Diagnostic value of tumor marker pro-gastrin-releasing peptide in patients with small cell lung cancer: a systematic review


CRD summary

This review concluded that pro-gastrin-releasing peptide 31-98 had high specificity for diagnosing small cell lung cancer with similar accuracy to pathology. The review had limitations in terms of the search, quality assessment and analysis. The results did not support the finding of similar accuracy to pathology. The authors’ conclusions are therefore unlikely to be reliable.

Authors’ objectives

To evaluate the diagnostic value of the serum tumour marker pro-gastrin-releasing peptide 31-98 in patients with suspected small cell lung cancer.

Searching

PubMed, EMBASE, CANCERLIT, China Biomedical Literature Database, Chinese Journals Full-text Database and China National Knowledge Infrastructure were searched from 1978 to 2009. Search terms were reported and included a diagnostic filter. Relevant journals were handsearched and bibliographies were screened for additional studies. The review was restricted to studies published in English or Chinese with an English abstract.

Study selection

Eligible studies evaluated the accuracy of pro-gastrin-releasing peptide 31-98 detected by ELISA (index test) compared to surgery and pathology (reference standard) for the diagnosis of small cell lung cancer. Studies had to report sufficient data to construct a 2x2 table of test performance.

Included studies were conducted in Japan, Germany, France, China and Spain. Most patients had non-small cell lung cancer. Agents manufacturers included the Peninsula Lab Belmont (CA), Japan Tonen Corporation, Germany Wak-Chemie Medical, Japan national cancer center and Japan Advanced Life Science Corporation.

The authors did not state how studies were selected for inclusion in the review.

Assessment of study quality

Study quality was assessed according to the following criteria: use of a reference standard; independent comparison of the index test with the reference standard; data analysed blindly; enrolment of consecutive patients and inclusion of grey cases; appropriate selection of threshold; reporting of sensitivity, specificity and likelihood ratios; detailed description of the study location, environment and population; information on disease status of subjects, disease course and subject medications provided. Studies were graded as A if they fulfilled all criteria, grade B if one or more of first five criteria were poorly described and grade C if one or more of first five criteria was not fulfilled.

Two reviewers independently assessed study quality.

Data extraction

Data were extracted to populate 2x2 tables of test performance. These data were used to calculate diagnostic odds ratios and sensitivity and specificity. The authors did not state how many reviewers performed the data extraction.

Methods of synthesis

Summary sensitivity, specificity, diagnostic odds ratios and positive and negative likelihood ratios (LR+ and LR-) were calculated; details on methods were not reported. A summary receiver operating curve was estimated and the area under the curve was calculated. Heterogeneity of the diagnostic odds ratios was assessed using I² and X². Subgroup analysis was conducted by pooling data according to peptide manufacturer.

Results of the review
Twenty two studies were included (6,759 patients, range 72 to 827). All studies were graded as C as none were interpreted blind and none enrolled consecutive patients.

Summary sensitivity was 72% (95% CI 70 to 75) and summary specificity was 93% (95% CI 92 to 94). There was strong evidence of heterogeneity ($I^2=87\%$, $p<0.001$). Data pooled separately for two of the manufacturers were also presented; results were similar to overall pooled values.

**Authors' conclusions**
Serum pro-gastrin-releasing peptide 31-98 was a valuable marker with a high specificity for diagnosis of small cell lung cancer with a similar diagnostic accuracy to pathology.

**CRD commentary**
The review addressed a clear question and inclusion criteria were defined although they lacked clarity for participants and study design. A range of databases was searched to locate studies published in English or Chinese but the use of very restrictive diagnostic filter (the term "diagnostic accuracy") and the restriction to studies published in these languages meant it was likely that relevant studies had been missed. Details on the review process were only reported for quality assessment and so it was not possible to determine whether appropriate steps were taken to minimise bias and errors. A formal quality assessment was conducted but the criteria used appeared to have been developed by the authors and lacked clarity.

Only limited details of the results of the quality assessment and the included studies in general were reported, especially in relation to participants, so the risk of bias and generalisability of the results was unclear. Methods used to pool the included studies were not described in detail but it appeared that the more robust models were not used. There was substantial heterogeneity across studies which was not adequately investigated. The authors' conclusions suggest that the accuracy of pro-gastrin-releasing peptide 31-98 was similar to that of pathology (the reference standard). This was not supported by the review which suggested moderate sensitivity and reasonable specificity but some way from complete agreement with being similar to pathology. This combined with the limitations in the review in terms of possibility of missing studies, limitations with the quality assessment, lack of study details and limited analysis meant the authors' conclusions were unlikely to be reliable.

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

**Practice:** The authors stated that serum pro-gastrin-releasing peptide 31-98 levels measured with an ELISA could be used to diagnose small cell lung cancer. However, limitations with the review meant this recommendation should be followed with caution.

**Research:** The authors stated that high quality studies were required in this area.

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