Initial Aspirin Dose and Outcome Among ST-Elevation Myocardial Infarction Patients Treated With Fibrinolytic Therapy

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Methods and Results—Using combined data from the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO I) and Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO III) trials (n=48,422 ST-elevation myocardial infarction patients), we compared the association between initial aspirin dose of 162 versus 325 mg and 24-hour and 7-day mortality, as well as rates of in-hospital moderate/severe bleeding. Results were adjusted for previously identified mortality and bleeding risk factors. Overall, 24.4% of patients (n=11,828) received an initial aspirin dose of 325 mg, and 75.6% (n=36,594) received 162 mg. The 24-hour mortality rates were 2.9% versus 2.8% (P=0.894) for those receiving an initial aspirin dose of 325 versus 162 mg. Mortality rates at 7 and 30 days were 5.2% versus 4.9% (P=0.118) and 7.1% versus 6.5% (P=0.017) among patients receiving the 325 versus 162 mg aspirin. After adjustment, aspirin dose was not associated with 24-hour (odds ratio [OR], 1.01; 95% CI, 0.82 to 1.25), 7-day (OR, 1.00; 95% CI, 0.87 to 1.17), or 30-day (OR, 0.99; 95% CI, 0.87 to 1.12) mortality rates. No significant difference was noted for myocardial infarction or the composite of death or myocardial infarction between groups. In-hospital moderate/severe bleeding occurred in 9.3% of those treated with 325 mg versus 12.2% among those receiving 162 mg (P<0.001). After adjustment, 325 mg was associated with a significant increase in moderate/severe bleeding (OR, 1.14; 95% CI, 1.05 to 1.24; P=0.003).

Conclusion—These data suggest that an initial dose of 162 mg aspirin may be as effective as and perhaps safer than 325 mg for the acute treatment of ST-elevation myocardial infarction. (Circulation. 2008;117:192-199.)

Key Words: aspirin ■ death ■ hemorrhage ■ myocardial infarction ■ prognosis
STEMI remain unknown. To date, there has been only a single randomized trial\(^1\) that compared initial aspirin doses among those receiving fibrinolytic therapy, but unfortunately, the trial stopped early after enrolling only 162 patients.

Given this paucity of information, we undertook a retrospective analysis of 2 large STEMI fibrinolytic trials, the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO I) and Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO III) clinical trials, with a combined database of 56,080 STEMI patients, to assess immediate aspirin dose (162 versus 325 mg) and short-term outcomes after STEMI. We hypothesized that aspirin dose (162 versus 325 mg) would be associated with less bleeding, not with cardiovascular events.

**Methods**

### Patient Population

The GUSTO I and GUSTO III studies were international fibrinolytic trials that enrolled 56,080 patients with STEMI <6 hours after symptom onset from 1990 through 1993 and 1995 through 1997, respectively. GUSTO I enrolled 41,021 patients; GUSTO III enrolled 15,059. Entry criteria and treatment protocols for these studies, nearly identical, have been described.\(^12\)\(^13\)

In GUSTO I, 35,529 patients received immediate chewable aspirin, of whom 31,575 (88.9%) received 160 mg and 3954 (11.1%) received 325 mg. In GUSTO III, 12,893 patients received immediate aspirin: 5019 (38.9%) received 126 to 162 mg and 7874 (61.1%) received 163 to 325 mg. For purposes of the present analysis, patients administered 126- to 162-mg doses are identified as having received 162 mg, and patients administered 163 to 330 mg are identified as having received 325 mg. We excluded 7658 patients (13.7%) because of missing or unknown data on immediate aspirin dose, 5492 (13.4%) from GUSTO I and 2166 (14.4%) from GUSTO III. This provided a final cohort of 48,422 patients for the present study. Aspirin dose was left to the discretion of the treating physician.

### Outcomes

Efficacy outcomes of interest were all-cause mortality, reinfarction, any stroke (both hemorrhagic and nonhemorrhagic), and the composite end points of death or reinfarction and death, reinfarction, or stroke. Safety outcomes of interest were GUSTO-defined bleeding (moderate, severe, or moderate/severe intensity) and requirement for blood transfusions. Events occurring within 24 hours, 7 days, and 30 days after randomization were evaluated, along with any bleeding events that occurred during initial hospitalization.

