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[Diagnostic Test Accuracy Review]

Blood CEA levels for detecting recurrent colorectal cancer

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ABSTRACT

Background

Testing for carcino-embryonic antigen (CEA) in the blood is a recommended part of follow-up to detect recurrence of colorectal cancer following primary curative treatment. There is substantial clinical variation in the cut-off level applied to trigger further investigation.

Objectives

To determine the diagnostic performance of different blood CEA levels in identifying people with colorectal cancer recurrence in order to inform clinical practice.

Search methods

We conducted all searches to January 29 2014. We applied no language limits to the searches, and translated non-English manuscripts. We searched for relevant reviews in the MEDLINE, EMBASE, MEDION and DARE databases. We searched for primary studies (including conference abstracts) in the Cochrane Central Register of Controlled Trials (CENTRAL), in MEDLINE, EMBASE, and the Science Citation Index & Conference Proceedings Citation Index – Science. We identified ongoing studies by searching WHO ICTRP and the ASCO meeting library.

Selection criteria

We included cross-sectional diagnostic test accuracy studies, cohort studies, and randomised controlled trials (RCTs) of post-resection colorectal cancer follow-up that compared CEA to a reference standard. We included studies only if we could extract 2 x 2 accuracy data. We excluded case-control studies, as the ratio of cases to controls is determined by the study design, making the data unsuitable for assessing test accuracy.

Data collection and analysis

Two review authors (BDN, IP) assessed the quality of all articles independently, discussing any disagreements. Where we could not reach consensus, a third author (BS) acted as moderator. We assessed methodological quality against QUADAS-2 criteria. We extracted binary diagnostic accuracy data from all included studies as 2 x 2 tables. We conducted a bivariate meta-analysis. We used the `xtmelogit` command in Stata to produce the pooled estimates of sensitivity and specificity and we also produced hierarchical summary ROC plots.

Main results

In the 52 included studies, sensitivity ranged from 41% to 97% and specificity from 52% to 100%. In the seven studies reporting the impact of applying a threshold of 2.5 µg/L, pooled sensitivity was 82% (95% confidence interval (CI) 78% to 86%) and pooled specificity 80% (95% CI 59% to 92%). In the 23 studies reporting the impact of applying a threshold of 5 µg/L, pooled sensitivity was 71% (95% CI 64% to 76%) and pooled specificity 88% (95% CI 84% to 92%). In the seven studies reporting the impact of applying a threshold of 10 µg/L, pooled sensitivity was 68% (95% CI 53% to 79%) and pooled specificity 97% (95% CI 90% to 99%).

Authors' conclusions

CEA is insufficiently sensitive to be used alone, even with a low threshold. It is therefore essential to augment CEA monitoring with another diagnostic modality in order to avoid missed cases. Trying to improve sensitivity by adopting a low threshold is a poor strategy because of the high numbers of false alarms generated. We therefore recommend monitoring for colorectal cancer recurrence with more than one diagnostic modality but applying the highest CEA cut-off assessed (10 µg/L).

PLAIN LANGUAGE SUMMARY

Detecting recurrent colorectal cancer by testing for blood carcino-embryonic antigen (CEA).

Background

After surgery for cancer in the colon or rectum (colorectal cancer), most people are intensively followed up for at least five years to monitor for signs of the cancer returning. When this occurs, it usually causes a rise in a blood protein called CEA (carcino-embryonic antigen). An increased level of CEA can be picked up by a blood test, which is normally done every three to six months after colorectal cancer surgery. Those people with raised CEA levels are further investigated by x-ray imaging (usually a scan of the chest, abdomen and pelvis). We conducted this review to help decide what level of blood CEA should lead to further investigation.

Key Results

This review shows that setting a low cut-off point will increase the number of genuine cases of colorectal cancer recurrence that are detected (true positives), but a low cut-off will also cause unnecessary alarm by incorrectly classifying too many cases that are not actually recurrences (false positives). In addition, this review shows that a rise in CEA does not occur in up to 20% of patients with a true recurrence (false negatives). The current evidence supports using the highest cut-off point assessed (10 µg/L), but that adding another diagnostic modality (e.g. a single scan of the chest, abdomen and pelvis at 12 to 18 months) is necessary in order to avoid the missed cases.