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Risk of cancer appearance among the incidence and prevalence of type 2 diabetes in Hungary

Doctoral (PhD) thesis

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1 Introduction

Type 2 diabetes (T2DM) has a high prevalence worldwide. The disease is associated with cardiovascular risks, and a higher incidence of cancers can also be observed.

Cancer is a growing burden worldwide, although different geographical areas are affected differently. In Hungary, cancer incidence is estimated to decrease by 0–0.9% per year.

Cancers and T2DM share many common risk factors. Glucotoxicity, hyperinsulinaemia, inflammation and oxidative stress are the main contributors to the development of long-term complications of T2DM. Obesity further increases the risk of T2DM and cancers.

Most data on the subject are available for prevalent T2DM patients. In newly discovered T2DM patients, the study of the incidence of cancers may provide a deeper insight into the characteristics of these diseases. The early appearance of cancers after the diagnosis of T2DM may indicate that the development of the disease can precede the diagnosis itself by years.

In this thesis, we examined the appearance of cancers in newly diagnosed T2DM patients. We examined only one year after the diagnosis, so the effect of long-term antidiabetic treatment on the development of cancers is negligible. The chance of developing a cancer can be compared to a control group with a big sample size. In this thesis, we examined the relationship between not only T2DM, but also gender and age, with the risk of developing cancers.

Cancer is the second most common cause of death worldwide, but it is the first in developed countries, so we found it justified to investigate the epidemiology of cancers in the case of prevalent T2DM patients as well.

Most of the previous studies focused on only one type of cancer or examined a small group of patients, but in this paper, we presented a robust, nationwide study of the appearance of cancers among T2DM patients. We examined the effect of gender and age, and the change in time for more than 20 cancer types.

2 Objectives

2.1 To investigate cancer incidence among newly diagnosed T2DM patients compared to the non-diabetic population.

1. How does the risk of developing a cancer differ in newly diagnosed T2DM patients compared to the diabetes-free population?
2. How does the risk of developing cancer differ in newly diagnosed T2DM patients compared to the diabetic-free population by gender and age group?
3. Did the risk of developing cancer change during the study period in newly diagnosed T2DM patients and in the diabetes-free population?
4. Is there a difference in the trend between the two subpopulations?
5. What are the most common types of cancers in the two subpopulations?

2.2 To investigate cancer incidence among previously diagnosed prevalent T2DM patients compared to the non-diabetic population.

1. How does the risk of developing cancer differ in prevalent T2DM patients compared to the diabetes-free population?
2. How does the risk of cancer develop in prevalent T2DM patients compared to the diabetic-free population by gender and age group?
3. Did the risk of cancer change during the study period in the case of prevalent T2DM patients and the diabetes-free population?
4. Is there a difference in the trend between the two subpopulations?
5. What are the most common types of cancers in the two subpopulations?

3 Materials and methods

The study was approved by TUKEB (Scientific Research Ethics Committee) under the permit number BMEÜ/325-1/2022/EKU

We determined ten-year age groups when we examined cancers independently of their localisation. In the case of each type of cancer, only the 18–59 and 60+ age groups were distinguished, because on the one hand, this is included in the WHO recommendation for determining the older population, and on the other hand, the 60+ age group includes a quarter of the non-diabetic population at risk, so a sufficiently large number of elements was available for the study. The NHIF does not release data for groups with less than 10 patients, so a more detailed split of age groups was impossible.

Two databases were used in the study. The data on adult T2DM and cancer patients came from the National Health Insurance Fund Management (NHIF) database. For the total number of the Hungarian population, we used the data on the website of the Central Statistical Office (HCSO). By comparing the two, we were able to determine the number of people in the diabetes and cancer-free population in each year.

The algorithm I developed can determine the time and type of diabetes diagnosis based on the reported ICD (International Classification of Diseases, version 10) codes and medications used. Based on a seven-step hierarchical algorithm, we determined the T1DM patients, excluding whom we obtained the examined T2DM patient base. We selected adult patients only for the study. We excluded those who were diagnosed with cancer between 2009 and 2014 from the analysis. To determine the cancer's type and time of appearance, we also used a method we developed earlier.

