

# Diabetes as a risk factor of hospitalization in the surgical ward due to cancer in the elderly and middle-aged population

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## Abstract

**Introduction:** Diabetes can be considered as a risk factor of several types of malignancy. Surgery is one of the primary methods of cancer treatment. The objective of this study was to evaluate the association between diabetes and hospital admissions to the surgery unit due to malignancy among elderly and middle-aged people.

**Material and methods:** Data for analysis were taken from the medical records of 7,694 patients aged > 45, hospitalized in the General Surgery Ward in the Specialist District Hospital in Stalowa Wola in the Subcarpathian (Podkarpatie) Province, Poland, in the years 2010–2013. Among them malignancy was diagnosed in 652 patients and diabetes in 370 subjects. Ninety-three patients suffered from both diabetes and cancer.

**Results:** Diabetes was associated with significantly elevated risk of hospitalization due to malignancy compared with the non-diabetic population, odds ratio (OR) 4.051 (95% confidence interval: 3.154–5.203),  $p < 0.001$ . Among people with diabetes, elderly patients (> 65 years) had higher risk of hospital admission due to cancer compared with the middle-aged population, OR = 5.238 (2.873–9.550),  $p < 0.001$ . Also, urban residents had higher risk compared with rural inhabitants, OR = 2.272 (1.375–3.752),  $p = 0.002$ .

**Conclusions:** Patients with diabetes, especially elderly and urban inhabitants, are at high risk of hospital admission due to malignancy. This indicates the need for oncological vigilance in such patients for early detection and treatment of cancers common in this population.

**Key words:** diabetes, cancer, surgery unit, hospitalization, risk factors.

## Introduction

The burden of diabetes has become one of the most important public health problems worldwide over the last few decades. According to the data from 2014 published by the International Diabetes Federation (IDF), it affects 387 million people worldwide. This number is expected to rise to 592 million in 2035. Also in Poland the number of diabetic subjects is continuously increasing, and according to these data, it is estimated to be 2.05 million [1]. This entails increasing costs of its treatment, and hospitalizations represent the major part of these expenditures [2]. These hospitalizations are mainly due to the vascular complications of diabetes

[3, 4]. However, also increased risk of hospitalizations due to malignancy in the diabetic population is observed [4].

The beginnings of interest of scientists in the mutual links between diabetes and cancer date back to the early 20<sup>th</sup> century [5]. Data from numerous reviews and meta-analyses published in the last decade clearly indicate that diabetes can be considered as a risk factor for at least several types of cancer. Hepatocellular, pancreatic, colorectal, gastric, kidney, bladder, endometrial and breast cancers, as well as non-Hodgkin lymphomas, are significantly more prevalent among diabetic subjects compared with the general population [6–14]. Conversely, the risk of prostate cancer is decreased among men with diabetes [15]. In a large retrospective, registry-based study in Poland an elevated risk of several site-specific cancers among diabetic patients was also found [16]. In addition, meta-analyses revealed significantly increased mortality due to malignancy among patients with diabetes compared to the non-diabetic population [17, 18].

One of the primary cancer treatment methods is surgery. Taking this into account, the aim of this study was to analyze whether, and to what extent, presence of diabetes is associated with an elevated risk of hospitalization in the surgery unit due to malignancy. This was presumed to reflect – with some limitations – the overall likelihood of cancer morbidity in diabetes. The analysis of the influence of other variables, such as age, gender and place of residence, was assumed to be helpful in identifying subjects at the highest cancer risk.

## Material and methods

Stalowa Wola is an industrial city (mainly iron and steel industry) in the Subcarpathian Province in south-eastern Poland, with over 65,000 inhabitants. It is the capital of the district, with a population of around 110,000 people. The Specialist District Hospital is the only hospital providing inpatient medical services for the residents of the county.

