Evaluation of bleeding and thrombotic risk in patients receiving triple antithrombotic therapy

Katharine Lundy PharmD
Elizabeth Meisberger PharmD, BCPS
Kris Howard PharmD, BCPS, AACC
Jennifer Sposito PharmD

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Evaluate bleeding and thrombotic risk in patients receiving triple antithrombotic therapy

Katharine Lundy, PharmD; Elizabeth Meisberger, PharmD, BCPS; Kris Howard, PharmD, BCPS, AACC; Jennifer Sposito, PharmD, BCPS

Parkview Regional Medical Center, Fort Wayne, Indiana

OBJECTIVE

Evaluate bleeding and thrombotic risk of patients receiving triple antithrombotic therapy (TAT) versus dual antithrombotic therapy (DAT) and characterize prescribing patterns.

BACKGROUND

- TAT is used in a subset of patients with indications for both dual platelet therapy (DAPT) and an oral anticoagulant (OAC).
- Indication for TAT is often due to development of acute coronary syndrome with an underlying condition requiring anticoagulation, such as atrial fibrillation, prosthetic heart valve, or venous thromboembolism (VTE).
- Studies have shown an increased risk of bleeding in patients receiving TAT (OAC + DAPT) compared to DAT (OAC + single antiplatelet therapy) with no significant differences in thrombotic events.
- Management of patients on TAT is not well addressed in current guidelines, especially regarding duration of therapy.

METHODS

- Retrospective chart review of subjects who received percutaneous coronary intervention (PCI) with either TAT or DAT prescribed at hospital discharge. Subjects were then followed for one year post-discharge or end of study period, whichever occurred first.
- Data was included from February 2015 through September 2018.
- Antiplatelet agents: aspirin, clopidogrel, prasugrel, and ticagrelor.
- OACs: warfarin, dabigatran, apixaban, and rivaroxaban.
- EDoxaban is non-formulary at the study site and was therefore not used in study subjects.
- Primary outcomes: Incidence of major bleeding within one year as defined by the Thrombolysis in Myocardial Infarction (TIMI) criteria
- Secondary outcomes:
  - Incidence of any thrombotic event identified using the International Classification of Diseases tenth revision (ICD-10) codes
  - Incidence of any bleeding event identified using ICD-10 codes
  - Time to de-escalation of TAT
  - Defined as discontinuation of at least one of the three antithrombotic agents comprising the TAT regimen

Subgroup analyses:
- Incidence of major bleeding among patients using warfarin versus a direct OAC (dabigatran, apixaban, and rivaroxaban)
- Incidence of major bleeding categorized by age of the subject
- Incidence of any gastrointestinal (GI) bleeding among subjects using a proton pump inhibitor (PPI) versus those without a PPI
- Indication for OAC among subjects with bleeding
- Bleeding events of various medication regimens

RESULTS

Table 1: Baseline Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>TAT n = 120</th>
<th>DAT n = 112</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>72 ± 16</td>
<td>73 ± 16</td>
</tr>
<tr>
<td>Number of male subjects</td>
<td>100 (83%)</td>
<td>95 (85%)</td>
</tr>
<tr>
<td>Mean CHA2DS2-VASc score</td>
<td>2.4 ± 1.7</td>
<td>2.7 ± 1.4</td>
</tr>
</tbody>
</table>

Table 2: Indications for OAC

- Indication for OAC: Subjects with bleeding
  - Apixaban/Flutab: 14 (15%)
  - VTE: 4 (15%)
  - Thromboprophylaxis: 4 (15%)
  - Multiple Indications: 4 (15%)

Table 3: Time to De-escalation

<table>
<thead>
<tr>
<th>Time to De-escalation</th>
<th>TAT n = 170</th>
<th>DAT n = 112</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-30 days</td>
<td>48 (28%)</td>
<td>30 (27%)</td>
</tr>
<tr>
<td>31-60 days</td>
<td>61 (36%)</td>
<td>46 (41%)</td>
</tr>
<tr>
<td>61-90 days</td>
<td>70 (41%)</td>
<td>67 (60%)</td>
</tr>
<tr>
<td>&gt; 90 days</td>
<td>19 (11%)</td>
<td>8 (7%)</td>
</tr>
</tbody>
</table>

Table 4: TIMI Major Bleeding by Age

<table>
<thead>
<tr>
<th>TIMI Major Bleeding</th>
<th>Subjects with bleeding n = 112</th>
<th>Subjects with bleeding n = 170</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAS-BLED (mean score ± SD)</td>
<td>2.4 ± 1.1</td>
<td>2.4 ± 1.1</td>
</tr>
</tbody>
</table>

Figure 1: Drug Regimen by Indication for OAC

Figure 2: Number of Bleeding and Thrombotic Events

Figure 3: Incidence of TIMI Major Bleeding with Warfarin vs DOAC

Figure 4: TIMI Major Bleeding by Age

Figure 5: Incidence of GI Bleeding

Figure 6: Classification of bleeding events by medication regimen

DISCUSSION & CONCLUSIONS

- There is a lack of consistency among providers regarding the management of patients receiving TAT.
- Subjects receiving DAT had a higher incidence of both major and overall bleeding events than patients receiving TAT which is contradictory to previous findings.
- Patients thought to be at a high risk of bleeding may empirically be prescribed DAT, which is reflected by the higher HAS-BLED score associated with the DAT group.
- These patients also had an increased risk of clotting as indicated by the higher CHA2DS2-VASc score in this group, but had a similar incidence of thrombotic events between the two groups.
- 62% of subjects on TAT at discharge were de-escalated to at least DAT or DAPT within 6 months, which is in alignment with available guidelines.
- The timing of de-escalation was often guided by the scheduling of the subject’s outpatient cardiology appointments.
- Incidence of GI bleeding events were higher in patients receiving a PPI.
- These subjects also had a slightly higher risk of bleeding as evidenced by the increased HAS-BLED score in this group.
- There was a higher percentage of bleeding events in subjects using an OAC for thromboprophylaxis or having multiple indications which could be a target area for intervention (16% of the study subjects).
- Of patients with bleeding, 34% used warfarin in alignment with guideline recommendations of use of warfarin + clopidogrel ± aspirin.
- The majority of bleeding events (66%) were among subjects using a DOAC, which is not a recommended therapy.

LIMITATIONS

- Retrospective chart review with limited documentation of outpatient medication use and compliance.
- Start/stop dates of agents were updated at appointments and may not reflect exact dates of therapy modification.
- Inconsistent use of ICD-10 coding for bleeding/thrombotic events.
- Future Research & Impact on Practice

- Creation of a guidance document to encourage consistency in prescribing TAT regimens and appropriate de-escalation.
- Continued study of this specific patient population to adequately characterize the risks and benefits of various treatment selection decisions.
- Further analysis of the 18% on TAT de-escalated at > 6 months.

REFERENCES


Additional information: Parkview Regional Medical Center, Fort Wayne, Indiana.