RESEARCH LETTER

# Does diabetes alter the risk of neoplasms?

## Real-world data analysis in Poland: incidence rates for selected neoplasms in patients with diabetes

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**Introduction** Neoplastic diseases are the second cause of death in developed countries and the third one in developing countries.[1] A comorbidity of neoplastic diseases in patients suffering from diabetes has been described in the literature, with particular emphasis on the survival and death rates in this population of patients.[2,3] Numerous published studies and meta-analyses have indicated an association between type 2 diabetes mellitus and an increased risk of neoplasms, including hepatocellular, endometrial, pancreatic, colorectal, breast, or urinary bladder carcinomas, with a decreased risk of prostate carcinoma.[4] The relationship is thought to be causal (associated with hyperglycemia, hyperinsulinemia, and other metabolic disorders) or to depend on common risk factors, such as obesity.

Carcinogenesis is a multi-level process sensitive to genetic stimuli. Diabetes can influence this process through several mechanisms, predominantly associated with increased concentrations of insulin, activation of signal pathways dependent on insulin-like growth factor (IGF), hormonal dysregulation of ovarian functions, and finally, chronic inflammation. Insulin and IGF influence cell survival and proliferation.[5] It has been proved that insulin concentrations in patients with neoplasms are directly, proportionally correlated with case fatality associated with neoplasm.[5,6] Should a causal relationship between hyperglycemia or hyperinsulinemia and the induction of carcinogenesis be found, the institutions responsible for public health should take this into consideration when planning intensified health-promoting actions. Due to the fact that diabetes and neoplasms are becoming chronic diseases, there is a need to assess how their incidence rates are distributed within patient populations, which is particularly important when assigning resources (human, equipment, or office space) for the coming years.

**Patients and methods** In order to select a population for further analysis, patients with known diabetes diagnosed within the scope of health care services (ICD-10: E10% to E14%; a „%" sign replaces each number and sign) or who filled the prescriptions for antidiabetic medications (from the ATC groups: A10A% and A10B%) and/or for glucose test strips, the data for which were reported to the National Health Fund in the period from May 1, 2009, to April 30, 2009, were identified from the National Health Fund databases.

Based on the unique patients' identifiers (patient ID), we checked whether neoplasms were diagnosed among the patients (ICD-10 C%, D% or Z51.1; Z51.2) in the previous period (before May 1, 2008; 30 5411 patients with reported neoplasms were excluded from further analysis). A cohort of patients included in the further analysis included 1 840 979 people. After 1 year (from January 1, 2010, to December 31, 2010), data from the same, still alive patients (a cohort of 1 740 967 people, including 754 552 men and 986 415 women) were analyzed once again for the diagnosis of a neoplasm. A total of 19 023 new cases of cancer were found (in the population with known diabetes), whereas among the 35 818 062 people from the general population without diabetes, only 107 165 of new cases of cancer were found. This means that the general incidence rate of cancer in

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Received: May 30, 2016.
Revision accepted: June 21, 2016.
Published online: June 29, 2016.
Conflict of interests: none declared.
Pol Arch Med Wewn. 2016; 126 (6): 435-437
doi:10.20452/pamw.3456

**TABLE 1** Incidence rates of cancer in the population with diabetes and in the population without diabetes per 100 000 population (source: internal databases of the Polish National Health Fund)

| Type of cancer | ICD-10 | Men | | Women | |
|---|---|---|---|---|---|
| | | population with diabetes | general population | population with diabetes | general population |
| total | – | 310.14 | 1 229.34 | 288.81 | 988.12 |
| stomach | C16 | 15.11 | 47.18 | 7.05 | 29.91 |
| large intestine and rectum | C18-C21 | 41.55 | 140.61 | 31.11 | 104.22 |
| liver | C22 | 2.64 | 22.00 | 1.78 | 16.73 |
| gallbladder | C23 | 0.49 | 6.49 | 3.03 | 16.22 |
| pancreas | C25 | 6.97 | 42.54 | 5.90 | 33.25 |
| larynx | C32 | 11.08 | 14.31 | 1.27 | 2.84 |
| lungs | C34 | 68.32 | 155.72 | 25.54 | 63.77 |
| skin | C44 | 13.21 | 92.90 | 13.50 | 87.49 |
| breast in women | C50 | – | – | 77.04 | 139.90 |
| uterine cervix | C53 | – | – | 14.50 | 32.54 |
| uterine body | C54 | – | – | 17.96 | 90.73 |
| ovary | C56 | – | – | 16.58 | 24.13 |
| prostate gland | C61 | 39.41 | 205.29 | – | – |
| kidney | C64 | 13.25 | 64.14 | 8.96 | 41.97 |
| urinary bladder | C67 | 27.36 | 116.23 | 7.69 | 27.27 |
| thyroid | C73 | 1.84 | 4.51 | 8.83 | 12.27 |