We set the index date so that the one-year follow-up period did not extend into 2020, when the COVID-related lockdowns may have biased the results. This incidence was 2015-2018 for incident and 2015-2019 for prevalent patients.

At the beginning of each calendar year, we determined the number of diabetes-free people as the population reported by the Central Statistical Office (HCSO) minus the diabetic patients already known from the NHIF database, and patients diagnosed with diabetes in that year.

3.1 Statistical analysis

The analysis was conducted using R version 4.3.1 and version 7.3-60 of the MASS package.

During the research, we examined whether cancer appeared within 365 days after the index date. T2DM patients and the control group were compared by binomial logistic regression, where the target variable was the appearance of the cancer, and the explanatory variables were the presence of diabetes, index year, gender, age group, and their interactions. In this way, we were able to estimate the risk of cancer for each gender and age group, as well as the odds ratio (OR) between T2DM patients and the control group, as well as the annual change in risk. When we examined the different cancer types, we considered only the appearance of the given cancer type as a positive case.

We calculated the above metrics for gender, age groups and the entire Hungarian population. For this, we used a parameterised bootstrap simulation. Using the estimates of the regression model and their standard error, as well as the covariance matrix of the model, we estimated the risks in each group with one million iterations. When summarising, we weighted it with the average number of people in each age group and gender. In this way, we obtained estimates, confidence intervals and p-values corrected for gender and age, which were valid for the Hungarian population. The fact that the distribution of the age group was very different in the diabetic and non-diabetic circles did not cause any bias in the estimates.

Some parts of the analysis included several comparisons, which may lead to the phenomenon of alpha inflation. To eliminate this, we used the Benjamini-Hochberg method for each sub-analysis. In addition to the 5% FDR (False Discovery Rate), we determined the p-value in each case, below which we make first-type errors in a maximum of 5% of the cases.

4 Results

4.1 Incident cancers of incident T2DM patients

In the years 2015–2018, we found 54,851, 52,592, 48,947, and 47,464 newly diagnosed adult T2DM patients who had no cancer at that time. The control group included 7,171,520, 7,115,034, 7,050,703 and 7,002,327 people, respectively.

4.1.1 Distribution of age groups

In terms of the group at risk, 39.35% of non-diabetics were under 40 years of age; the proportion of certain age groups was monotonously decreasing, with only 3.98% in the 80– year age group. In the case of incident T2DM patients, the distribution of the age group was completely different. The proportion of people under 40 was only 4.49%, which rose and reached a maximum of 31.45% among 60-69-year-olds, and then decreased to 9.35% among those over 80. The age distribution of the two patient groups was much more similar among new cancer patients.

4.1.2 Crude incidence

In T2DM patients, the raw case numbers per 1000 people at risk in each year ranged from 3.57 to 4.32 under 40 years of age, compared to only 0.86 to 0.95 in the non-diabetic population. The risk was highest in the two age groups over 70. In T2DM patients, we saw values between 38.72 and 48.37, while in the case of non-diabetic patients, the crude incidence was roughly half of this, 19.90 to 21.74.

4.1.3 Time to onset of cancers among T2DM patients

30% of the cancers occurring within a year occurred within a very short time after the diagnosis of diabetes, within a month, instead of the 8% expected time proportionally. Depending on the type of cancer, this value varied between 16.5% and 48.5%. The largest proportion was detected within a month for oesophageal cancers. All types of cancers were characterised by a higher than time-proportional frequency already in the first month. The average time to appearance was 117.9 days.

4.1.4 Cross-sectional image, all cancers

The probability of developing a cancer was 4.32 (4.14–4.53; $p<0.0001$) in the overall population. For men, the odds ratio was 4.7 (4.43–5.02; $p<0.0001$) and 3.94 (3.70–4.22; $p<0.0001$) for women. There was no significant difference between the sexes.

In terms of age groups, we saw a significant difference between the young and the elderly. People aged 18–39 had the highest odds ratio, OR=4.22 (2.45–7.92). Moving towards the elderly, the odds ratio decreased monotonously, but even for those over 80 years of age, it was 1.97 (1.75–2.22).

