Prevalence of diabetes in Japanese patients with cancer

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ABSTRACT

Cancer patients with diabetes experience a poorer prognosis, yet the population burden of this multimorbidity remains unknown. This study aimed to estimate the latest incidence and prevalence of cancer with diabetes mellitus in Japan. We used projection of cancer incidence and latest survival data from population-based cancer registries. The incidence of cancer associated with diabetes was estimated separately for patients with pre-existing diabetes and those without diabetes, and used to estimate the 5-year cancer prevalence for those with and without diabetes. The prevalence of pre-existing diabetes in cancer patients at any cancer site was estimated to be 20.7% (647,160 men and women). Among cancer sites, diabetes prevalence was high in patients with liver and pancreatic cancers in both sexes. In conclusion, our study shows a large burden of diabetes in cancer patients in Japan, which warrants further attention by health practitioners and policy-makers.

INTRODUCTION

In recent years, associations between diabetes mellitus and cancer have been reported in multiple meta-analyses, including reports from Japan[1–3]. As the prevalence of diabetes continues to rise as a result of population aging and sedentary lifestyle, the burden of cancer associated with diabetes is also expected to grow in the coming decades[4]. For instance, cancer accounted for approximately 38% of overall causes of death in diabetes patients in Japan between 2001 and 2010[5]. Cancer patients with diabetes are known to experience a poorer prognosis than those without diabetes[6–8], which will considerably impact treatment practices and cancer survivorship.

To date, however, no convincing evidence on the current magnitude of the prevalence of diabetes among cancer patients has yet appeared. Here, we aim to estimate the latest incidence and prevalence of cancer in patients with diabetes in Japan.

METHODS

Data on the incidence of cancer for 2015–2019 were obtained from the long-term projection of cancer incidence from 2015 to 2039, available from the Cancer Information Services website of the National Cancer Center, Japan[9]. The projection used the national estimates of cancer incidence between 1985 and 2014 derived from seven to 32 prefectures in the cancer registry as part of the Monitoring of Cancer Incidence in Japan Project[10]. Cancer cases were classified by sex, 5-year age group and cancer sites that are known to be associated with diabetes in Japanese individuals[2] according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision. Observed survival for cases diagnosed between 2006 and 2008 were obtained from the Monitoring of Cancer Incidence in Japan Project[11,12]. We obtained population projections for Japanese individuals with the medium-fertility and medium-mortality assumption from the National Institute of Population and Social Security Research[13]. Estimates of the prevalence of diabetes in Japanese individuals as of 2015 were obtained from a report by Charvat *et al.*[14], in which diabetes is defined by either a glycated hemoglobin of ≥6.5% (48 mmol/mol) or fasting plasma glucose level of ≥126 mg/dL and/or 2-h plasma glucose of ≥200 mg/dL in a 75-g oral glucose tolerance test. Summary estimates of the association between pre-existing diabetes and the risk of cancer were obtained from a meta-analysis of eight large-scale cohort studies carried out in Japan, which used self-reported diabetes status as exposure[2]. Of note, a validation study carried out in one of the participating studies showed that 94% of cases of self-reported diabetes were consistent with diabetes reported in medical records[15]. Both the prevalence estimates of diabetes and relative risks of cancer in patients with pre-existing diabetes pertain to diabetes of all types, albeit that type 2 diabetes accounts for the substantial

Table 1 | Estimated incidence of cancer by cancer site and diabetes status in Japan, 2019

Cancer site	ICD-10	Incidence (overall)		Incidence (with pre-existing diabetes)		Incidence (without pre-existing diabetes)	
		No. cases	Crude incidence rate[†]	No. cases	Crude incidence rate[†]	No. cases	Crude incidence rate[†]
Men, aged ≥20 years							
All sites	C00–C96	564,530	1065.6	125,910	2277.7	438,620	978.1
Colon	C18	49,690	93.8	13,760	248.9	35,930	80.1
Liver	C22	28,080	53.0	9,360	169.3	18,720	41.7
Pancreas	C25	19,790	37.4	5,510	99.7	14,280	31.8
Women, aged ≥20 years							
All sites	C00–C96	412,300	724.9	84,610	1293.2	327,690	684.9
Liver	C22	14,840	26.1	4,580	69.9	10,260	21.4
Pancreas	C25	19,450	34.2	7,490	114.4	11,960	31.2
Both sexes, aged ≥20 years							
All sites	C00–C96	976,830	889.2	210,520	1744.1	766,310	826.8
Liver	C22	42,920	39.1	13,940	115.5	28,980	31.3
Pancreas	C25	39,240	35.7	13,000	107.7	26,240	28.3

[†]Crude incidence rates are expressed per 100,000. ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th Revision.

majority of diabetes cases in both studies[2,14]. Hence, the definition of diabetes in the current report follows the definition used in these studies. The study was approved by the institutional review board of the National Cancer Center in Tokyo (approval number 2004-061).

