Lost in Translation: randomised controlled trial and systematic review evidence of intracoronary vs intravenous abciximab in ST-elevation myocardial infarction

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Introduction

In the evaluation of healthcare interventions, systematic review and meta-analysis of randomized controlled trials (RCTs) has been regarded as the highest level of evidence. However, these methodologies have limitations that are inherent to potential bias and heterogeneity that may be present in the source data. Furthermore, meta-analyses can constitute a form of sequential analysis as in principle a new systematic review can be conducted each time trial is published. This study seeks to demonstrate the implications for the consideration of findings of statistical significance from meta-analysis via an examination of RCT and meta-analyses findings of intracoronary with intravenous abciximab in ST-elevation myocardial infarction (STEMI) patients.

Results

- To date, the efficacy and safety of intracoronary versus intravenous administration of abciximab in STEMI patients has been evaluated in eight RCTs (Table 1).
- With the exception of one (Iversen et al), none reported statistically significant differences in mortality between intracoronary and intravenous abciximab.
- Since 2010, ten meta-analyses have been published (Figure 1). The earliest meta-analysis reported a statistically significant reduction in the risk of death with intracoronary abciximab when compared with intravenous administration (OR 0.57; 0.35, 0.94).

![Figure 1](image)

Table 1 Characteristics of the RCTs

<table>
<thead>
<tr>
<th>Year</th>
<th>Trial</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>Bellandi</td>
<td>30 days</td>
</tr>
<tr>
<td>2006</td>
<td>Galache Osuna</td>
<td>&gt;1 year</td>
</tr>
<tr>
<td>2008</td>
<td>LIPIA</td>
<td>30 days</td>
</tr>
<tr>
<td>2009</td>
<td>Dominguez-Rodriguez</td>
<td>30 days</td>
</tr>
<tr>
<td>2010</td>
<td>Iversen</td>
<td>30 days</td>
</tr>
<tr>
<td>2010</td>
<td>EASY-MI</td>
<td>1 year</td>
</tr>
<tr>
<td>2010</td>
<td>CICERO</td>
<td>30 days</td>
</tr>
<tr>
<td>2012</td>
<td>AIDA STERI</td>
<td>90 days</td>
</tr>
</tbody>
</table>

![Figure 2](image)

Conclusions

It is important to take into account the essentially sequential nature of the meta-analysis. The total number of trial that will be conducted is not fixed, and we should allow for the fact that multiple meta-analyses may be conducted, although not always reported, as trials are conducted.

Methods

A systematic review of RCTs and meta-analyses comparing intracoronary with intravenous administration of abciximab in STEMI patients. Data on mortality reported in the RCTs were pooled using:

1. cumulative meta-analysis, which does not take into consideration potential false-positive findings due to repeated significance tests as new trials are added; and
2. sequential meta-analysis, which allows for the possibility that the meta-analysis was repeated after each trial was published.

The results of the two approaches were examined, and reasons for discrepancies between the RCTs and meta-analyses were explored.

- Similar findings were reported by subsequent meta-analyses; these findings were in contrast to those reported in individual RCTs. However, the four most recent meta-analyses that included the AIDA STEMI trial did not show statistically significant reduction in mortality associated with intracoronary compared with intravenous abciximab.
- In the cumulative meta-analysis, inclusion of all existing evidence prior to the publication of the AIDA STEMI trial gave a summary estimate of OR 0.49 (95% CI 0.27, 0.90) – a statistically significant reduction in the risk of mortality (Figure 2). Six of the ten systematic reviews were published during this period and reported a statistically significant effect.
- Four further meta-analyses were published after the AIDA-STEMI trial had been published. In contrast to the earlier meta-analyses these did not show a statistically significant reduction in mortality. No further trials or meta-analyses were published before 2010.
- We also conducted a sequential meta-analysis. This analysis is similar to that undertaken in trials where the sample size is not fixed and sequential analysis is undertaken. The sequential meta-analysis allows for the possibility that the meta-analysis was repeated after each trial was published. Consequently, the confidence intervals are wider. In this case, the sequential analysis did not indicate a statistically significant reduction in mortality at any point.

References: