Author's response to reviews

Title: Improving the management of non-ST elevation acute coronary syndromes: systematic evaluation of a quality improvement programme
European Quality Improvement Programme for Acute Coronary Syndrome: The EQUIP-ACS project

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Author's response to reviews: see over
RE: MS: 1172684250273695 - Response to Reviewer's report

Manuscript title: Improving the management of non-ST elevation acute coronary syndromes: systematic evaluation of a quality improvement programme
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Dear Trials Journal

Thank you for reviewing our manuscript. We have carefully considered the Reviewers’ report and provide our response in the text below. Please note that no revisions have been made to the manuscript.

Reviewer's report:
A unique characteristic of this protocol is the randomization of hospitals to participate (or not) in an intensive quality improvement program related to acute coronary syndromes. The description of the background is extensive, the hypothesis is clear, and the protocol is well described.

My only regret is that the protocol focuses on the performance of angiography (after risk certification) and long term treatment. I believe that it would appropriate to also include time to diagnosis as a quality criterion and the initiation of multiple drug therapy once a tentative or final diagnosis has been made (aspirin, clopidogrel, anti coagulant, beta blocker, statin, nitrates).

Authors’ response:
We appreciate the Reviewers’ comments.

In selecting appropriate quality metrics for the study, the EQUIP Steering Committee considered a range of possible treatments. The 8 treatments selected are based on Class I recommendations (with level of evidence A or B) from the ESC 2007 guidelines as referenced in the protocol.

We agree that time to diagnosis is an important metric but we feel that formal risk stratification, as measured in EQUIP, provides an appropriate surrogate as it is based on important diagnostic elements such as the electrocardiogram,
biochemical markers, clinical history and risk factors. The EQUIP protocol defines ‘early risk stratification’ as occurring within 24 hours of admission to hospital.

Initiation of several evidence based drug therapies both in hospital and at discharge is measured, along with an estimate of when these therapies are started (see Table) where these were recommended in the Guidelines\textsuperscript{1}. Where the evidence supports early initiation of a treatment, i.e. statins and clopidogrel loading dose, this has been specified in the protocol but initiation of other drug therapy at discharge is in agreement with the literature. The following evidence-based drug therapy and respective timings are stipulated in our protocol:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoagulation</td>
<td>In-hospital</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>At discharge</td>
</tr>
<tr>
<td>Statins</td>
<td>Within 4 days of admission</td>
</tr>
<tr>
<td>ACE-inhibitors</td>
<td>At discharge</td>
</tr>
<tr>
<td>Clopidogrel loading dose</td>
<td>Within 24 hours of admission</td>
</tr>
<tr>
<td>Clopidogrel maintenance dose</td>
<td>At discharge</td>
</tr>
</tbody>
</table>

The list of features indicating patients who should undergo early angiography is too simple. For example, patients with elevated troponin levels were enrolled in the ICTUS study (De Winter) in which a systematic invasive approach was not superior to a initial medical approach (with a relatively high proportion of 40% revascularisation in the medical court).

We agree in principle that we have used simple, often dichotomous criteria, but as stated above these criteria for early angiography are firmly based on the ESC 2007 guidelines’ definition for intermediate to high risk patients. In addition any criteria that are intended to be used in a routine clinical manner need to be simple, but of course the final judgement for angiography and PCI has to be at the discretion of the interventional cardiologist. The definition used in our study includes patients with elevated troponin levels but also several other clinical risk factors (a full list of criteria is provided in protocol). We understand that in the ICTUS trial patients with ACS and elevated troponins were randomised to an early invasive or early conservative strategy and no advantage was demonstrated for the early invasive strategy. This contrasts with the available evidence from pooling similar trials and the widely held belief that an early invasive approach is desirable in higher risk patients. Thus we feel our pragmatic approach to selecting patients who should be eligible for early angiography, while simple, is based on current European guidelines. The EQUIP study will test whether a simple quality improvement intervention can improve angiography rates in appropriate patients.
References


We look forward to your response and hope you will accept our manuscript for publication.

Kind regards

Marcus Flather

*On behalf of the EQUIP Steering Committee*