<th>Risk Factor:</th>
<th>Validated OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac disease</td>
<td>39.5</td>
<td>17.9-87</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>2.7</td>
<td>1.5-4.9</td>
</tr>
<tr>
<td>Prolonged QT</td>
<td>5.5</td>
<td>2.8-10.9</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Data Set:</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV 2+ factors</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Derivation</td>
<td>51.6%</td>
<td>93.7%</td>
<td>90.9%</td>
<td>97.1%</td>
</tr>
</tbody>
</table>
  CI 41.1-62       | CI 92.4-94.8  | CI 62.3-98.4| CI 96.2-97.9   |
| Validation       | 75.4%         | 82.3%       | 51.5%          | 97.8%     |
  CI 63.1-85.2     | CI 79.9-85.1  | CI 34.5-68.6| CI 96.4-98.7   |
We have internally validated the previously-derived risk prediction rule for ACVE in patients with acute drug overdose. The rule performed with slightly improved sensitivity and negative predictive value in the validation cohort. Use of these risk factors as a clinical decision rule, if externally validated, may allow for safer disposition of lower risk patients as well as ICU triage for those at highest risk. External validation in distinct settings nationwide is underway via the ToxIC Registry under a NIDA R01 (PI: Manini). We intentionally analyzed a heterogeneous study population in an attempt to enhance generalizability for ED clinicians taking care of acute drug overdoses. Future validation is needed to assess risk across all overdose intents, as well as for both single- and multi-drug exposures. Future studies should evaluate treatment modalities (e.g., Mg sulfate, antidysrhythmics) for those identified by this study to be high-risk.
Co-Investigators

▶ Robert S. Hoffman, MD
   NYU, Director, Division of Medical Toxicology

▶ Lynne Richardson, MD
   Mount Sinai, Chief, EM Research Division

▶ David Vlahov, PhD
   UCSF, Dean School of Nursing

▶ National Institute on Drug Abuse
   PO Jag Khalsa, PhD
Results: Toxicology

- Serum Toxicology Screens
  - 15 aspirin positive
  - 73 APAP positive
  - 179 ethanol co-ingestion
  - 172 other (specific screens positive)

- Urine Toxicology Screens
  - Benzos 109
  - Cocaine 89
  - Opiates 87
  - Cannabis/Cannabinoids 46
  - Methadone 40
  - Barbs 16
  - PCP 13
  - Amphetamine 7
  - Other 36 (specific screens positive)
Methods

- **Design**: This prospective cohort study was conducted over 17 months (2012-2014)
- **Setting**: 2 urban academic teaching hospitals.
- **Population**: Patients were adults with suspected acute drug overdose enrolled from the emergency department.
- **Prediction Rule**: included factors in Table 1 as previously derived.²
- **Sample size**: Was predetermined in order to calculate the rule test characteristics with 95% confidence interval (CI) widths <5%
  - We calculated the need to analyze 900 patients.