In the years 2010–2013 in the General Surgery Ward with Urology and Vascular Surgery subdivisions in the Specialist District Hospital in Stalowa Wola there were 10,289 hospital admissions. Among them 7,674 patients were aged  $\geq 45$ . Based on the analysis of the hospital medical records and charts, prevalence of diabetes and malignant neoplasms in this group, as well as patients' age, gender, place of residence (rural or urban) and also diabetes treatment, were evaluated. Characteristics of the study group are presented in Table I.

The study was approved by the institutional Bioethics Committee at the University of Rzeszów and by all the appropriate administrative bodies.

## Statistical analysis

Statistical analysis of the data was performed using SigmaPlot for Windows version 12.5 (Systat Software Inc., San Jose, CA, USA). Numerical data are presented as numbers and percentage (in parentheses) or as mean and standard deviation (SD). The continuous data comparing two groups of patients were analyzed using an unpaired two-tailed Student's *t*-test or by a Mann-Whitney rank sum test where appropriate. The categorical data were analyzed using the  $\chi^2$  test. The likelihood of hospitalization due to cancer among different populations was estimated using odds ratios (OR) and 95% confidence intervals (CI) in univariate and in multiple logistic regression models. A *p*-value  $< 0.05$  was considered statistically significant.

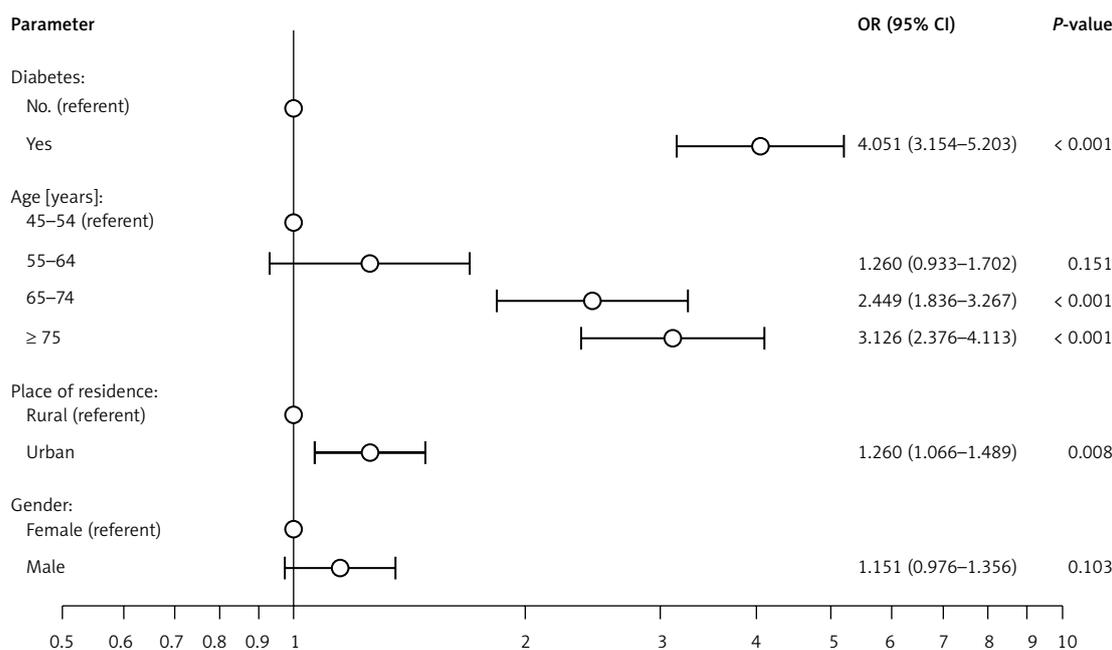
## Results

Malignancy was diagnosed in 652 (8.5%) persons among 7,674 elderly and middle-aged patients hospitalized in the surgery ward. The most frequent cancer sites were as follows: urinary bladder (31.7%), colon and rectum (24.4%), mammary gland (7.8%), skin (7.5%), prostate (6.1%) and stomach (4.6%).

