Author's response to reviews

Title: A simple statistical model for prediction of acute coronary syndrome in chest pain patients in the emergency department

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Author's response to reviews: see over
Replies to editorial board comments

1) Small sample.

The size of the sample may limit our abilities to detect characteristics of low prevalence that nevertheless are important for ACS classification. A note on this dilemma has been added to Limitations of the study on page 15. To diminish somewhat the problem with low statistical power, we left variables with odds ratios above 2.5 or below 0.4 in the statistical model even if they were non-significant, which is mentioned in Statistical analyses on page 6.

2) Very narrow definition of ACS.

The definition of myocardial infarction used in our study is the older WHO definition. The new definition by ESC/ACC is indeed broader since it now categorizes lower values of cardiac markers (e.g. Troponin T) as AMI. With the new definition, many patients previously classified as having unstable angina are now classified as having AMI. However, the total number of ACS patients is probably little affected by the new definition.

This is now stated in Limitations of the study:
“An old definition of AMI was used in the present study. Newer definitions of AMI have lower cut-off values for biochemical markers, and some of the unstable angina diagnoses in this study would currently be classified as AMI (ref Trevelyan et al). However, the total number of ACS cases would probably be little changed”.

3) The sample includes patients with STEMI. The relevant clinical question for emergency doctors is identifying ACS in patients without STEMI so I would have excluded them from the sample. This drops the ACS prevalence to 16% with impacts of PPV and NPV.

We agree that the diagnosis of STEMI can be quite obvious for the experienced doctor in a patient with typical ECG changes, and the biggest challenge is often to detect the patients with NSTEMI and unstable angina in the acute setting. But STEMI can be difficult to detect by the inexperienced physician and it is a very serious diagnosis to miss. In one of our own studies, interns reading ECGs attained a sensitivity of only 68% for STEMI (Olsson et al 2006, Clin Physiol Funct Imaging 26, pp 151–156). Since our model is intended primarily for decision support to personnel inexperienced in ECG reading (see eg Conclusions), we feel it is relevant to include the STEMI patients in the sample.

4) I do feel strongly, that the authors should remove any recommendations to hospitalize patients based on the risk estimate. The model is not sufficiently validated to warrant this type of recommendation.

We agree that a prospective validation is absolutely essential before the model can be used as a basis for any recommendation regarding patient management. Our view on this is now further emphasized in Conclusions, last sentence:
“However, the model must be prospectively validated before it can be used in clinical practice.”
Also, we have changed to the following in *Discussion* (p13, lines 8-10): “However, if a simple prediction model with automated ECG reading, like ours, can maintain a NPV of 96% in a larger prospective study, we believe it can be useful in real-life routine care.”

And on page 14, last para: “If our model can be validated in prospective studies, it is thus probably best used as support for discharging patients in settings where the ACS prevalence is low, e.g. in primary care, in the initial ED triage or in telemedicine situations, where information is limited.”

**Replies to Dr Ludbrook**

1) *Software*

The statistical analyses were conducted using SPSS release 12.0.1 (SPSS Inc, Chicago, U.S.), which is now mentioned in *Statistical analyses* on page 6.

2) *Model interpretation*

The reported odds ratios in table 3 can indeed be used to calculate the risk of ACS for an individual patient, which we also exemplify for two hypothetical patients. Our calculation procedure is 100% equivalent to the procedure described by Hosmer & Lemeshow (2000), page 87-88. The difference in procedure is simply a matter of taste. We believe that it is easier to start with the baseline odds for ACS and then multiply with the odds ratios for the risk factors that a given patient has in order to obtain the patient’s odds for ACS. The corresponding risk for the patient is then calculated as Odds / (1+Odds). The equivalent procedure by Hosmer & Lemeshow is in our opinion a bit harder for a non-statistician to follow. Here, you should start with the regression intercept (the natural logarithm of our reported baseline odds) and add all regression coefficients (the natural logarithm of our reported odds ratios) for the risk factors that a given patient has. The obtained sum (“\(g \hat{h}\)” in the notation by Hosmer & Lemeshow) can then be converted to the ASC risk as \(\exp(Sum) / (1+ \exp(Sum))\).

Irrespective of calculation procedure, our handling of the age variable in the models might have caused some confusion. In order to obtain meaningful baseline odds for ACS in the models, we namely chose 40 years old (rather than age zero) as reference value for age. Thus, we therefore used the number of years above 40 as age variable in the models and allowed for both positive (patients above 40) and negative (patients below 40) numbers. This has now been clarified in *Statistical analyses* on page 6 and when exemplifying risk calculations on pages 9-10.

**Replies to Dr McManus**

1) Positioning of citations has been revised

**Additional changes**

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