Bile Acids

How do bile acids reflect the relationship between diet and colorectal cancer risk?

Epidemiological evidence clearly demonstrates a correlation between diet and the incidence of colorectal cancer (CRC). The correlation appears to be related, at least in part, to bile acid metabolism. Consuming a diet rich in fat and animal protein and low in fiber results in a 2- to 5-fold increase in the excretion of secondary or unconjugated bile acids.\(^1\)\(^4\)

Owen et al.\(^5\) concluded that the lithocholic acid:deoxycholic acid ratio (LCA:DCA) may be an important discriminate marker in CRC susceptibility. Their study revealed that 75% of CRC patients exhibited a secondary bile acid ratio >1.0, whereas 85% of healthy controls had a ratio <1.0.

What is the significance of an elevated bile acid ratio?

A secondary bile acid ratio >1.0 is associated with gallstones, cholecystectomy, and increased risk of breast and colorectal cancers.\(^2\)\(^3\)\(^4\)

Is lithocholic acid more toxic than deoxycholic acid?

Evidence supports the role of both secondary bile acids in promoting CRC. However, LCA is considered to be more toxic than DCA. LCA has a greater inhibitory effect on the enzyme glutathione-S-transferase than does DCA. The inhibition of glutathione-S-transferase results in the persistence of mutagens in colonocytes, which is linked to a greater frequency of neoplasia-associated mutations.\(^4\)\(^5\)\(^6\)\(^9\)\(^10\)

What can be done to reduce the ratio?

Supplementation with fiber and probiotics can help reduce an elevated bile acid ratio. Fiber increases cholesterol absorption, which in turn reduces the concentration of secondary bile acids in the stool. Taking probiotics on a regular basis also has a beneficial effect on a high LCA: DCA ratio.\(^2\)\(^3\)\(^5\)\(^11\)\(^13\)

Which type of fiber is most effective in lowering the bile acid ratio?

Resistant starch, the insoluble fiber contained in wheat bran, legumes, and certain vegetables, decreases the level of secondary bile acids. Resistant starch enhances short-chain fatty acid production in the proximal colon, which lowers intestinal pH. A reduction in the colonic pH inhibits bacterial 7 alpha-hydroxylase activity, reducing the concentrations of LCA, DCA, and the LCA:DCA ratio.\(^4\)\(^12\)\(^14\)

What are Bile Acids?

Bile acids are end products of hepatic cholesterol metabolism that play an important role in fat emulsion and detoxification. High levels of bile acids can result from an excess of dietary fat and animal protein, and may be associated with increased risk of gallstones and certain cancers.

Turn-around Time 14 days
**What other dietary interventions can modify levels of secondary bile acids?**

Other dietary interventions to modify levels of secondary bile acids include increasing vegetable intake, reducing dietary fat, and supplementing with calcium.

Studies have shown that 30%-40% of secondary bile acids bind to lignin, a constituent of vegetable fiber. Plant sterols, in particular beta-sitosterol, can inhibit cholesterol absorption, which is thought to influence the absorption of cholesterol in the intestine. Conversely, diets low in vegetables can augment cholesterol absorption, which in turn increases the synthesis of the primary bile acid chenodeoxycholic acid (CDCA). An increase in CDCA raises levels of the secondary bile acid LCA, which in turn elevates the LCA:DCA ratio.15

Reducing dietary fat can also help reduce CDCA synthesis in the liver. High-fat diets induce changes in the colonic flora, increasing levels of 7alpha-dehydroxylase. This enzyme is involved in the conversion of primary bile acids into the more toxic secondary bile acids.2,5,7

A study by Lupton et al. found that calcium is able to modify the bile acids, via a mechanism that reduces CDCA in bile. Dietary calcium, along with the luminal concentrations of calcium-binding substances such as phosphate and fatty acids, determines the availability of ionized calcium. In its ionized form, calcium is able to form insoluble soaps with bile acids.19

**What other analytes can evaluate the relationship between bile acids and Colorectal Cancer risk?**

Other important analytes on the CDSA 2.0 to consider when assessing the bile acid ratio are calprotectin, beta-glucuronidase, pH, n-butyrate, and occult blood. When calprotectin results are above 100 µg/g, one should further investigate the etiology, as elevated levels may be associated with neoplastic disease. Beta-glucuronidase, pH, and n-butyrate are all modifiable markers that indicate an increased risk for colorectal cancer and breast cancer. A positive occult blood warrants further investigation, and should ideally commence with collecting three consecutive samples for repeat testing.

**What other tests might be indicated?**

- **Food Antibody Assessment**—oat and wheat antibodies
- **Anti-Gliadin Antibody Assay**—gluten intolerance
- **Bacterial Overgrowth of the Small Intestine Breath Test**
- **Estrogen Metabolism Assessment** (2/16 a-hydroxyestrone ratio)—to assess additional breast cancer risk factors
- **DetoxiGenomic™ Profile**—to test for glutathione-S-transferase polymorphisms

**How do I order this test?**

For CDSA 2.0 test kits, Interpretive Guidelines or information, please call a GSDL Accounts Receivable representative at 888-201-8333 or use our secure web contact center at www.gsdl.com/billing.
References