

Research reveals why patients with diabetes have poorer prognosis for prostate cancer

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Men with type 2 diabetes are less likely to develop prostate cancer than patients without diabetes. However, the mortality rate is higher. Researchers of the German Center for Diabetes Research (DZD) from Tübingen and experts of Helmholtz Zentrum München and the Urology Department of Tübingen University Hospital were able to show that in the affected individuals the androgen receptor and the mitogenic forms of the insulin receptor were more strongly expressed. This could explain why patients with diabetes have a poorer prognosis for prostate cancer. The current results were published in the journals *Molecular Metabolism* and *Endocrine Related Cancer*.

Prostate cancer and type 2 diabetes are among the most common diseases in men. Although studies indicate that people with diabetes suffer more frequently from cancer, men with diabetes do not increasingly suffer from prostate cancer. On the contrary, meta-analyses of studies have shown that diabetes patients are less likely to develop this carcinoma. However, the mortality rate is higher. This is also confirmed by current research carried out by researchers at the Institute for Diabetes Research and Metabolic Diseases (IDM) of Helmholtz Zentrum München at the University of Tübingen, a partner of the DZD, in cooperation with the Department of Urology at Tübingen University Hospital. The research team recently analyzed the data of patients who had their prostate removed due to cancer. As expected, among them were fewer patients with diabetes than in the general population. However, prostate cancer patients with diabetes were significantly more likely to have metastases in the lymph nodes. In addition, the proportion of patients who are at very high risk according to the guidelines of the National Comprehensive Cancer Network (NCCN) was significantly higher among those with diabetes.

But how do prostate carcinomas differ in men with and without diabetes? What makes prostate carcinoma in patients with metabolic disease so aggressive? The researchers investigated these questions in another study. For this purpose, they analyzed 70 tumor samples from patients without diabetes and 59 samples from patients with type 2 diabetes.

Since male sex hormones (androgens) play an important role in the development of prostate cancer, the scientists investigated the androgen signaling chain. We conducted a gene expression analysis of key proteins and found that in men with diabetes, the androgen receptor (AR) was increased," said Dr. Martin Heni, who led the study at the IDM. The signaling pathway mediated by AR was also more strongly activated.

The scientists identified another difference: "Insulin receptors of isoform A are increasingly expressed in the prostate carcinomas of patients with diabetes," said Dr. Stefan Lutz, first author of the study. These can bind insulin-like growth factors (IGFs). This contributes to increased cell growth and cell division. Normally, adults mainly express the isoform B, which does not bind IGF.

In addition, in patients with diabetes, the steroid biosynthesis in the tumor is also altered. Less protective estrogen receptor ligands are formed.

This further strengthens the androgen signaling pathway in tumors.

Our research provides new insights into why prostate cancer is so aggressive in men with type 2 diabetes," said Dr. Heni, summarizing the results. Prostate carcinoma in men with type 2 diabetes has a poorer prognosis and must therefore be diagnosed and treated earlier and more comprehensively than prostate cancer in nondiabetics," said Professor Arnulf Stenzl, MD, head physician of the Urology Department of Tübingen University Hospital.

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