The PREPIC Trial- Fact or Fiction?

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The PREPIC Study Group

The PREPIC Trial—Study Design

- First prospective, randomized trial comparing anticoagulation to IVC filters
- From 9/91-2/95 in 44 French centers
- 400 patients with DVT “at risk” for PE
- Randomized to
  - UH or LWMH
  - IVC filter or no IVC filter
    - Greenfield, Cardial, LGM, or Bird's nest filter
- All patients placed on oral anticoagulation at discharge when possible

No Disclosures

The Last 10 IVC Filters Developed and Approved by the FDA

Prevention du Risque D'Embolie Pulmonaire Par Interruption Cave (PREPIC) study

Circulation

Eight-Year Follow-Up of Patients With Permanent Vena Cava Filters in the Prevention of Pulmonary Embolism
The PREPIC (Prevention du Risque d'Embolie Pulmonaire par Interruption Cave) Randomized Study

The PREPIC Study Group

PREPIC – Study Design

- Primary outcome
  - Pulmonary Embolism
- Secondary outcomes
  - Deep venous thrombosis
  - Death
  - Major filter complications
  - Major bleeding
- Data published at 2 (NEJM 1998) and 8 years (Circulation 2005)
PREPIC - Critical Appraisal

- Now thought of as a study of filter randomization in patients with DVT but actually included randomized treatment to unfractionated and LMW heparins
  - Weak study design

PREPIC - Critical Appraisal

- Statistical analysis is subject to criticism
  - The analysis failed to correct for multiple comparisons (UH vs LMWH, Filter vs no filter)
    - Bonferroni correction would call for a p value of < 0.0125 to be statistically significant
  - PREPIC data show that PE can occur remotely from the incident event (VTE) and that filters are protective
    - Retrieval of IVC filters does NOT provide protection from late events

PREPIC 2 - Design

- Do patients with acute PE and high risk of recurrence benefit from an IVC filter in addition to anticoagulation alone?
  - Multicenter, randomized, controlled trial, 2006-2012, Intention-to-treat analysis
  - 399 patients, 200 IVC filter, 199 no filter, all anticoagulated
  - Risk factors: age>75, CHF, COPD, cancer, RV dysfunction, MI, stroke, bilateral DVT, iliocaval thrombus
  - All filters retrieved at 3 months
  - Follow up at 3 and 6 months
PREPIC 2 - Results

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Event Rate</th>
<th>SE</th>
<th>Relative Risk</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>11.5%</td>
<td>1.05</td>
<td>1.50 (0.51-5.0)</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Hospital</td>
<td>8.8%</td>
<td>1.03</td>
<td>1.95 (0.5-7.6)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Community</td>
<td>13.8%</td>
<td>1.10</td>
<td>1.80 (0.63-5.3)</td>
<td>1.9</td>
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<tr>
<td>Community versus Hospital</td>
<td>26.1%</td>
<td>1.10</td>
<td>1.75 (0.53-5.9)</td>
<td>3.6</td>
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<tr>
<td>Main analysis</td>
<td>8.8%</td>
<td>1.03</td>
<td>1.95 (0.5-7.6)</td>
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- Increasing concerning evidence
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- Hospital
- Community
- Community versus Hospital
- Main analysis
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- Main analysis

PREPIC - Fact or Fiction

- Interesting study with controversial findings
- The data from PREPIC suggest that patients with IVC filters have:
  - Increased risk of DVT long-term
  - Decrease risk of PE long-term
- No other data to suggest that removal of IVC filters lowers the risk of DVT long-term
- PREPIC 2 did little to answer these questions