### Statistical Analysis

Baseline characteristics are reported as percentiles for discrete variables and as medians (25th and 75th percentiles) for continuous factors. The distribution of key baseline characteristics, in-hospital medications, and procedures was compared for the 2 dose groups through the use of a \(\chi^2\) test for categorical and a Wilcoxon sign-rank test for continuous variables. Hochberg’s procedure for multiple tests of significance was performed on the baseline characteristics.\(^14\) After adjustment for multiple comparisons, only those factors with values of \(P<0.001\) are statistically significant. Models had been previously developed, validated, and published for moderate to severe bleeding,\(^15\) in-hospital death or myocardial infarction,\(^16\) stroke,\(^17,18\) and mortality\(^19,20\) using the GUSTO I and III databases. All factors found to be predictive in the death or MI model were included in a logistic model for covariate adjustment for the end point of in-hospital reinfarction alone. For the composite end point of death, reinfarction, or stroke, all factors found in the published models for death, death or reinfarction, or stroke were included as potential confounders. The aspirin dose (325 versus 162 mg) was included in each of these models to assess the association between dose and outcome after adjustment for differences in baseline risk. This association was assessed at 24 and 168 hours (7 days) after randomization for all outcomes of interest. In addition, the association between aspirin dose and mortality was evaluated out to 30 days after randomization. Logistic modeling techniques were used for all of the adjusted and unadjusted modeling. The effect of trial was evaluated 2 ways: by including trial as a covariate and by stratifying on trial.

A value of \(P<0.05\) was used to declare statistical significance, bearing in mind the hypothesis-generating nature of this study. SAS version 8.2 (SAS Institute Inc, Cary, NC) was used for all statistical analyses.

All authors had access to the data and the statistical analysis report. Each author approved the final manuscript and attests to the validity of the results.

### Results

Information on immediate aspirin dose and short-term outcomes was available for 48,422 patients (86%). An immediate aspirin dose of 162 mg was given to 36,594 patients (75.6%). Patients from GUSTO I were more likely to receive 162 mg, whereas patients from GUSTO III were more likely to receive 325 mg. Baseline characteristics according to aspirin dose are presented in Table 1. It is evident that there were some imbalances between the groups. Patients receiving 162 mg were more frequently enrolled from North America, more likely to be current smokers and diabetic, less likely to have a family history of cardiac disease or history of MI, and more likely to have an inferior MI than those receiving 325 mg. Treatment and procedural characteristics are depicted in Table 2. Patients who received 162 mg were more likely to receive streptokinase; were less likely to receive tenectaplaste and reteplase; had significantly higher measured activated partial thromboplastin times at 6, 12, and 24 hours; and were more likely to undergo invasive procedures. In-hospital medications also were significantly different between the groups (Table 2).

At 24 hours, there were 1370 deaths (2.8%): 2.9% among the 325-mg and 2.8% among the 162-mg (\(P=0.894\)) groups. After adjustment for baseline imbalances, there was no significant association of aspirin 325 versus 162 mg on 24-hour mortality (odds ratio [OR], 1.01; 95% CI, 0.82 to 1.25). When stratified by clinical trial, no significant association was noted for aspirin dose and 24-hour mortality for GUSTO I (OR, 0.88; 95% CI, 0.66 to 1.17) and GUSTO III (OR, 1.29; 95% CI, 0.88, 1.72). MI and stroke occurred more frequently in patients receiving 325 mg (Table 3). However, after multivariable adjustment, there was no significant association between aspirin dose and risk of MI (OR, 1.22; 95% CI, 0.89 to 1.67) or stroke (OR, 1.16; 95% CI, 0.87 to 1.53). In addition, there was no association between aspirin dose and the composite of death, MI, or stroke at 24 hours.

At 7 days, there were 2393 deaths (4.9%): 5.2% among the 325-mg and 4.9% among the 162-mg (\(P=0.118\)) groups. After adjustment for baseline imbalances (Figure), there was no significant association of aspirin 325 versus 162 mg on 7-day mortality (OR, 1.00; 95% CI, 0.87 to 1.17). When stratified by clinical trial, no association was noted for aspirin dose and 7-day mortality in GUSTO I (OR, 0.97; 95% CI, 0.79 to 1.19) or GUSTO III (OR, 1.07; 95% CI, 0.84 to 1.36). The individual frequency of MI was similar in the 2 groups; however, stroke was more frequent in patients receiving 325 mg (Table 4). After multivariable adjustment, there was no...
significant association between aspirin dose and the risk of MI (OR, 1.00; 95% CI, 0.87 to 1.15) or stroke (OR, 1.14; 95% CI, 0.91 to 1.41). In addition, there was no association between aspirin dose and the composite of death, MI, or stroke at 7 days. At 30 days, mortality rates were higher in the 325-mg group compared with the 162-mg group (7.1 versus 6.5%; \( P=0.017 \)). However, after adjustment for baseline imbalances, there was no significant association between aspirin dose and 30-day mortality.

