

METFORMIN USE AND ALL-CAUSE AND PROSTATE CANCER SPECIFIC MORTALITY AMONG DIABETIC MEN.

David Margel^{1,4,6}, David Urbach^{*,2,3,4,5}, Lorraine Lipscombe^{4,6}, Chaim M. Bell^{4,6,7}, Girish Kulkarni^{1,4}, Peter C. Austin^{4,6} and Neil Fleshner¹

¹Division of Urology, Department of Surgical Oncology, Princess Margaret Hospital, University Health Network, Toronto, Ontario, Canada

²Departments of Surgery and Health Policy Management and Evaluation, University of Toronto

³Division of Clinical Decision Making and Health Care, Toronto General Hospital Research Institute

⁴Institute for Clinical Evaluative Sciences (ICES)

⁵Cancer Care Ontario

⁶Institute for Health Policy Management and Evaluation, University of Toronto

⁷Department of Medicine and Keenan Research Centre in the Li Ka Shing Knowledge Institute, St. Michael's Hospital.

⁸Department of Medicine, Women's College Hospital and Research Institute, University of Toronto.

* Both David Urbach and Neil Fleshner contributed evenly to the manuscript.

Abstract

Purpose- To evaluate the association between cumulative duration of metformin use after prostate cancer diagnosis and all-cause and prostate cancer-specific mortality among diabetic patients.

Methods- We used a population-based retrospective cohort design. Data were obtained from several Ontario health care administrative databases. Within a cohort of men over the age of 66 with incident diabetes who subsequently developed prostate cancer, we examined the effect of duration of anti-diabetic medication exposure, after prostate cancer diagnosis, on all-cause and prostate cancer-specific mortality. Crude and adjusted hazard ratios were calculated using a time-varying Cox proportional hazard model to estimate effects.

Results- The cohort consisted of 3837 patients. Median age (interquartile range IQR) at diagnosis of prostate cancer was 75 (72-79) years. During a median (IQR) follow up of 4.64 (2.7-7.1) years, 1343 (35%) died, and 291 patients died of prostate cancer (7.6%). Cumulative duration of metformin treatment, after prostate cancer diagnosis, was associated with a significant decreased risk of prostate cancer-specific and all-cause mortality in a dose-dependent fashion. The adjusted hazard ratio, for prostate cancer-specific mortality was 0.76 (95% confidence interval, 0.64-0.89) for each additional six months of metformin use. The association with all-cause mortality was also significant but declined over-time from a HR of 0.76 in the first 6 months to 0.93 between 24-30 months. There was no relationship between cumulative use of other anti-diabetic drugs and either outcome.

Conclusions- Increased cumulative duration of metformin exposure after prostate cancer diagnosis was associated with decreases in both all-cause and prostate-cancer-specific mortality among diabetic men