The odds ratio of men was 20% compared to women in the overall population. In terms of age, the biggest difference was between men and women aged 40–49. There was practically no difference between the ages of 50 and 69, and then over the age of 80, and the odds ratio of men with T2DM was only 70% compared to women with T2DM.

4.1.5 Trends, all cancers

In the non-diabetic group, the mean annual change in risk was -1.86% (-2.29%–-1.44%; $p<0.0001$), in terms of gender, -1.94% (-2.55%–-1.34%; $p<0.0001$) in men and -1.79% (-2.38%–-1.20%; $p<0.0001$) in women, i.e. we saw a definite decrease in incidence over the four-year period studied.

In contrast, in newly diagnosed T2DM patients, a slight but not significant increase was observed in the overall population of 0.27% (-2.32%–2.60%; $p=0.9291$). However, this did not differ significantly from the trend of non-diabetics (ORR=1.02; 0.99–1.05; $p=0.1174$). Due to the much smaller number of cases, the estimates were much more uncertain, which was also the reason why we did not find any significant differences.

In the case of T2DM patients, we saw a slightly larger decrease in the 40-49 age group compared to the others, which was not significant.

In the non-diabetic population, the change in the 70–79 age group differed from the average of the others, because it decreased less in this age group.

4.1.6 Age group distribution for each type of cancer

In the case of melanoma and breast cancer, we observed a rate below 0.5. Younger T2DM patients were underrepresented in these two localisations. The rate was above 0.7 for lung cancer, non-Hodgkin lymphoma, pancreatic cancer, uterine cancer, kidney and prostate cancer. These had a higher proportion of younger T2DM patients than the average.

4.1.7 Distribution of cancer types between the incident T2DM patients and non-diabetics.

There was a striking difference in the distribution of cancers in the case of breast cancer, where the incidence rate in T2DM patients was only 8% instead of 13.8%, in non-diabetic patients. Pancreatic cancer rates, on the other hand, were 11.7% for T2DM compared to 3% in non-diabetics.

Kidney cancer (4.5% vs. 3.1%) and liver cancer (2.5% vs. 1.3%) were also at least one percentage point more common in T2DM patients. In the non-diabetic population, melanoma (2.1% vs. 4.2%), oral cavity cancer (1.8% vs. 4.1%) and cervical cancer (0.8% vs. 2%) were more common.

4.1.8 Cross-sectional image, stratified by cancers

If we examined the occurrence of the individual cancers, we found significant differences. The odds ratio for pancreatic cancer was outstandingly high: 17.43. This was followed by liver (8.81), kidney (6.67), uterine (5.99), gallbladder (5.52), bladder (5.47), stomach (5.12) and brain cancer (5.10), with an odds ratio of more than five.

4.1.9 Trends, stratified by cancer types

In the non-diabetic group, we mostly saw a decrease, significantly in the case of eight cancers. There were also significant changes stratified by gender and age group. Breast cancer differed in the 18–59 age group, where the risk was increased. In contrast, the picture was mixed in the case of newly diagnosed T2DM patients. There was a significant change only in the 18–59-year-old group for myeloma.

If we split the two populations by gender, the incidence of myeloma in the non-diabetic group increases in men and decreases in women. There was no other significant difference between the sexes.

Comparing the T2DM patient and non-diabetic populations by cancer, there was a significant difference only in the case of colorectal cancer, where the incidence increased in T2DM patients while it decreased in non-diabetic patients.

4.2 Incidence of cancers in prevalent diabetic patients

In the years 2015–2019, we found 564,486, 584,891, 602,844, 615,259, and 625,811 prevalent adult T2DM patients who had no cancer at that time. The control group included 7,171,520, 7,115,034, 7,050,703, 7,002,327 and 6,973,636 people, respectively.

4.2.1 Distribution of age groups

Considering the group at risk, 39.06% of non-diabetics were under 40 years of age, the proportion of each age group was monotonously decreasing, with only 3.97% in the 80-age group.