Moderate or severe bleeding occurred in 11.5% of the population (Table 4). In unadjusted analysis, there were fewer moderate/severe bleeding episodes and blood transfusions in
the 325-mg group. However, using the previously validated GUSTO I moderate- or severe-bleeding prediction model,15 325 mg was associated with an independent increase in the risk of moderate or severe bleeding (OR, 1.14; 95% CI, 1.05 to 1.24) compared with 162 mg (Figure). When stratified by clinical trial, the association between aspirin dose and moderate or severe bleeding remained significant for both GUSTO I (OR, 1.14; 95% CI, 1.02 to 1.27) and GUSTO III (OR, 1.24; 95% CI, 1.06 to 1.44). In addition, increased risk of moderate or severe bleeding in those receiving 325 mg aspirin was similar between patients who did (OR, 1.11; 95% CI, 0.99 to 1.24) and did not (OR, 1.12; 95% CI, 0.95 to 1.33) undergo cardiac catheterization.

**Discussion**

There are 2 major findings of the current analyses. First, in the acute setting of STEMI, there is no significant association between initial aspirin dose (162 versus 325 mg) and risk of...
death, MI, or stroke. Second, the initial dose of 325 mg is associated with a significant increase in the risk of moderate or severe bleeding compared with 162 mg in the initial treatment of STEMI. Our data are consistent with prior aspirin studies that have shown similar efficacy and increased bleeding risk with a higher aspirin dose. The present study extends these findings and demonstrates that even the initial dose of aspirin may have clinical implications and therefore should not be overlooked. Our study raises the hypothesis that lowering the initial dose of aspirin from 325 to 162 mg may substantially lower the risk of bleeding without loss of efficacy.

**Aspirin Dose: Mechanism of Action**

Aspirin irreversibly inhibits platelet cyclooxygenase-1, thereby preventing the conversion of arachidonic acid to prostaglandin H₂, which, under normal circumstances, is then converted to thromboxane (TX) A₂ and other bioactive prostanoids. TXA₂ is synthesized and released by platelets and acts as a platelet aggregator and vasoconstrictor. By preventing TXA₂ formation, aspirin irreversibly blocks platelet function. At higher doses, aspirin suppresses vascular endothelial cell production of prostacyclin, which, if unopposed, results in inhibition of platelet aggregation and induces vasodilation.

A wide range of aspirin doses have been evaluated to determine the best way to achieve maximal antiplatelet activity in the acute setting. In a study that evaluated the acute effect of 40-, 100-, 300-, and 500-mg doses of aspirin, the 100-, 300-, and 500-mg doses were found to inhibit platelet aggregation at 2 hours, with no difference observed between the 100- and 300-mg doses. Serum TXB₂ was significantly reduced 2 hours after administration in each group, yet only 300 and 500 mg exerted >99% inhibition of TXB₂ synthesis. In another study comparing 81, 162, and 324 mg aspirin, maximal platelet inhibition after 15 minutes was greatest in the 162- and 324-mg groups. No significant difference in production of TXB₂ was noted between the 162- and 324-mg groups. Moreover, such a dose-response relationship is substantially identical in healthy subjects and in patients with atherosclerosis. For complete inhibition of thromboxane synthesis, Patrono et al suggested a loading dose of at least 120 mg.

