

Is Your Liver Fat?

The link between fatty liver and cancer

Cancer is one of the major concerns most of us have as we age. We perform screening tests to try to detect it early so it can be treated, but there are many cancers without good screening tests. What are the signs that we are at increased risk of cancer developing? Is cancer simply a random occurrence, or are there lifestyle changes we can make to reduce our risk? Are there links between genetics, lifestyle, and cancer risk and how can we reduce our risk? What causes fatty liver and how is a finding of fatty liver related to cancer risk?



Abstract

BACKGROUND: Metabolic dysfunction-associated fatty liver disease (MAFLD) is a significant health issue closely associated with multiple metabolic dysfunctions. The association between MAFLD and cancer risk is yet unknown.

METHODS: UK Biobank study participants were diagnosed for the presence of MAFLD at baseline. A multivariable Cox regression model was performed to examine the associations of MAFLD with incident events in 24 specific cancers.

RESULTS: We included 352,911 individuals (37.2% with MAFLD), among whom 23,345 developed cancers. Compared with non-MAFLD, MAFLD was significantly associated with 10 of the 24 examined cancers, including corpus uteri (hazard ratio [HR] = 2.36, 95% CI 1.99-2.80), gallbladder (2.20, 1.14-4.23), liver (1.81, 1.43-2.28), kidney (1.77, 1.49-2.11), thyroid (1.69, 1.20-2.38), esophagus (1.48, 1.25-1.76), pancreas (1.31, 1.10-1.56), bladder (1.26, 1.11-1.43), breast (1.19, 1.11-1.27), and colorectal and anus cancers (1.14, 1.06-1.23). The associations of MAFLD with liver, esophageal, pancreatic, colorectal and anal and bladder cancers and malignant melanoma were strengthened in males, and associations with kidney, thyroid, and lung cancers were increased in females. The associations of MAFLD with the risk of liver, kidney, and thyroid cancers remained significant after further adjusting for the waist circumference or body mass index and the number of metabolic syndrome components based on the main models. The risk-increasing allele of PNPLA3 rs738409 significantly amplified the association of MAFLD with the risk of liver and kidney cancers.

CONCLUSION: MAFLD is associated with an increased risk of a set of cancers, but the effect substantially varies by site. MAFLD deserves higher priority in the current scheme of cancer prevention.

Fatty liver disease is associated with obesity, hyperlipidemia, and type 2 diabetes and is termed metabolic dysfunction-associated fatty liver disease. It currently affects over 1 billion people worldwide with the incidence increasing. This study analyzed data from UK Biobank study on the association of metabolic dysfunction-associated fatty liver disease with 24 different cancer types. The researchers found that this fatty liver disease increased the risk of 10/24 cancers examined. An increased risk was found for uterine, gallbladder, liver, renal, thyroid, esophageal, pancreatic, bladder, breast, and colorectal cancers. It did not lower the risk of any cancers. The relationship between fatty liver and cancer was stronger in men than women. Additionally, they found a link between a specific gene which amplified the risk. This specific gene directs cells to break down subcutaneous fat and send it to the liver and muscle, leading to increased fat in the liver which worsens the fatty liver disease and possibly increases unfavorable outcomes.

During my visits, we often discuss metabolic dysfunction and insulin resistance. These two conditions are really part of the same problem. Chronically elevated blood glucose levels lead to insulin resistance. Insulin resistance leads to obesity as we cannot burn fat when insulin levels are high, dyslipidemia (elevated atherogenic particles), and eventually type 2 diabetes. These conditions together are termed metabolic dysfunction and have been linked to increased risk for several medical conditions including heart disease and strokes. Externally, we often see weight gain, abdominal obesity (apple

shape), and elevated blood pressure readings. This study shows us that early findings of metabolic dysfunction should be taken seriously as the later outcomes include not only heart disease, strokes, high blood pressure, and diabetes, but cancers, many of which don't have good screening tests. The best we can do is prevention. This starts early in life by preventing metabolic dysfunction and addressing it early when we see signs of development.

[Metabolic dysfunction-associated fatty liver disease and the risk of 24 specific cancers](#)

Metab. Clin. Exp. 2021 Dec 14;[EPub Ahead of Print].