Patients with malignancy were significantly older compared to the remaining subjects,  $70.4 \pm 11.1$  vs.  $65.5 \pm 11.9$  years respectively ( $p < 0.001$ ). In the univariate analysis probability of hospitalization due to cancer increased together with increasing age ( $p_{\text{trend}} < 0.001$ ) and elderly patients ( $\geq 65$ ) had significantly higher risk compared with the middle-aged group, OR = 2.436 (2.048–2.897). The strongest association with the likelihood of hospitalization due to malignancy was found for

**Table I.** Characteristics of patients with malignancy regarding age, presence of diabetes, place of residence and gender

Parameter	Value	
Study group, <i>n</i>	7,674	
Age [years]	45–64	$\geq 65$
	3,815 (49.7%)	3,859 (50.3%)
Gender	Female	Male
	3,215 (41.9%)	4,459 (58.1%)
Place of residence	Urban	Rural
	4,573 (59.6%)	3,101 (40.4%)
Cancer	Yes	No
	652 (8.5%)	7,022 (91.5%)
Diabetes	Yes	No
	370 (4.8%)	7,304 (95.2%)



**Figure 1.** Probability of hospitalization in the surgical ward due to malignancy regarding presence of diabetes, age, place of residence and gender

diabetes. A significant relationship was also revealed for urban residence. Gender had no significant impact (Figure 1).

In the multivariate logistic regression analysis taking into account age category (45–54, 55–64, 65–74 and ≥ 75 years), presence of diabetes, place of residence and gender, diabetes remained the strongest predictor of hospitalization due to cancer, OR = 3.891 (3.016–5.019),  $p < 0.001$ . Other variables also appeared to be significantly associated with the likelihood of hospitalization: every one-step increase in age category, OR = 1.512 (1.396–1.638),  $p < 0.001$ , urban residence, OR = 1.308 (1.103–1.551),  $p = 0.002$ , and male gender, OR = 1.227 (1.037–1.451),  $p = 0.017$ .

Among patients with cancer diabetic subjects were significantly older compared to people without diabetes, and women were significantly older than men. No significant difference regarding age of urban and rural inhabitants was found (Table II).

Among hospitalized patients, 370 (4.8%) subjects suffered from diabetes. In this group women were significantly older than men (70.5 ± 11.4 vs. 66.0 ± 10.4 years respectively,  $p < 0.001$ ). Also urban residents were significantly older than rural inhabitants, 69.2 ± 10.6 vs. 66.2 ± 11.4 years respectively,  $p = 0.020$ . Proportions between men and women, and between urban and rural inhabitants, were not significantly different compared with the rest of the study population.

Ninety-three (1.2%) patients were diagnosed with both diabetes and cancer. They comprised 14.3% of all patients with malignancy. The most

**Table II.** Age of patients with malignancy regarding presence of diabetes, place of residence and gender

Parameter	Age, mean ± SD		P-value
Diabetes	Yes	No	< 0.001
	74.1 ± 8.2	69.8 ± 11.4	
Place of residence	Urban	Rural	0.374
	70.2 ± 11.4	70.9 ± 11.0	
Gender	Female	Male	0.009
	71.8 ± 10.6	69.6 ± 11.4	

frequent cancer site in this group was bladder (29.0%). Subsequent sites by frequency were as follows: colon and rectum (23.7%), breast (12.9%), skin (8.6%), kidney (7.5%) and stomach (6.5%).

Mean age of patients in this group was significantly higher compared with diabetic subjects without malignancy (Table III). No significant difference regarding age between women and men in this group was found (75.7 ± 7.6 vs. 72.8 ± 8.6 years respectively). Not surprisingly, the likelihood of hospitalization due to malignancy among diabetic subjects increased with increasing age,  $p_{\text{trend}} < 0.001$  (Figure 2), and patients aged 65 or more had over 5-fold higher risk compared with middle-aged diabetic subjects, OR = 5.238 (2.873–9.550).