In the case of prevalent T2DM patients, the age group distribution was quite different. The proportion of people under 40 was only 0.19%, which rose and reached a maximum of 38.03% among 70-79-year-olds, and then decreased to 16.9% among those over 80. The age distribution of the two groups of patients was much more similar between patients with new cancer than between those at risk.

4.2.2 Crude incidence

We found that the raw case numbers per 1000 people at risk in each year, stratified by gender and at the same time, ranged from 1.55 to 2.51 in T2DM patients under 40 years of age, compared to only 0.81 to 0.95 in the non-diabetic population. The risk was highest in the two age groups over 70. In T2DM patients, we saw values between 20.01 and 23.29, and in the case of non-diabetic patients, the crude incidence was similarly 19.52–21.74.

4.2.3 Time to appearance of cancers

The appearance of cancers was examined every year in the 365 days after the first of January. During this time, the appearance of cancers occurred essentially evenly. The proportion of appearances within one month was between 8.2 and 10.4%, and 8.9% for all cancers. The average time to appearance was 178.4 days, with a value ranging from 168.9 to 186.4 for different cancer types.

4.2.4 Cross-sectional image, all cancers

The odds ratio of developing a cancer was 2.50 (2.46–2.55; $p<0.0001$) in the overall population. For men, the odds ratio was 2.76 (2.70–2.82; $p<0.0001$) and for women 2.27 (2.22–2.33; $p<0.0001$). There was a significant difference between the sexes, and the risk for men is higher.

We also saw a significant difference between the young and the elderly regarding age groups. People aged 18–39 had the highest odds ratio, OR=2.23 (1.58–3.25; $p<0.0001$). Moving towards older people, the odds ratio typically decreased: 1.26 and 1.27 in the 40–49 and 50–59 age groups, respectively, and 1.08 in both the 60–69 and 70–79 age groups. There was no significant difference for those over 80 years of age: OR=0.98 (0.94–1.03; $p=0.4568$).

4.2.5 Trends, all cancers

In the control group, the mean annual changed in risk was -1.79% (-2.07%–-1.52%; $p<0.0001$), by gender -1.91% (-2.31%–-1.52%; $p<0.0001$) in men and -1.68% (-2.06%–-1.29%; $p<0.0001$) in women, i.e. we saw a clear decrease in incidence in the five-year period under review. Split by age group, but without gender, we experienced a significant decrease everywhere except for the 70-79 age group.

In the case of prevalent T2DM patients, a slight but not significant decrease was also observed in the overall population, -0.50% per year (-1.12%–0.10%; $p=0.0991$). Stratified by age, there was a significant decrease among 50–59-year-olds (-2.63%; -4.59%–-0.66%; $p=0.0091$).

4.2.6 Age group distribution for each type of cancer

In the case of prevalent T2DM patients, due to the higher number of cases, we were able to examine the age group distribution in more detail.

In the case of all types of cancer, we saw that the proportion of juvenile cancer is higher among non-diabetics. The biggest difference was seen in the case of cervical cancer and melanoma.

4.2.7 Distribution of cancer types between prevalent T2DM patients and non-diabetics

There was a striking difference in the distribution of cancers in the case of breast cancer, where the proportion of incidence T2DM patients was only 7.9% instead of 13.8% in non-diabetic patients. The rate of pancreatic cancer, on the other hand, was 11.9% in T2DM compared to 3% in non-diabetics.

Kidney (4.6% vs. 3.1%) and liver cancer (2.5% vs. 1.3%) were also at least one percentage point more common in T2DM patients. Melanoma (2.1% vs. 4.2%), oral cancer (1.8% vs. 4.8%) and cervical cancer (0.7% vs. 2%) were more common in the non-diabetic population.

4.2.8 Cross-sectional image, stratified by cancer

If we examined the occurrence of the individual cancers, we found significant differences. Liver and pancreatic cancer were on the top of the list here as well, but now liver cancer had come first: OR = 5.65 (5.08–6.29; $p<0.0001$) and 4.35 (4.06–4.67; $p<0.0001$). These were followed by gallbladder (3.66; 3.17–4.28; $p<0.0001$), uterine (3.60; 3.20–4.06; $p<0.0001$), kidney (3.40; 3.11–3.73; $p<0.0001$) and stomach (3.13; 2.83–3.48; $p<0.0001$) with odds ratio of more than three. In the case of the examined cancers, we saw different behaviour in the case of the cervix and testicles, where the odds ratio was lower in diabetic patients than in the control, the latter significantly: (0.87; 0.67–1.14; $p=0.3203$ and 0.49; 0.36–0.67; $p<0.0001$).