**Aspirin Dose and Efficacy**

The ideal dose of aspirin for the prevention of vascular events has been the subject of much debate. Direct comparison of aspirin dose has been evaluated in a small number of random-

### Table 3. Twenty-Four–Hour Adverse Events

<table>
<thead>
<tr>
<th>Clinical Events</th>
<th>All Patients (n=48 422)</th>
<th>162 mg (n=36 594)</th>
<th>325 mg (n=11 828)</th>
<th>P</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>2.8</td>
<td>2.8</td>
<td>2.9</td>
<td>0.894</td>
<td>1.01 (0.89–1.14)</td>
<td>1.01 (0.82–1.25)</td>
</tr>
<tr>
<td>MI</td>
<td>0.6</td>
<td>0.5</td>
<td>0.7</td>
<td>0.057</td>
<td>1.28 (0.99–1.66)</td>
<td>1.22 (0.89–1.67)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.7</td>
<td>0.7</td>
<td>0.9</td>
<td>0.017</td>
<td>1.33 (1.05–1.67)</td>
<td>1.16 (0.87–1.53)</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>0.5</td>
<td>0.5</td>
<td>0.6</td>
<td>0.067</td>
<td>1.30 (0.98–1.72)</td>
<td>1.04 (0.75–1.45)</td>
</tr>
<tr>
<td>Nonhemorrhagic</td>
<td>0.2</td>
<td>0.1</td>
<td>0.2</td>
<td>0.034</td>
<td>1.68 (1.03–2.74)</td>
<td>1.68 (0.94–2.99)</td>
</tr>
<tr>
<td>Death/MI/stroke</td>
<td>4.0</td>
<td>3.9</td>
<td>4.2</td>
<td>0.111</td>
<td>1.09 (0.98–1.21)</td>
<td>1.05 (0.91–1.21)</td>
</tr>
<tr>
<td>Death or MI</td>
<td>3.5</td>
<td>3.4</td>
<td>3.6</td>
<td>0.362</td>
<td>1.05 (0.94–1.18)</td>
<td>1.04 (0.89–1.21)</td>
</tr>
</tbody>
</table>

### Figure

Adjusted OR for 7-day events of those who received 325 mg (versus 162 mg) aspirin for the initial treatment of STEMI. Bleeding and blood transfusion are recorded as in-hospital results.
bleeding.4 Other studies of aspirin in the acute setting of
stroke without substantially increasing the risk of major
thrombosis.11 No effect of aspirin dose in STEMI. The Duke University Clinical
Cardiology Group Study-II (DUCCS-II) compared the efficacy
between aspirin dose and cardiovascular efficacy may reflect the
inverse relationship of aspirin dose on clinical outcomes was noted; however,
there is considerable evidence that the side effects of aspirin
dose dependent.3,8,38,39 A UK study group found that
patients with higher aspirin dose were more likely to have both gastrointestinal tract symptoms and gastrointestinal hemorrhage.29 In the Dutch TIA trial,27 risk of bleeding was higher in patients receiving 283 mg compared with those receiving 30 mg. Observational data from the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) investigators40 noted increased bleeding risks with increasing aspirin dose (<100 mg, 1.9%; 101 to 199 mg, 2.8%; >200 mg, 3.7%; P = 0.0001). In a recent analysis of 31 randomized controlled trials, major, minor, gastrointestinal, and fatal bleeding all increased with increased aspirin dose.41

Our analysis extends the importance of aspirin dose and risk of bleeding to the initial dose. The reason for this increased risk after a single dose is not entirely clear. Aspirin is rapidly absorbed in the upper gastrointestinal tract and results in a measurable inhibition of platelet function within 60 minutes.42 This antiplatelet effect occurs even before acetylsalicylic acid is detectable in the peripheral blood.

There has been only 1 single randomized study11 that directly compared aspirin dose in STEMI. The Duke University Clinical Cardiology Group Study-II (DUCCS-II) compared the efficacy of 81- and 325-mg aspirin doses in 162 patients with STEMI treated with front-loaded tissue plasminogen activator or anisoylated plasminogen streptokinese activator complex.11 No effect of aspirin dose on clinical outcomes was noted; however, because of its early termination, the study was severely underpowered to do so. The majority of data supporting the use of aspirin in the acute setting of myocardial infarction are from ISIS-2.4 In this study, 162.5 mg aspirin reduced vascular mortality, reinfarction, and stroke without substantially increasing the risk of major bleeding.4 Other studies of aspirin in the acute setting of myocardial infarction have been severely underpowered to address the clinical efficacy and safety profile of aspirin in this setting.34–37