Compared with the non-diabetic population, diabetes was associated with significantly higher risk of hospitalization due to cancer in both

**Table III.** Characteristics of patients with diabetes regarding age, gender, place of residence and anti-diabetic medications use

Parameter	Total	Malignancy	No malignancy	P-value*
Patients with diabetes, n	370	93	287	
Age, mean ± SD [years]:	67.8 ±11.1	74.1 ±8.2	65.7 ±11.1	< 0.001
45–64	154 (41.6%)	15 (16.1%)	139 (50.2%)	< 0.001
≥ 65	216 (58.4%)	78 (83.9%)	138 (49.8%)	
Gender:				NS
Male	220 (59.5%)	51 (54.8%)	169 (61.0%)	
Female	150 (40.5%)	42 (45.2%)	108 (39.0%)	
Place of residence:				0.002
Urban	205 (55.4%)	65 (69.9%)	140 (50.5%)	
Rural	165 (44.6%)	28 (30.1%)	137 (49.5%)	
Diabetes treatment:				< 0.001
Insulin ± oral drugs	228 (61.6%)	33 (35.5%)	195 (70.4%)	
Oral drugs	142 (38.4%)	60 (64.5%)	82 (29.6%)	

NS – non-significant, \*between malignancy and non-malignancy groups.

age groups. Among middle-aged subjects this risk was 2-fold higher, OR = 2.050 (1.179–3.565),  $p = 0.016$ , while among elderly patients it was almost 5-fold higher, OR = 4.913 (3.649–6.614),  $p < 0.001$ .

Gender distribution was not significantly different between diabetic patients with and without malignancy, while likelihood of hospitalization due to cancer was significantly elevated among urban residents compared with rural inhabitants, OR = 2.272 (1.375–3.752),  $p = 0.002$ . Significantly fewer patients with diabetes and malignancy were treated with insulin compared to diabetic subjects hospitalized due to other reasons,  $p < 0.001$  (Table III). Among patients treated with oral medications proportions of sulfonylurea derivatives and metformin users were not significantly different

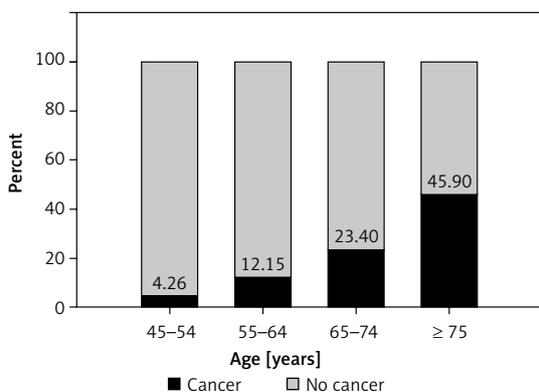
between patients with and without cancer (48 vs. 66 users of sulfonylureas, and 20 vs. 28 users of metformin respectively).

Among patients with diabetes prevalence of kidney and breast cancers was significantly higher compared to the remaining subjects with malignancy, OR = 4.144 (1.564–10.980),  $p = 0.002$  and OR = 2.021 (1.016–4.021),  $p = 0.041$  respectively. No significant differences were found for other cancer sites.

### Discussion

Current evidence indicates that both morbidity and mortality due to malignancy are elevated among diabetic patients compared with the general population [17–21]. Our study demonstrated another kind of association between diabetes and cancer – an elevated risk of hospitalization in the surgery ward due to malignancy.

Data from the literature addressing risk of hospitalization due to malignancy in diabetes are scarce. In the paper by Fu *et al.* diabetes was associated with increased risk of the first and also re-hospitalization due to cancer by 37% and 58% respectively. Interestingly, higher risk (60%) was observed in the age group < 65 years [4]. In our study presence of diabetes, among different analyzed variables, appeared to be the strongest predictor of the risk of hospitalization in the surgery unit. However, contrary to Fu *et al.*, elderly patients were at higher risk compared with the middle-aged population, and this relationship was significantly more pronounced among patients with diabetes.



