Intensive insulin-glucose infusion regimens with long-term or standard glucose control did not differ for reducing mortality in type 2 diabetes mellitus and MI


Clinical impact ratings: Hospitalists ★★★★★☆☆ Cardiology ★★★☆☆☆☆☆ Endocrinology ★★★★★★★☆

**Question**
In patients with type 2 diabetes and acute myocardial infarction (MI), does an insulin-glucose regimen followed by insulin-based therapy reduce mortality and morbidity (group 1) more than an insulin-glucose infusion followed by standard care (group 2) or standard care alone (group 3)?

**Methods**

**Design:** Randomized controlled trial (Diabetes Mellitus, Insulin Glucose Infusion in Acute Myocardial Infarction [DIGAMI 2]).

**Allocation:** [Concealed]*

**Blinding:** Blinded [outcome assessors]*

**Follow-up period:** Median 2.1 years.

**Setting:** 44 centers in Sweden, Norway, Denmark, Finland, England, Scotland, and the Netherlands.

**Patients:** 1253 patients (mean age 68 y, 67% men) with type 2 diabetes or blood glucose > 11.0 mmol/L (198 mg/dL) with suspected acute MI (chest pain > 15 min in the previous 24 h) or recent electrocardiogram signs (new Q-waves or ST-segment deviations in ≥ 2 leads).

**Intervention:** Intensive insulin-glucose infusion to reach a target fasting blood glucose level (5 to 7 mmol/L [90 to 126 mg/dL]) and a nonfasting blood glucose level (< 10 mmol/l [180 mg/dL]) and insulin-based long-term glucose control (group 1) (n = 474); intensive insulin-glucose infusion and standard glucose control (group 2) (n = 473); or local routine metabolic management (group 3) (n = 306).

**Outcomes:** All-cause mortality between group 1 and group 2. Secondary outcomes were all-cause mortality between group 2 and group 3, and morbidity (e.g., nonfatal reinfarction, congestive heart failure, and stroke) among all 3 groups.

**Patient follow-up:** 100% (intention-to-treat analysis).

**Main results**

Overall, 277 patients (22%) died. All-cause mortality did not differ between group 1 and group 2 or between group 2 and group 3 (Table). Group 1 did not differ from groups 2 or 3 for stroke (hazard ratio [HR] 1.41, 95% CI 0.76 to 2.62 and HR 1.21, CI 0.62 to 2.37, respectively) or MI (HR 1.34, CI 0.94 to 1.90 and HR 1.36, CI 0.91 to 2.03, respectively). Group 1 and group 3 did not differ for time to first major event (death, reinfarction, or stroke) (HR 1.22, CI 0.95 to 1.56).

**Conclusion**

In patients with type 2 diabetes and acute myocardial infarction, an insulin-glucose regimen with long-term insulin control was not better than an insulin regimen with standard glucose control for improving survival.

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**Acute insulin-glucose infusion regimen (IIR) with long-term glucose control (group 1) vs an IIR with standard glucose control (group 2), or group 2 vs routine metabolic management (group 3) for type 2 diabetes mellitus and acute myocardial infarction at median 2.1 years**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>RRR (95% CI) NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>23%</td>
<td>23%</td>
<td>—</td>
<td>3.5% (18 to 31) Not significant</td>
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<tr>
<td></td>
<td></td>
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<tr>
<td>RRI (CI) NNT</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>23%</td>
<td>19%</td>
<td>17% (11 to 56) Not significant</td>
<td></td>
</tr>
</tbody>
</table>

**Commentary**

Elevation of glucose in the acute phase of such conditions as MI can increase the risk for vascular events and mortality. However, few conclusive data exist to show that lowering glucose in such conditions can prevent major vascular events and mortality. 2 preliminary trials that investigated glucose lowering with insulin (the first DIGAMI trial [1] and another trial in ICU patients [2]) indicated lower mortality. However, these trials were modest in size and, although statistically significant, the CIs of the apparent benefit were wide and thus uncertain. In patients with diabetes, no strong evidence exists that lowering glucose prevents macrovascular disease, although it can clearly prevent microvascular disease. Nevertheless, given the consistent epidemiologic association, it is reasonable to expect that lowering glucose levels in acute conditions should lead to clinical benefit.

The study by Malmberg and colleagues was an attempt to partially replicate and extend the findings of the first DIGAMI trial. Unfortunately, the study could not achieve its critical operational goals. Problems included failure to recruit the originally projected number of patients and inability to obtain a major difference in glucose levels between the treatment groups. Thus, although the overall results of the study showed little difference in major outcomes, the study should be interpreted as being inconclusive rather than as proof that glucose lowering is not beneficial.

The questions addressed by Malmberg and colleagues are of utmost importance and must be addressed in large, well-designed studies.

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**References**