In the case of young people, the risk of gallbladder cancer was significantly higher. This was followed by cancers of the prostate, kidneys, uterus, lungs, pancreas, oesophagus and colon, where the risk of younger people was significantly higher, at least threefold. Only in the case of testicular cancer was the risk of younger people significantly lower.

There were minor differences between the sexes. In the case of melanoma, liver cancer, bladder cancer, colon and lung cancer, the risk was significantly higher for men, while for oral cancer, it was higher for women.

4.2.9 Trends, stratified by cancer

In the non-diabetic group, we mostly saw a decrease, which was significant in the case of ten cancers, while the incidence of non-Hodgkin lymphoma showed an increasing trend. There were also significant changes in the gender and age group stratums. Of these, the risk of breast and thyroid cancer were higher in the 18–59 age group.

In contrast, the picture was mixed in the case of prevalent T2DM patients. There was a significant change in the 60-year-old group and in men, as well as overall in gastric cancer. In the case of young people, the risk of liver cancer was reduced. It can be observed that due to the much smaller number of cases, the estimates were much more uncertain, which was also the reason why we did not find any significant differences.

In the case of T2DM patients, there was a significant difference in liver cancer between the age groups 18-59 years and older. The incidence decreased more among younger people.

In the non-diabetic population, cancers of the liver, lungs, breast, thyroid, oral cavity, larynx and cervix showed significantly different trends in the two age groups. In the case of breast and thyroid cancer, there was an increase in younger people, but in other cases, their trend was more favourable. If we divided the two populations by gender, the incidence of lung cancer in the non-diabetic group decreased more in men than in women. There was no other significant difference between the sexes.

5 Discussion

The main strength of our study is that we were able to map the entire adult Hungarian population based on the data of the National Health Insurance Fund and the Central Statistical Office. Based on the data of the health insurance company, it could be determined quite accurately who and how long had been suffering from diagnosed diabetes and cancer, so the results of the study provided an accurate estimate of the entire adult Hungarian population. We had the opportunity to detect gender and age differences both in the case of all cancers together and in the case of the individual organs, examining both cross-sectional and temporal changes.

However, due to the data protection rules of the NHIF, it did not release data for groups of less than 10 patients, so it was impossible to examine rare cases. Another limitation was that results of laboratory examinations (e.g. HbA_{1c}) or data on the physical status of patients (e.g. BMI, body weight) were not available in the database, so they could not be corrected in the models. There was a big difference in the age distribution of the two groups, but we were able to manage these differences by choosing a statistical method.

We examined both newly discovered and prevalent T2DM patients. Although the risk in the two groups was different in absolute terms compared to the diabetes-free control group, the trends were the same: diabetics were exposed to an increased risk and the incidence of cancer in the control group shows a slight decrease, while in diabetic patients this was not the case. Different organs were affected in a similar proportion between the old and new patients, while in the diabetes-free population, we experienced different proportions.

An important finding of the thesis was that in the case of younger diabetics, the risk is higher, and timely initiated screening tests can save lives among them, despite the fact, that, due to the low absolute risk, there are fewer actual cases of the disease than in older age groups.

5.1 Incident cancers of incident T2DM patients

We examined the general and organ-specific cancer incidence and its annual change among newly diagnosed T2DM patients in the first year after diagnosis, compared to the diabetes-free population between 2015 and 2018. We corrected the results for gender and age. The control group was the entire Hungarian diabetes-free population. To my knowledge, this was the first study to specifically examine the cancer incidence of T2DM patients for four consecutive years.

During the study, we found that in the case of diabetic patients, the number of cases per 1,000 people was 32.11, while in the case of controls, it was significantly lower, only 6.75, and the odds ratio is 4.32.