**Figure 2.** Proportion of patients with malignancy among subjects with diabetes according to age range

Antidiabetic medications are considered to modulate cancer risk in diabetic subjects. Existing evidence indicates a protective role of metformin in malignancy development and outcomes [22], whilst exogenous insulin use seems to be associated with an elevated cancer risk [23], which was also revealed in one of our studies [24]. In the present study the number of diabetic patients with malignancy treated with insulin was significantly lower compared to the rest of patients with diabetes. This phenomenon can be explained by the specific surgery ward and patient profile, where atherosclerotic complications (including lower extremity ulcerations) were the leading cause of hospitalization other than cancer. Lack of data regarding diabetes duration and control did not allow this relationship to be analyzed further. Distribution of oral drug use was similar in both groups of diabetic patients.

Our study revealed that people living in an urban environment are at significantly higher risk of hospitalization due to cancer compared with rural inhabitants, which was also more apparent among patients with diabetes. This can be explained by the greater availability of medical services among urban inhabitants, and possibly higher detection of malignancies. However, in another study conducted in the Polish population among urban residents also higher breast cancer incidence was observed compared to rural inhabitants [25], which may indicate the important role of different environmental factors (e.g. disruptive chemicals present in food, air and water) in cancer development [26]. The impact of male gender on this risk, although notable, was less pronounced.

Urinary bladder was the most prevalent cancer site, both among all studied patients and among diabetic subjects. The high number of urinary tract cancers can be explained by the profile of the surgery unit, which has a large urology subdivision. Also due to the ward profile many patients with other site-specific cancers were not hospitalized in the general surgery unit, and they were usually referred to more specialized clinical units. In our study the highest risk of hospitalization for site-specific cancers in diabetic population was found for kidney and breast cancers, which is in line with findings presented in meta-analyses indicating higher risk of cancer incidence in diabetes for many cancer sites, including kidneys and mammary gland [10, 13]. Prostate cancer is known to be less prevalent among diabetic men, which was also, although insignificantly, observed in our study [16].

There are several limitations of our study. The first of them is its retrospective and registry-based design and the fact that not all important data were available, e.g. metabolic control of diabetes,

diabetes duration, smoking habits, body mass index and family history of malignancy. Moreover, not all comorbidities were listed in the hospital charts, which did not allow us to analyze other associations. The second limitation is the fact that patients with many types of cancer were not hospitalized in this particular surgery unit (lung cancer, gynecological cancers, oral cavity and laryngeal cancers, leukemia, etc.), and probably also several patients with malignancies were hospitalized in other, more specialized oncological wards elsewhere. Thus, selection bias cannot be completely excluded. Nevertheless, this study has also several strengths. One of them is the large number of patients included in the analysis, exceeding 7,500 subjects. Due to the fact that the Specialist District Hospital is the only hospital providing inpatient medical services for the residents of the county, these patients, with the mentioned earlier limitation, seem to be a group representative for the population of the district.

In summary, in our study diabetes showed a significant association with elevated risk of hospitalization in the surgery unit due to malignancy. Such a relationship has not been studied previously, and these results shed some new light and broadened our knowledge on certain links between diabetes and cancer. In addition, this study showed the important role of older age and urban place of residence in cancer risk, which was more pronounced among diabetic patients in the studied population.

In conclusion, amongst patients admitted to this particular surgery ward our study identified elderly, urban inhabitants with diabetes as a group at the highest risk of hospitalization due to malignancy. Therefore, it is advisable to make major efforts for early detection of the cancers common in this population. Early detection and early radical treatment of malignancy may allow us to improve patients' outcome and reduce the future costs spent on the therapy of more advanced neoplasm and subsequent hospitalizations due to malignancy [27, 28].

### Acknowledgments

This work was presented as a poster during the 16<sup>th</sup> Congress of the Polish Diabetes Society held in Wroclaw on 21–23 June 2015.

### Conflict of interest

The authors declare no conflict of interest.

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