Prognostic role of troponin T versus troponin I in unstable angina pectoris for cardiac events with meta-analysis comparing published studies


Authors' objectives
To assess the risk of nonfatal acute myocardial infarction (AMI) and cardiac death in patients with unstable angina pectoris (UAP) with elevated troponin T or I.

Searching
MEDLINE was searched from January 1985 to July 1997 using the keywords 'troponin' and 'unstable angina pectoris'. The references in published clinical trials, published abstracts from national and international meetings, and review articles were also scrutinised. Where indicated, attempts were made to obtain additional data from the authors of relevant abstracts and articles. Studies reported in any language were considered.

Study selection
Study designs of evaluations included in the review
The included studies were required to have specified the collection of blood samples within 12 to 48 hours of hospital admission or chest pain onset.

Specific interventions included in the review
No inclusion criteria relating to the specific test methods were specified. The assay methods used for troponin T were first- and second-generation enzyme immunosorbent assays; those for troponin I included Opus Plus immunoaassay analyser, Stratus II fluorometric enzyme immunoassay and the Access assay. The cut-off values depended on the assay technique and ranged from 0.03 to 3.1 microg/L.

Reference standard test against which the new test was compared
No inclusion criteria relating to the reference standard were specified. The occurrence of AMI or cardiac death during follow-up was used as the reference standard. The median follow-up was 30 days (range: 4 to 1,095) for troponin T studies and 42 days (range: 10 to 365) for troponin I studies.

Participants included in the review
The included studies had to be exclusively on patients with UAP, or to report separate data on a subgroup of patients with UAP.

Outcomes assessed in the review
The included studies had to report sufficient data to calculate the sensitivity and specificity of troponin T or troponin I for the prediction of AMI or cardiac death.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed each study, with the final selection made by consensus.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.
Methods of synthesis
How were the studies combined?
A cumulative meta-analysis was performed with troponin T and troponin I grouped separately. Studies in the troponin T group were arranged in order of publication. The odds ratios (ORs) were computed for the risk of AMI and cardiac death. The overall sensitivity and specificity rates were estimated. For a statistical comparison of the sensitivity and specificity of troponin T and troponin I, a summary receiver operating characteristic (sROC) curve was generated.

How were differences between studies investigated?
Potential causes of heterogeneity were discussed.

Results of the review
Twelve studies (2,847 patients) of troponin T and 9 studies (1,901 patients) of troponin I were included in the review.

Troponin T: the cumulative OR was 2.7 (95% confidence interval, CI: 2.1, 3.4, P<0.001) for the risk of AMI and cardiac death. The cumulative sensitivity attributable to troponin T for adverse cardiac events was 57%, with a cumulative specificity of 68%.

Troponin I: the cumulative OR was 4.2 (95% CI: 2.7, 6.4, P<0.001) for the risk of AMI and cardiac death. The cumulative sensitivity attributable to troponin I for adverse cardiac events was 63%, with a cumulative specificity of 71%.

Comparative analysis of troponin T versus troponin I: the sROC curve showed no statistically-significant difference between the sensitivity and specificity of troponin T and I.

Authors' conclusions
Troponin T and troponin I were equally sensitive and specific prognostic indicators for AMI or cardiac death in patients with UAP. The review supported their role in risk stratification.

CRD commentary
The aim of the review was clearly stated, though the definition of the inclusion criteria was limited. The search strategy was limited to one electronic database and some additional sources. No attempt to identify unpublished data was reported, and publication bias was not assessed. The authors reported that all but one of the studies included in their review were reported in English; it was unclear whether language had been used as a selection criteria. Given the problems with the search strategy, it is possible that not all of the available relevant data were included in this review.

The validity of the primary studies was not assessed and UAP was not defined. In addition, the methods used to determine the outcomes of AMI and cardiac death, and to extract the data, were not provided. It was unclear why the troponin T studies were arranged in order of publication in the cumulative meta-analysis, or how the order of the troponin I studies was determined.

The authors acknowledged several methodological limitations to their review: heterogeneity of the patient population; the use of different sensitivity levels for troponin T and I in the various studies; flaws in the assumptions made when extracting the population of patients with UAP from more general patient populations; the lack of uniformity in the laboratory assay techniques used; and differences in the cut-off levels used. Given the acknowledgement of these limitations, it is surprising that no formal assessment of study heterogeneity was reported, no analysis of the effect of differing cut-off levels was included in the sROC curve analysis, and no attempt was made to investigate sources of heterogeneity. In addition, the derivation of the summary values for sensitivity and specificity was unclear. The sROC curves were presented for troponin T and troponin I and it was stated that these curves showed no statistically-significant difference in sensitivity and specificity between the two tests. The data presented could be used to support a lack of significant difference between the ORs for the two tests, but cannot demonstrate a lack of significant difference between the individual components of sensitivity and specificity used to calculate the OR.

The authors' conclusions should be treated with caution given the considerable limitations in the primary data and
Implications of the review for practice and research
The authors considered that in the light of newer, improved assay techniques, the clinical significance of elevated troponin T in patients with renal failure is uncertain.

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