Restarting Oral Anticoagulation After Intracranial Hemorrhage

To the Editor:

In their recent article, Eckman and colleagues highlight a difficult clinical decision: whether it is safe to restart anticoagulation for atrial fibrillation after intracerebral hemorrhage, and they cite the lack of published data addressing the issue. We agree that decisions must be made based on the relative risks versus benefits in individual patients, which will vary depending on the site of hemorrhage, continuing risk factors for further hemorrhage, and indication for anticoagulation. In the decision analysis model, untreated atrial fibrillation was assumed to carry a risk of thromboembolism of 4.5% per year. The decision to restart anticoagulation is particularly difficult for patients with prosthetic heart valves (PHV) for whom the risk of thromboembolism without anticoagulation may be as high as 22% per year.

To our knowledge there have been no prospective studies determining the specific risk of recurrent intracranial hemorrhage after restarting oral anticoagulation (OAC). Lau et al reported 4 patients with OAC-related intracranial hemorrhage and PHV. All patients had anticoagulation reversed at diagnosis. Two patients died immediately; 2 patients survived and were restarted on OAC after 5 and 7 days without rebleeding after 9 weeks and 3 years' follow-up. Babikian et al reported 6 patients with PHV who restarted OAC after intracranial hemorrhage with no rebleeding after a mean 6 months of follow-up. More recently, Punthakee et al reviewed 20 patients with OAC-related intracranial hemorrhage. In 6 patients restarted on OAC for whom follow-up data were available, no further hemorrhages were recorded after a mean time of 2.8 years.

We have previously published data for 35 patients who suffered an intracranial hemorrhage while on oral anticoagulation with warfarin, including 16 patients with PHV. Nineteen (54%) patients had international normalized ratios (INRs) within the therapeutic range at the time of bleeding. After rapid reversal of anticoagulation, warfarin was withdrawn for a median 7 days (0 to 19 days). No patient with PHV had evidence of thromboembolism as a result of cessation of warfarin during this period. Two patients died as an immediate result of the intracranial bleed. Thirteen patients with PHV restarted anticoagulation after intracranial hemorrhage and were followed for a median 23.5 months (6 to 47 months) after the initial bleed. Follow-up data are summarized in the Table. The site of bleeding was intracerebral (4), subdural (7), intraspinal (1), or subarachnoid (1). One patient died of acute myocardial infarction at 8 months. One patient suffered a nonfatal, recurrent subdural hematoma while the INR was 3.5 (target 3.0 to 4.0) at 1 year. Four patients (23%) suffered recurrent ischemic neurological events (1 fatal). Of the 4 patients with intracerebral hemorrhage, none suffered recurrent intracranial bleeding and 2 suffered thromboembolic events (1 myocardial infarction, 1 cerebral infarct) after 8, 12, 28, and 39 months follow-up, respectively.

The target INR was lowered in 9 of 13 patients, including all 3 patients suffering thromboembolic events, although patient numbers were too small to demonstrate whether this was causal.

To our knowledge this is the largest published series of patients restarting anticoagulation after intracranial hemorrhage and demonstrates that careful reintroduction of oral anticoagulation is appropriate for patients at high risk of recurrent thrombosis. We conclude that restarting anticoagulation did not result in a high rate of fatal bleeding in the 2-year period after the initial intracranial bleed.

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Follow-Up Data on 13 Patients Restarting Oral Anticoagulation After Intracranial Hemorrhage

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age, y</th>
<th>Type of Bleeding</th>
<th>Site of Bleeding</th>
<th>Postbleed Target INR</th>
<th>Follow-Up, mo</th>
<th>Late Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>58</td>
<td>ICH</td>
<td>R temporoparietal</td>
<td>2.0–3.0</td>
<td>12</td>
<td>Ischemic stroke at 3 months postbleed</td>
</tr>
<tr>
<td>2</td>
<td>61</td>
<td>SAH</td>
<td></td>
<td>2.0–3.0</td>
<td>28</td>
<td>Multiple transient ischemic attacks</td>
</tr>
<tr>
<td>3</td>
<td>56</td>
<td>Intraspinal</td>
<td>Cauda equina</td>
<td>3.0–4.0</td>
<td>47</td>
<td>Ischemic stroke at 26 months postbleed (fatal)</td>
</tr>
<tr>
<td>4</td>
<td>59</td>
<td>SDH</td>
<td></td>
<td>2.0–2.5</td>
<td>27</td>
<td>Ischemic stroke at 26 months postbleed (fatal)</td>
</tr>
<tr>
<td>5</td>
<td>73</td>
<td>SDH</td>
<td></td>
<td>2.0–4.0</td>
<td>23</td>
<td>Ischemic stroke at 25 months</td>
</tr>
<tr>
<td>6</td>
<td>61</td>
<td>SDH</td>
<td></td>
<td>2.0–3.0</td>
<td>7</td>
<td>Myocardial infarction (fatal)</td>
</tr>
<tr>
<td>7</td>
<td>44</td>
<td>ICH</td>
<td>R temporal</td>
<td>3.0–4.5</td>
<td>39</td>
<td>Ischemic stroke at 26 months postbleed (fatal)</td>
</tr>
<tr>
<td>8</td>
<td>61</td>
<td>SDH</td>
<td></td>
<td>2.0–2.5</td>
<td>35</td>
<td>Ischemic stroke at 25 months</td>
</tr>
<tr>
<td>9</td>
<td>64</td>
<td>SDH</td>
<td></td>
<td>2.0–2.5</td>
<td>6</td>
<td>Myocardial infarction (fatal)</td>
</tr>
<tr>
<td>10</td>
<td>70</td>
<td>ICH</td>
<td>R temporoparietal</td>
<td>2.5–3.0</td>
<td>8</td>
<td>Myocardial infarction (fatal)</td>
</tr>
<tr>
<td>11</td>
<td>59</td>
<td>SDH</td>
<td></td>
<td>2.0–3.0</td>
<td>30</td>
<td>Recurrent nonfatal subdural hemorrhage while INR 3.5</td>
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<tr>
<td>12</td>
<td>56</td>
<td>ICH</td>
<td>R parietal</td>
<td>3.0–3.5</td>
<td>28</td>
<td>Recurrent nonfatal subdural hemorrhage while INR 3.5</td>
</tr>
<tr>
<td>13</td>
<td>53</td>
<td>SDH</td>
<td></td>
<td>3.0–4.0</td>
<td>12</td>
<td>Recurrent nonfatal subdural hemorrhage while INR 3.5</td>
</tr>
</tbody>
</table>
We believe it is premature, however, to conclude from the 4 described intracerebral hemorrhage subjects that “careful reintroduction of oral anticoagulation is appropriate for patients at high risk of recurrent thrombosis.” Our analysis suggests that this is a complex decision in which all options carry substantial risk.

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