We have experienced an increased risk for almost all types of cancer, except for cervical and testicular cancer. In this study, too, the additional risk of pancreatic cancer was the highest.

In 30% of cases, the cancer was diagnosed in the first month. This might also be due to the fact, that diabetes itself was discovered late, when its complications had already developed. It was also possible that the cancer was discovered first. Metabolic changes associated with hyperglycaemia might promote the development of cancers even in prediabetic conditions, as evidenced in the literature.

However, it should be taken into consideration, that reverse causality was also possible, especially in the case of pancreatic cancers, when the beta cells responsible for insulin production and secretion were damaged and became inoperable, leading to diabetes. The latter possibility cannot be ruled out in the case of other types of cancers.

On the other hand, the appearance of a cancer within a few months of the diagnosis of T2DM could also be caused by a bias. After the diagnosis of T2DM, a more thorough examination routinely follows, during which an already existing but not yet diagnosed cancer could be detected. Although this might cause distortions in epidemiological research, it could be extremely important from a medical point of view. Namely, within six months of the diagnosis of T2DM, it might be worth performing basic cancer screening procedures (abdominal ultrasound, chest X-ray, stool blood test, gynaecological screening, etc.).

Given that the incidence of T2DM was also increasing among young people, screening for T2DM may lead to more and more early-diagnosed cancers in the future and thus to saved lives. We saw the same pattern among young, new T2DM patients here as well as in cardiovascular comorbidity and mortality.

We found that the incidence of cancers did not change during the four years studied among new T2DM patients, while it decreased slightly in the diabetes-free population. The latter was in line with the estimated very slight annual decrease in the age-standardized incidence rate of cancers (without melanoma), which was between -0.2% globally (CI: -0.9%–0.5%) and in Hungary as well as -0.9% and 0% between 2010 and 2019. This showed that T2DM patients may contribute to stagnation.

5.2 Incident cancers of prevalent diabetic patients

We examined the incidence of general and organ-specific cancers and their annual change among prevalent T2DM patients compared to the diabetes-free population between 2015 and 2019. We corrected the results for gender and age. The control group was the entire Hungarian diabetes-free adult population.

We found that men with T2DM had a higher risk than women. Different age groups were affected differently in the T2DM and control groups. In the diabetes-free population, cancer incidence decreased, which was detectable separately in several age groups, while a similar phenomenon was not confirmed in the T2DM group.

The distribution of cancer-affected organs was also different in the two groups, for example, kidney, pancreatic, and liver cancers were more common, while breast and testicular cancers were less common among T2DM patients. The greatest additional risk was for cancers of the liver, pancreas, gallbladder, uterus, kidneys and stomach, respectively.

In most types of cancer, the additional risk of younger people was higher than that of older people. In the non-diabetic group, the incidence of gallbladder, stomach, colon, bladder, lung, oesophagus, oral cavity, larynx and cervical cancer is significantly reduced, while in T2DM patients, only stomach cancer is reduced. A significant increase was seen only in non-diabetic patients with non-Hodgkin lymphoma.

We checked whether there was a positive association between T2DM and cancers, as assumed by the literature. The additional risk we measured in T2DM patients was typically higher than what can be found in the literature, and there are several reasons for this. Obesity, for example, is a well-known risk factor for the development of both cancer and T2DM may appear as a confounder in the study of the relationship between

T2DM and cancers. In several studies, they have corrected for various markers, such as BMI, which is a marker of obesity, and this may have significantly changed their results. In this study, we did not correct for BMI or any other anthropometric parameter, as the NHIF database did not contain such data. For example, this could cause a discrepancy between my data and the literature data. In addition, demographic and ethnic factors could also influence differences compared to data from other countries.

According to our data, in the diabetes-free population, a decrease in cancer incidence could be seen in almost all age groups during the five years examined, while in the T2DM group, there was no verifiable overall change. Only in the 50-59 age group was a significant decrease. Metabolism-related cancers were increasing worldwide (AAPC=0.74; 0.71–0.76). The "Global Burden of Disease" study placed Hungary in the category of -0.9-0% average annual percentage change, while according to my data, this value was -1.78 for the diabetes-free and -0.5 for the T2DM population.

