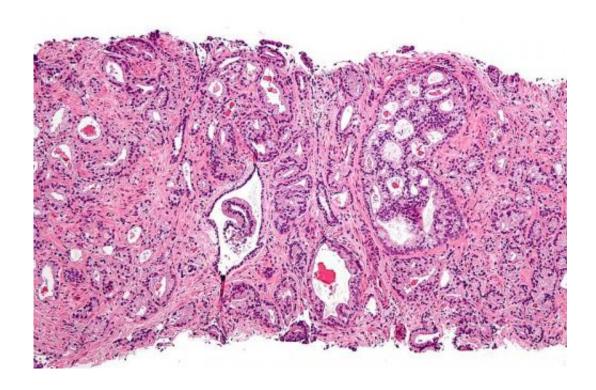


Statins may lower mortality in high-risk prostate cancer patients

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Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, <u>CC BY-SA 3.0</u>

Among high-risk prostate cancer patients—those with high PSA and Gleason scores of 8 or more—many will develop a difficult-to-treat disease. Preliminary research suggests that two commonly prescribed medications, cholesterol-lowering statins and the diabetes therapy metformin may have anticancer effects. However, it is unclear which of these two medications—commonly prescribed together—contributes the



most and whether they can impact high-risk prostate cancer. New research shows that statins, alone or with metformin, increase survival in men with high-risk prostate cancer.

"Both metformin and statins have been associated with <u>longer life</u> in <u>prostate</u> cancer patients, yet because they are commonly prescribed together, no study we know of has looked at these two medications separately," says senior author Grace Lu-Yao, Ph.D., associate director of Population Science at the Sidney Kimmel Cancer Center—Jefferson Health, one of only eight NCI-designated cancer centers nationwide with a prostate cancer program of excellence.

The study, published in *Cancer Medicine* on Feb 8th, looked at a number of statin therapies, and metformin, an anti-diabetic medication, in high-risk prostate cancer populations.

Using data from the Surveillance, Epidemiology and End Results (SEER-18) database linked with Medicare files, Dr. Lu-Yao and colleagues looked at patients diagnosed with cancer from 2007 through to 2011. Based on 12,700 patients, the researchers observed that statins alone or in combination with metformin was significantly associated with reduced mortality from all causes.

Dr. Lu-Yao and colleagues saw the highest median survival of 3.9 months in men who took both metformin and statins, 3.6 with statins alone and 3.1 years with metformin alone. The median survival for those who did not use either drug was also 3.1 years.

"With respect to prostate mortality, metformin plus statin was associated with a 36% reduction in risk of death followed by statins alone," says Dr. Lu-Yao. "Those taking metformin alone were relatively rare, and there was no significant association with all-cause mortality."



Interestingly, the study revealed that men who took atorvastatin, pravastatin, or rosuvastatin—but not lovastatin—demonstrated a reduction in mortality compared with non-users, which is consistent with the findings from a recent population-based cohort study using Taiwan National Health Insurance Research Data. The Taiwanese research showed that these three statins are more effective at lowering triglycerides and low-density lipoprotein cholesterol and raising high-density lipoprotein cholesterol than other statins in patients with hypercholesterolemia.

Of the three statins studied, men on atorvastatin did have a longer median time to progression on androgen deprivation therapy compared to those who weren't treated with statins. "Although the exact mechanisms remain unknown, it is worth noting that atorvastatin exhibits a potent lipid-lowering effect per dose of any statin, and has the greatest bioavailability and one of the longest half-lives," says to Dr. Lu-Yao.

The data presented in the current study provide crucial insight for the design of future randomized clinical trials of <u>statin</u> for high-risk patients with prostate cancer. Based on the existing evidence, a well-designed clinical trial is warranted to investigate the roles of statins and combination statins/<u>metformin</u> to reduce the mortality cancer of the prostate.

"Our study showed that the effects were more pronounced in patients taking statins after the diagnosis of prostate cancer, 54% reduction in PCA mortality among patients with high-risk prostate cancer," says Lu-Yao. "This magnitude of reduction is comparable to the results of men treated with androgen signaling inhibitors." Statins are relatively inexpensive with good safety records. Further studies to understand the mechanisms of the observed association and its potential clinical utility are warranted.



More information: Xiang-Lin Tan et al, Individual and joint effects of metformin and statins on mortality among patients with high-risk prostate cancer, *Cancer Medicine* (2020). DOI: 10.1002/cam4.2862

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