Table 4. In-Hospital, 7-Day, and 30-Day Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>All Patients (n=48 422)</th>
<th>Aspirin 162 mg (n=36 594)</th>
<th>Aspirin 325 mg (n=11 828)</th>
<th>P</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At 7 d</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>5.0</td>
<td>4.9</td>
<td>5.2</td>
<td>0.118</td>
<td>1.08 (0.98–1.18)</td>
<td>1.00 (0.86–1.17)</td>
</tr>
<tr>
<td>MI</td>
<td>3.1</td>
<td>3.1</td>
<td>3.2</td>
<td>0.650</td>
<td>1.03 (0.91–1.16)</td>
<td>1.0 (0.87–1.15)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.2</td>
<td>1.2</td>
<td>1.4</td>
<td>0.0528</td>
<td>1.20 (1.0–1.43)</td>
<td>1.14 (0.91–1.41)</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>0.67</td>
<td>0.65</td>
<td>0.76</td>
<td>0.1807</td>
<td>1.18 (0.93–1.51)</td>
<td>0.96 (0.72–1.29)</td>
</tr>
<tr>
<td>Nonhemorrhagic</td>
<td>0.41</td>
<td>0.38</td>
<td>0.51</td>
<td>0.0663</td>
<td>1.32 (0.98–1.80)</td>
<td>1.54 (1.08–2.20)</td>
</tr>
<tr>
<td>Death/MI/stroke</td>
<td>8.4</td>
<td>8.4</td>
<td>8.6</td>
<td>0.403</td>
<td>1.03 (0.96–1.11)</td>
<td>1.0 (0.91–1.10)</td>
</tr>
<tr>
<td>Death or MI</td>
<td>7.7</td>
<td>7.7</td>
<td>7.8</td>
<td>0.570</td>
<td>1.02 (0.95–1.11)</td>
<td>0.99 (0.90–1.10)</td>
</tr>
<tr>
<td><strong>In hospital</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe bleeding</td>
<td>1.2</td>
<td>1.2</td>
<td>1.1</td>
<td>0.328</td>
<td>0.91 (0.74–1.10)</td>
<td>1.08 (0.85–1.38)</td>
</tr>
<tr>
<td>Moderate bleeding</td>
<td>10.3</td>
<td>11.0</td>
<td>8.3</td>
<td>&lt;0.001</td>
<td>0.73 (0.68–0.79)</td>
<td>1.15 (1.05–1.26)</td>
</tr>
<tr>
<td>Moderate/severe bleeding</td>
<td>11.5</td>
<td>12.2</td>
<td>9.3</td>
<td>&lt;0.001</td>
<td>0.74 (0.69–0.79)</td>
<td>1.14 (1.05–1.24)</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>9.4</td>
<td>10.0</td>
<td>7.5</td>
<td>&lt;0.001</td>
<td>0.74 (0.68–0.79)</td>
<td>1.09 (0.99–1.20)</td>
</tr>
<tr>
<td><strong>At 30 days</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>6.7</td>
<td>6.5</td>
<td>7.1</td>
<td>0.017</td>
<td>1.10 (1.02–1.20)</td>
<td>0.99 (0.87–1.12)</td>
</tr>
</tbody>
</table>

Aspirin Dose and Safety
The major risk of aspirin therapy is the risk of bleeding, and there is considerable evidence that the side effects of aspirin are dose dependent.3,8,38,39 A UK study group found that patients with higher aspirin dose were more likely to have both gastrointestinal tract symptoms and gastrointestinal hemorrhage.29 The Acetylsalicylic Acid and Carotid Endarterectomy (ACE) trial reported that the risk of stroke, MI, or death within 3 months of undergoing a carotid endarterectomy is significantly lower for patients receiving 81 or 325 mg aspirin daily than for those receiving 650 or 1300 mg.31 In the largest investigation to date, which compiled data from >250 antiplatelet trials, the Antiplatelet Trialists’ Collaboration (ATC) demonstrated that when aspirin use was divided into dosage categories of 75 to 150, 160 to 325, and >500 mg, the reduction in vascular events was 32%, 26%, and 19%, respectively.1,2 Although not significant, the protective effect of aspirin decreased with higher doses. A more recent examination of the ATC data in patients with acute coronary syndrome showed a greater benefit at lower doses compared with higher doses in a nonrandomized comparison. This potential inverse relationship between aspirin dose and cardiovascular efficacy may reflect the progressive inhibition of prostacyclin, similar to cyclooxygenase-2 inhibitors, thereby inducing platelet aggregation and vasoconstriction.23,33

