Carcinoembryonic antigen (CEA)

What is carcinoembryonic antigen?

Carcinoembryonic antigen (CEA) is a glycoprotein, which is present in normal mucosal cells but increased amounts are associated with adenocarcinoma, especially colorectal cancer. CEA therefore has a role as a tumour marker. Sensitivity and specificity are low, however, so it is of more use for monitoring and is not useful as a diagnostic or screening test.

CEA levels are useful in assessing prognosis (with other factors), detecting recurrence (especially for disease that cannot be evaluated by other means) and monitoring treatment in people with colorectal cancer.[1] CEA is particularly recommended for postoperative follow-up of patients with colorectal cancer.[2]

Conditions which may have elevated CEA[2]

CEA may be elevated in colorectal cancer, which is where it is most clinically useful. However, it may also be elevated in a wide variety of other malignant and benign conditions.

Malignant conditions which may have elevated CEA include:

- Colorectal cancer.
- Breast cancer.
- Ovarian cancer.
- Lung cancer.
- Cancer of the stomach.
- Cancer of the oesophagus.
- Cancer of the pancreas.

- Mesothelioma.
- Medullary thyroid carcinoma.
- Skeletal metastases (may occasionally be a useful screening tool for distinguishing skeletal metastases of tumours above from primary bone or haematological malignancy).[3]

Non-malignant conditions which may have elevated CEA include:

- Non-malignant liver disease, including cirrhosis, chronic active hepatitis, viral hepatitis and obstructive jaundice.
- Chronic kidney disease.
- Pancreatitis.
- Inflammatory bowel disease (Crohn's disease; ulcerative colitis).
- Irritable bowel syndrome.
- Diverticulitis.
- Respiratory diseases - eg, pleural inflammation, pneumonia.
- Smoking.

Normal range

Individual laboratory normal ranges vary but CEA level is usually deemed to be normal at 2.5-5 µg/L. Increasing levels of CEA suggestive of active disease may be more clinically helpful than absolute level.[4] Levels exceeding 10 µg/L are rarely due to benign disease or the moderate elevation that may occur due to smoking.[5]

Sensitivity[4] [5]

Sensitivity in early-stage colorectal cancer is very low and increases with the stage of the disease. Studies reporting sensitivity vary in the cut off for what constitutes a normal CEA level so results are varied. Using a cut-off point of 5 µg/L, the proportions of patients with increased values are 3%, 25%, 45% and 65% for patients with Dukes' A, B, C and D disease respectively. Around 72% of cases with unresectable or metastatic disease have elevated CEA levels.

Indications for CEA measurement

Colorectal cancer [2] [5]

Due to the low sensitivity and specificity of the CEA test, it is not recommended that it be used for screening of healthy individuals or for the diagnosis of early colorectal cancer. A CEA level should be ordered only after malignancy has been confirmed.

- Prognosis:
    - The CEA test is of much more use in determining prognosis than it is as an early diagnostic test for colon cancer.
    - CEA levels are more likely to be elevated in advanced disease.
- Staging:
    - CEA in combination with other tumour markers (eg, mucin tumour markers CA19-9, CA242) can be used in pre-operative staging and thereby assist in the planning of the type of surgery required and future management options. [6]

- Monitoring treatment:

    - The major role for CEA levels is in following patients for relapse after intended curative treatment of colorectal cancer.
    - CEA levels typically return to normal within four to six weeks after successful surgical resection. The CEA level can also be used to assess the response to chemotherapy.
    - The National Institute for Health and Care Excellence (NICE) recommends that for people who have had potentially curative surgical treatment for non-metastatic colorectal cancer, follow-up for detection of local recurrence and distant metastases for the first three years should include CEA and CT scan of the chest, abdomen and pelvis.[7]
    - Clinical trials have shown improvement in survival after five years in patients who underwent CEA monitoring as part of post-treatment management.[4]
    - However, a Cochrane review found no overall survival benefit for intensifying the follow-up of patients after curative surgery for colorectal cancer. More participants were treated with salvage surgery with curative intent in the intensive follow-up groups, but this was not associated with improved survival. Harms related to intensive follow-up and salvage therapy were not well reported.[8]
    - Normal levels do not necessarily indicate that recurrence has not occurred.[9]

Breast cancer

Similar considerations apply to the diagnosis of breast cancer. The sensitivity of CEA is too low for it to be used as a primary diagnostic test. Although the prognosis for operable breast cancers is reportedly worse if serum CEA and cancer antigen 15-3 (CA15-3) levels are above normal, the usefulness of this prognosis is limited due to the low sensitivity and specificity. In addition, the optimal cut-off levels remain unknown.[10]

Some studies have shown that, in conjunction with other tumour markers (CA27.29, tissue polypeptide antigen and especially CA 15-3), CEA may however be helpful in the following:

- Disease surveillance.[11]
- Identifying patients with skeletal metastases.[12]
- Predicting response to chemotherapy.[13]

It is not recommended in the routine surveillance of breast cancer and should not be used in isolation for monitoring in advanced disease.[4]

Further reading

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