Prediction of the severity of acute pancreatitis on admission by urinary trypsinogen activation peptide: a meta-analysis

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CRD summary
The authors concluded that the urinary trypsinogen activation peptide marker had the potential to assess the severity of acute pancreatitis on hospital admission. The robustness of the review was limited by the small sample size and variation between the studies; these methodological concerns may limit the reliability of the authors’ conclusion.

Authors’ objectives
To evaluate the predictive value of urinary trypsinogen activation peptide in determining the severity of acute pancreatitis on admission to hospital.

Searching
MEDLINE, EMBASE, Cochrane CENTRAL, and Science Citation Index were searched for published English language articles in peer-reviewed journals from January 1990 to February 2013. Search terms were reported. Manual searches of abstract supplements and relevant international meetings were carried out.

Study selection
Eligible for inclusion were studies evaluating the diagnostic accuracy of urinary trypsinogen activation peptide in predicting the severity of acute pancreatitis. Severe acute pancreatitis was defined using the Atlanta classifications, or by the development of organ failure and/or local complications. Studies of serum or plasma trypsinogen activation peptide were excluded.

The included studies were conducted in China, USA, Finland, or across multiple centres. More men than women were included. The mean age of patients ranged from 52 to 69 years. Most patients had mild disease and aetiology was mainly biliary in origin, followed by alcoholic, endoscopic retrograde cholangiopancreatography, and idiopathic. For the meta-analysis, only those studies with a cut-off value of 35nmol/L were included.

Two reviewers independently selected the studies for inclusion. Disagreements were resolved by consensus, or with the involvement of a third reviewer where necessary.

Assessment of study quality
Study quality was assessed using Standards for Reporting of Diagnostic Accuracy (STARD) initiative guidelines. High quality was defined when a STARD score of at least 16 was reached.

Two reviewers independently carried out the quality assessment.

Data extraction
Data were extracted on diagnostic accuracy parameters (true and false positives, true and false negatives), and sensitivity and specificity were calculated with their 95% confidence intervals for the capacity of urinary trypsinogen activation peptide to predict the severity of acute pancreatitis. Diagnostic parameters were also extracted for plasma C-reactive protein and for the Glasgow, Acute Physiology and Chronic Health Evaluation (APACHE) II score at the highest diagnostic values during the first two days after admission (where reported).

Two reviewers independently extracted the data.

Methods of synthesis
Pooled sensitivity, specificity, and diagnostic odds ratios, together with 95% confidence intervals, were calculated in meta-analyses (fixed-effect where there was no heterogeneity and random-effects where heterogeneity was present). A summary receiver operating characteristic curve was presented, and area under curve (AUC) was calculated. Statistical heterogeneity was assessed with Cochran’s Q and I² (I² over 50% indicated the presence of heterogeneity).
bias was assessed with a funnel plot.

Sensitivity analyses were conducted by excluding each study in turn to evaluate the relative effect on overall results. Subgroup analyses explored the influence of high quality studies, sample size at least 50 in each study, single centre studies, and severity of pancreatitis defined by the 1992 Atlanta Classification.

**Results of the review**

Six studies (775 patients, sample size range 41 to 190) were included in the meta-analysis. Methodological quality was reported to be high with a STARD score at least 16 (full results were not reported).

Pooled results using all studies for the diagnostic accuracy of urinary trypsinogen activation peptide in predicting the severity of acute pancreatitis on hospital admission were: sensitivity 71% (95% CI 63 to 78; I²=81%); specificity 75% (95% CI 72 to 79; I² = 69%); the area under curve value was 0.83 and the diagnostic odds ratio was 8.67 (95% CI 3.70 to 20.33) with substantial heterogeneity (I²=69%). It was concluded that urinary trypsinogen activation peptide had the potential to predict the severity of acute pancreatitis.

Pooled results for severity stratification of urinary trypsinogen activation peptide versus the APACHE II score within the first 48 hours after hospital admission were: sensitivity 64% versus 69%; specificity 77% versus 61%; area under curve value 0.82 versus 0.73; and DOR 6.27 versus 4.61 (three studies, 422 patients). It was concluded that urinary trypsinogen activation peptide was comparably better than APACHE II in predicting the severity of acute pancreatitis.

The prognostic efficacy for severity stratification of urinary trypsinogen activation peptide versus plasma C-reactive protein within 48 hours of hospital admission was judged to be similar for the two markers (three studies; 440 patients).

Substantial heterogeneity remained in sensitivity and sub-group analyses (results reported in the paper).

There was evidence of publication bias.

**Authors’ conclusions**

Urinary trypsinogen activation peptide had the potential to act as a stratification marker on hospital admission for differentiating disease severity of acute pancreatitis.

**CRD commentary**

The review question was clear and inclusion criteria were adequately specified for all aspects apart from the study population. The search strategy included relevant sources, but language and publication restrictions may mean that studies were missed. The review process was conducted with efforts to minimise error and bias.

Study quality was assessed (with emphasis on reporting standards), although results of this were not fully presented, so it was difficult to verify the authors’ judgement. Study details were presented. Sensitivity and specificity were combined separately in meta-analyses (not generally considered to be reliable); the results from the summary receiver operating characteristic curves may be more reliable. The authors acknowledged limitations of the review with small sample size, heterogeneity, and possible publication bias.

These methodological concerns may limit the reliability of the authors’ conclusion.

**Implications of the review for practice and research**

**Practice:** The authors stated that the results of this meta-analysis encourage the use of urinary trypsinogen activation peptide in routine clinical practice. Peer review comments (included in the paper) suggested a more cautious approach to widespread use of urinary trypsinogen activation peptide for prognostic scoring of acute pancreatitis, as other equivalent tests were available.

**Research:** The authors stated that use of urinary trypsinogen activation peptide in routine clinical practice needed to be established in further well-designed studies with possible comparisons to the new severity classification systems.

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