Aspirin is rapidly absorbed in the upper gastrointestinal tract and results in a measurable inhibition of platelet function within 60 minutes.42 This antiplatelet effect occurs even before acetylsalicylic acid is detectable in the peripheral blood. The plasma half-life of aspirin is only 20 minutes; however, because platelets cannot generate new cyclooxygenase, the effects of aspirin last for the duration of the life of the platelet (~10 days).3 Whereas platelet thromboxane synthesis is blocked completely with a single dose of 100 mg, higher doses would be expected to inhibit cyclooxygenase-2-dependent thromboxane synthesis in vascular endothelium, monocytes, and macrophages.3,42 This could contribute to the impairment of hemostasis in patients using higher doses of aspirin. Another explanation for the increase in bleeding is the aspirin-dose–induced loss of the cytoprotective effects of prostaglandin E2 on the gastric mucosa.3 Consistent with this, it is imperative to examine the absolute thrombotic versus hemorrhagic risk of the individual.
patient and to determine the lowest effective dose of aspirin in each clinical setting.

**Study Limitations**

There are several limitations to our study. First, our study was a post hoc analysis of prospectively collected data within the context of 2 clinical trials. As such, the dose of aspirin was not prescribed by the study protocol, nor was it randomized. In general, treatment effects cannot be reliably estimated by observational studies, even when good adjustment models are available. However, the data with respect to both efficacy and safety are mechanistically consistent. Second, we could not explore the indications for a specific aspirin dose. Nevertheless, the main determinant of the dose used in patients in GUSTO I and GUSTO III was the routine approach of centers and specific countries (Table 1). This argues against the possibility that the selection of dose may be related to the risk profile of patients, thus confounding the differences in efficacy or safety between dose groups. Third, trial differences and regional differences in patient populations and practice patterns are reflected by significant differences in the baseline characteristics of the patients (Table 1) and in additional treatments. However, after adjustment for these differences, including the use of fibrinolytics and other antithrombotics, and stratification by clinical trial and region, a dose response between aspirin and bleeding complications is still observed. Fourth, it was unknown whether the patient was on aspirin before the infarction. Finally, GUSTO I and III were performed 10 to 15 years ago, before clopidogrel and glycoprotein IIb/IIIa use, which may limit the generalizability of the results. Nevertheless, with the current use of dual and triple antiplatelet therapy in STEMI, great focus remains on minimizing bleeding risk.

**Conclusions**

This analysis of ~50,000 patients with STEMI receiving fibrinolytic therapy from GUSTO I and III demonstrated that the initial dose of aspirin is significantly (and independently) associated with patient outcome. Specifically, a single initial dose of 325 mg was associated with a significant increase in the risk of moderate or severe in-hospital bleeding compared with 162 mg. Aspirin dose, however, was not significantly associated with a difference in the incidence of death, MI, or stroke. Although these data are nonrandomized, they suggest that for the first dose of aspirin, 162 mg may be as effective as and safer than 325 mg for the acute treatment of STEMI. This higher associated bleeding risk reinforces the importance of finding the lowest effective aspirin dose as an important goal in each clinical setting.

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**Disclosures**

None.

**References**


Berger et al

Aspirin Dose in ST-Elevation Myocardial Infarction


CLINICAL PERSPECTIVE
The International Study of Infarct Survival (ISIS-2) trial demonstrated that treatment with 162.5 mg aspirin reduces morbidity and mortality in ST-elevation myocardial infarction (STEMI). On the basis of these data, the American College of Cardiology, American Heart Association, and European Society of Cardiology gave a class I level of evidence A to immediate use of 162 mg of aspirin. Nevertheless, the most common initial dose of aspirin in the immediate setting of STEMI is 325 mg (class I level of evidence C). Given the uncertainty of immediate aspirin dose, we performed a retrospective analysis of 2 large STEMI fibrinolytic trials (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries [GUSTO I] and Global Use of Strategies to Open Occluded Coronary Arteries [GUSTO III]) to assess the relationship between aspirin dose (162 versus 325 mg) and short-term outcomes after STEMI. We demonstrated no significant association between initial aspirin dose (162 versus 325 mg) and risk of death, myocardial infarction, or stroke. However, the initial dose of 325 mg was associated with a significant increase in the risk of moderate or severe bleeding compared with 162 mg. Although these data are nonrandomized, they suggest that for the first dose of aspirin, 162 mg may be as effective as and safer than 325 mg for the acute treatment of STEMI. Until future randomized data are provided to support the use of 325 mg in the setting of STEMI, it may be worthwhile to use 162 mg, a dose previously established to lessen cardiovascular morbidity and mortality in this setting.
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