

Prediabetes Associated With Increase in Cancer Risk

Pam Harrison | September 09, 2014

Prediabetes — even at lower levels of impaired fasting glucose (IFG) as defined by the American Diabetes Association (ADA) — is associated with a significant increase in cancer risk that is independent of the effects of obesity, according to the results of a large new meta-analysis.

Yuli Huang, MD, PhD, from First People's Hospital of Shunde, Foshan, China, and colleagues found that prediabetes was associated with a 15% increased risk for cancer overall, based on data derived from 16 prospective cohort studies, with differing risks depending on the type of cancer. The risk was particularly increased for liver cancer and stomach or colorectal cancer.

"Epidemiological studies have shown that diabetes increases the incidence of cancer and mortality from it, but we thought that maybe not only diabetes but prediabetes may be associated with an elevated cancer risk," Dr. Huang told *Medscape Medical News*.

"And considering the high prevalence of prediabetes as well as the robust and significant association between prediabetes and cancer we demonstrated in our study, a successful lifestyle intervention could have a major public-health impact on cancer prevention," he added.

"This information is important to health professionals and those engaged in the prevention of cancer," Dr. Huang and colleagues stress.

The study was published online September 8 in *Diabetologia*.

Screen for Prediabetes Using ADA Criteria for Cancer Prevention

A total of 891,426 participants from the 16 studies, 4 of which were from Asia, 11 from the United States and Europe, and 1 from Africa, were included in the meta-analysis. Prediabetes included individuals with impaired glucose tolerance (IGT), IFG, or a combination of the 2.

Over 10 years ago, the ADA lowered its definition of prediabetes to that of a fasting plasma glucose concentration ranging from 5.6 to 6.9 mmol/L, but other organizations have maintained their definition at a higher level, as a fasting plasma glucose concentration between 6.1 and 6.9 mmol/L.

The risks of site-specific cancer among individuals with prediabetes was highest for liver cancer (relative risk [RR], 2.01), followed by colorectal and stomach cancer (RR, 1.55 for both), endometrial cancer (RR, 1.60), and breast as well as pancreatic cancer (RR, 1.19 for both).

But prediabetes was not associated with cancer of the bronchus, lung, prostate, ovary, kidney, or bladder.

The risks were increased even when a lower fasting plasma glucose value of 5.6 to 6.9 mmol/L was used, as well as in participants with IGT — "an interesting finding," investigators note, "and one that reaffirms the importance of screening for prediabetes using the ADA criteria with a view to cancer prevention."

As the authors point out, obesity — in itself a key risk factor for diabetes — has also been linked to cancer.

To rule out obesity as a potential confounder, the authors did a sensitivity analysis that included only studies that adjusted for body mass index (BMI).

After controlling for BMI, "we found that...the presence of prediabetes remained associated with an increased risk of cancer by 22%," they state. "So we believe that the increased risk of cancer in individuals with prediabetes is independent of obesity."

"Our study indicates that, on the basis of a snapshot blood glucose measurement, prediabetes is associated with an increased risk of cancer," they state.

Need for Trials of Metformin to Prevent Cancer

Speculating on the reasons for the association between prediabetes and increased cancer risk, Dr. Huang and colleagues suggest that chronic hyperglycemia and resulting states, including chronic oxidative stress and the accumulation of advanced glycated end products, may serve as carcinogens.

Alternatively, increased insulin resistance characteristic of prediabetes increases insulin secretion, and increased insulin levels may promote the growth of cancer cells.

Certain genetic mutations may also predispose individuals with prediabetes to an elevated cancer risk, they suggest.

As the authors point out, it is noteworthy that metformin is associated with an approximately 30% reduction in the lifetime risk of cancer in diabetic patients.

"Considering the protective anticancer properties of metformin in patients with diabetes, as well as its ability to delay progress to diabetes in patients with prediabetes, we feel studies are urgently needed to explore the effects of metformin on cancer risk in people with prediabetes, and [if shown to be protective], metformin might be recommended in select high-risk individuals, especially those with IGT or a combination of IGT and IFG," they conclude.

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