the population of patients with diabetes amounts to 1 092.61 per 100 000 people with diabetes, and in the case of the population without diabetes, it amounts to 299.19 per 100 000 people without diabetes. Confidence intervals were not determined because data from the entire available population (the actual data) were collected for the analysis.

**Results** The results of the incidence rate of cancer in both populations in 2010 standardized by the number of male patients with diabetes and without diabetes (754 552 and 17 429 462, respectively) and by the number of female patients with diabetes and without diabetes (986 415 and 18 388 599, respectively) are presented in TABLE 1. Moreover, for the survey population of patients with diabetes, the mean and the median age when medical services were first provided to the patient were calculated on the basis of the date of birth. The results for the beginning of the survey (2008) were: the mean age, 63.3 years, and the median age, 65 years, whereas for the end of the survey (2015), they were 64.4 years and 65 years, respectively. Although the mean age of the patients increased during the study period, the median age remained at the same level. The incidence of cancers in the population of patients with diabetes was 3.6-times more frequent compared with the incidence of cancers in the population without diabetes. In the male population with diabetes, a higher incidence of neoplasms of the prostate, lung, large intestine, and rectum could be observed. In the female population (both in the populations with and without diabetes), the highest incidence was noted for the neoplasms of the breast, large intestine, and rectum as well as the uterine body. An increase in the number of new neoplasms in the population with known diabetes differed depending on the type of neoplasm. In the male population with known diabetes, compared with the population without diabetes, the highest incidence of neoplasms was observed for the gallbladder (multiplication factor, 13.3), liver (multiplication factor, 8.3), and skin (multiplication factor, 7); while in women, for the liver (multiplication factor, 9.4), skin (multiplication factor, 6.5), and pancreas and gallbladder (multiplication factor, 5.4).

The results obtained indicate that the prevalence of prostate carcinoma in patients with diabetes is higher compared with that in the general population, although literature data suggest that the prevalence of this carcinoma in diabetes patients is equal or lower compared with that in the general population.[7] The analysis does not explain this phenomenon; it may result from overdiagnosis of this neoplasm associated with a greater number of control visits at primary physician's office due to diabetes, which can provide an occasion to educate the patient on screening for prostate carcinoma and be associated with higher detection of an asymptomatic increase in prostate-specific antigen levels. However, higher incidence rates for hepatocellular and pancreatic neoplasms

have been demonstrated in studies involving the populations of diabetes patients.[8,9] The analysis of women with known diabetes in Poland has indicated a lower incidence of breast carcinoma compared with that in the general population, which is an opposite result to literature data.[10,11] However, a higher incidence of uterine carcinoma compared with that in the general population has been reported in the literature, which can be explained by the common risk factor (obesity).[12]

**Conclusions** The obtained results are particularly valuable because they concern the entire population of Poland, which is almost completely ethnically homogeneous. The method used in this analysis does not allow the assessment of the influence of hypoglycemia treatment, concomitant diseases, or environmental factors on the occurrence of neoplasm. The results concern a 1-year follow-up of the cohort, and it will be undoubtedly interesting to conduct the same analysis on the same patient population after several years, using the same method.

Considering the above, it is not possible to assess with any certainty whether after several years the statistical indicators of the risk of developing neoplasms at certain sites will change or not. However, our results clearly indicate that physicians should take into consideration the more frequent incidence of certain neoplasms in patients with diabetes when providing care for these patients. Additionally, it has been confirmed that the adapted method of data analysis based on the reporting of health care services may be applied to the population of patients with diabetes and coexistent neoplastic disease. After developing additional verification algorithms within the scope of health care services burdened with a considerable risk of uncertainty (especially primary health care), it will be possible to apply our results in further analyses on populations suffering from diseases other than diabetes as well as concomitant diseases.

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