6 My theses

I. "Investigation of the incidence of cancer among newly diagnosed T2DM patients compared to the non-diabetic population" (**Abonyi-Tóth, Z.**, Rokszin, G., Fábián, I., Kiss, Z., Jermendy, G., Kempler, P., Lengyel, C., Wittmann, I., Molnár, G. A., Sütő, G. (2024). Incident Cancer Risk in Patients with Incident Type 2 Diabetes Mellitus in Hungary (Part 1). CANCERS, 16(9). http://doi.org/10.3390/cancers16091745)

IF: 4.5

1. Newly diagnosed adult T2DM patients had a 4.32 times higher chance of discovering a cancer within a year compared to the people without diabetes.
2. Stratified by age group, the additional risk was the highest in the case of 18–39-year-olds (OR=4.22), which decreased monotonously towards the elderly, even for those over 80 years of age, it is 1.97.
3. The additional risk of men and women did not differ significantly.
4. In the case of new T2DM patients, the incidence increased slightly but not significantly, while among those without diabetes, it decreased significantly.
5. There were significant differences between the different types of cancers. The greatest additional risk was for pancreatic, liver and kidney cancers.
6. Instead of the 8% expected on a time-proportional basis, 30% of the cancers discovered within a year appear in the first month.

II. "Investigation of the incidence of cancer among previously diagnosed prevalent T2DM patients compared to the non-diabetic population" (**Abonyi-Tóth, Z.**, Rokszin, G., Sütő, G., Fábián, I., Kiss, Z., Jermendy, G., Kempler, P., Lengyel, C., Wittmann, I., Molnár, G. A. (2024). Incident Cancer Risk of Patients with Prevalent Type 2 Diabetes Mellitus in Hungary (Part 2). CANCERS, 16(13). http://doi.org/10.3390/cancers16132414)

IF: 4.5

1. Prevalent adult T2DM patients had a 2.5-fold higher chance of discovering a cancer within a year than people without diabetes.
2. Stratified by age group, the additional risk was the highest in the case of 18–39-year-olds (OR=2.33), which decreased with the elderly, and was no longer significant for those over 80 (OR=0.98).

3. The additional risk of men was significantly higher that of women's.
4. In the case of prevalent T2DM patients, the incidence was slightly but not significantly reduced, while in the case of non-diabetic patients, the incidence was significantly reduced.
5. There were significant differences between the different types of cancers. The greatest additional risk was for cancers of the liver, pancreas and gallbladder.

7 Conclusions

Overall, the additional risk of cancer occurrence in patients with incident T2DM was 4.45-fold. There were eighteen organs whose cancers were more common in diabetic patients, including the pancreas, liver and kidneys, with the highest additional risk. In the case of young patients, a significantly higher additional risk could be observed, similarly to the cardiovascular events. During the follow up of the study, the cancer incidence decreased slightly in the diabetes-free population, but it was unchanged among T2DM patients. Age, sex, and organ-specific results require further investigations. It may be worth re-evaluating the current screening strategy for cancers in recently diagnosed T2DM patients, especially in younger ones.

We also observed a 2.5-fold increase in the risk among prevalent T2DM patients. Our results show that the distribution of the age group and the distribution of organs affected by the cancer differed compared to the control group. The temporal reduction was also smaller in T2DM patients. Overall, it could be concluded that T2DM patients belong to a risk group in terms of cancer, so it is advisable to have regular cancer screening.

8 Publications

8.1 Publications related to the theses

Abonyi-Tóth, Z., Rokszin, G., Fábián, I., Kiss, Z., Jermendy, G., Kempler, P., Lengyel C., Wittmann I., Molnár G. A., Sütő, G. (2024). Incident Cancer Risk in Patients with Incident Type 2 Diabetes Mellitus in Hungary (Part 1). CANCERS, 16(9). http://doi.org/10.3390/cancers16091745 (impact factor = 4,5)

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The overall impact factor of the publications related to the theses is 9.

8.2 Publications not related to the theses

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The cumulative impact factor of publications not related to the theses is 133.281.

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