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Carcinoembryonic Antigen (CEA) and Cancer Antigen 19.9 (CA19-9) for Gastrointestinal Cancers

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CEA and CA19-9

- CEA was discovered in 1965 by Gold and Freeman
- CA19-9 was identified from a human colorectal cancer cell line

- CEA and CA19-9 are glycoproteins
  - MW_{CEA}: 150 – 300 KDa with 45 – 50% carbohydrate
  - $MW_{CA19\text{-}9}$: 200 – 1000 KDa, exists as a mucin in serum

- Tumor markers
  - CEA: Colorectal cancer
  - CA19-9: Pancreatic cancer

Cancer Statistics

Colorectal Cancer

- The 3rd most common cancer in both men and women (9%)
- The 3rd most common cause of cancer death for both men and women (9%)
- New cases and mortality decreased significantly since the 1980s

Pancreatic Cancer

- The 10th and 9th most common cancer in men and women respectively, in the U.S
- The 4th most common cause of cancer death for both men and women
- Little improvement has been shown in survival in the past 30 years

Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013.
CA Cancer J Clin 2013;63:11-30.

Specificity of CEA and CA19-9

	CEA	CA19-9
Specificity	Low for colorectal | pancreatic cancer Elevated in conditions below	
Non-neoplastic conditions	Cigarette smoking, peptic ulcer disease, inflammatory bowel disease, pancreatitis, hypothyroidism, biliary obstruction, liver cirrhosis	Inflammatory conditions of the hepatobiliary system, many benign conditions (e.g., thyroid disease)
Malignancies	Breast, lung, gastric, pancreatic, bladder, medullary thyroid, head and neck, cervical and hepatic cancer, lymphoma, and melanoma	Tumors of the upper gastrointestinal tract, ovarian cancer, hepatocellular cancer, and colorectal cancer

Analytical Perspectives

- CEA reference range
  - Non-smokers: 0 – 2.5 ng/mL
  - Smokers: 0 – 5 ng/mL
  - Benign condition: < 10 ng/mL
- CA19-9 upper reference limit: 37 U/mL
  - Benign condition: < 1,000 U/mL

CEA Utilities in Colorectal Cancer

- Screening: Not recommended
- Staging/Treatment Planning: Yes
- Post-surgery follow up: Yes
- Therapy monitoring: Yes

CEA Utilities – Screening and Staging

- Screening: Not recommended
  - Cutoff at 2.5 ng/mL → Sensitivity = 36% and Specificity = 87%
  - Low prevalence
- Staging/Treatment Planning:
  - CEA may be ordered preoperatively to assist staging and planning of surgical treatment
  - CEA > 5 ng/mL may correlate with a poorer prognosis, but not enough evidence to use this level to trigger additional treatment
  - Poorly-differentiated colorectal cells may produce less CEA than well-differentiated cells

Duffy MJ. Clin Chem 2001;47:624-30.
Locker GY, et al. Journal of Clinical Oncology 2006;24:5313-27.

CEA Utilities – Post surgery & monitoring

- Post-surgery follow-up
  - Typically back to normal level 4 – 6 weeks after successful surgery
  - Every 3 months in patients with stage II/III disease for a minimum of 3 years
  - Elevated CEA (confirmed after retesting) suggests further evaluation for metastasis, but not sufficient to justify therapy
- Therapy monitoring
  - Should be measured at the beginning of the therapy
  - Every 1-3 months during treatment
  - Persistently rising CEA values → restaging and alternative therapy

Locker GY, Hamilton S, Harris J, Jessup JM, Kemeny N, Macdonald JS, et al. Asco 2006 update of recommendations for the use of tumor markers in gastrointestinal cancer. J Clin Oncol 2006;24:5313-27.

Surveillance Using Serial CEA

Arguments in favor of CEA

- Provide a lead time of 1.5 – 6 months
- Some data reflect a significant increase in survival using CEA as part of follow-up

Arguments against CEA

- 30 – 40% recurrence not associated with elevated CEA
- Only benefits a small group of patients
- No data to show improvement in quality of life

CA19-9 Utilities: Pancreatic Cancer

- Screening: Not recommended
  - One systematic review based on 2283 patients
  - Median sensitivity: 79%
  - Median specificity: 82%
  - Median positive predictive value 72%
  - Median negative predictive value 81%
- Operability: Not used alone
  - When CA19-9 > 1000 U/mL, 96% of tumors → unresectable
- Post-surgery recurrence:
  - Combined with imaging studies and/or biopsy

Locker et al. ASCO 2006 update of recommendations for the use of tumor markers in gastrointestinal cancer. J Clin Oncol 2006;24:5313-27.
Molina V, et al. Ca 19-9 in pancreatic cancer. Tumour Biol 2012;33:799-807.

CA19-9 Utilities: Pancreatic Cancer

- Therapy Monitoring: Not confirmative
  - Should be measured at the start of treatment
  - Every 1-3 months during treatment
  - Serial elevation → progressive disease
    - Should be confirmed with other studies before actions
- One caveat
  - CA19.9 is not expressed in Lewis null blood type (le a^-b^-)patients (~ 5% population)

Locker GY, Hamilton S, Harris J, Jessup JM, Kemeny N, Macdonald JS, et al. Asco 2006 update of recommendations for the use of tumor markers in gastrointestinal cancer. J Clin Oncol 2006;24:5313-27.

Summary

- CEA → colorectal cancer
- CA19-9 → pancreatic cancer
- Neither is sufficient as a screening test
- Both show utilities in detecting post-surgery recurrence and monitoring of treatments
- CEA is most useful for early detection of liver metastasis
- CA19-9 can aid in assessing patient's resectability

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