In the analyses, we decomposed the crude incidence rates for different cancer sites separately for patients with pre-existing diabetes before diagnosis of cancer and for patients without diabetes[16]. Furthermore, we estimated the prevalence of cancer defined as the number or proportion of patients with a diagnosis of cancer within the past 5 years of a given time point[17,18], for all patients including both those with and without diabetes. Full details of the analyses are provided in Appendix S1. All analyses were carried out using Stata SE 15 (StataCorp, College Station, TX, USA).

RESULTS

Table 1 shows the incidence of all cancer sites and cancers associated with diabetes in 2019. Among patients with pre-existing diabetes, the incidence for all cancers in 2019 was 125,910 (crude incidence rate: 2277.7 per 100,000) in men and 84,610 (1293.2 per 100,000) in women, whereas the incidence for all cancers among non-diabetic patients was 438,620 (978.1 per 100,000) in men and 327,690 (684.9 per 100,000) in women.

Table 2 shows the estimated 5-year prevalence of cancer by diabetes status in Japanese adults in 2019. The prevalence of pre-existing diabetes in cancer patients at any cancer site was estimated to be 21.8% (377,190 persons with diabetes among 1,728,710 with cancer) in men and 19.4% (269,970 with diabetes among 1,394,820 with cancer) in women. When we

Table 2 | Estimated prevalence of cancer by cancer site and diabetes status in Japan, 2019

Cancer site	ICD-10	Prevalent cancer cases (overall) $n^{†}$	Prevalent cancer cases with pre-existing diabetes $n^{†}$	Prevalence of pre-existing diabetes in cancer patients %
Men, aged ≥20 years				
All sites	C00–C96	1,728,710	377,190	21.8%
Colon	C18	179,380	48,940	27.3%
Liver	C22	67,760	22,310	32.9%
Pancreas	C25	19,470	5,240	26.9%
Women, aged ≥20 years				
All sites	C00–C96	1,394,820	269,970	19.4%
Liver	C22	33,290	10,080	30.3%
Pancreas	C25	17,490	6,470	37.0%
Both sexes, aged ≥20 years				
All sites	C00–C96	3,123,530	647,160	20.7%
Liver	C22	101,050	32,390	32.1%
Pancreas	C25	36,960	11,710	31.7%

[†]Estimated prevalence is expressed in absolute numbers. ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th Revision.

compared across cancer sites, diabetes prevalence was higher in patients with liver cancer among men (32.9%), and higher in patients with pancreatic cancer among women (37.0%).

Table 3 shows the age-specific prevalence of cancer among patients according to diabetes status in 2019. For both men and women, diabetes prevalence in cancer patients showed a rapid increase after age 45 years, with cancer patients aged ≥65 years having a diabetes prevalence of >20%.

Table 3 | Estimated prevalence of cancer[†] in patients with pre-existing diabetes by age group in Japan, 2019

Cancer site	ICD10	Cancer prevalence by age group														
		20–44 years			45–54 years			55–64 years			65–74 years			≥75 years		
		Overall prevalence of cancer	Patients with pre-existing diabetes	Percentage	Overall prevalence of cancer	Patients with pre-existing diabetes	Percentage	Overall prevalence of cancer	Patients with pre-existing diabetes	Percentage	Overall prevalence of cancer	Patients with pre-existing diabetes	Percentage	Overall prevalence of cancer	Patients with pre-existing diabetes	Percentage
Men, aged ≥20 years																
All sites	C00–C96	51,300	1,860	3.6%	97,440	10,200	10.5%	272,030	50,420	18.5%	640,810	148,760	23.2%	667,130	165,950	24.9%
Colon	C18	3,610	190	5.3%	9,680	1,310	13.5%	27,770	6,460	23.3%	65,220	18,660	28.6%	73,080	22,320	30.5%
Liver	C22	870	70	8.0%	3,610	630	17.5%	11,830	3,350	28.3%	25,020	8,610	34.4%	26,430	9,660	36.5%
Pancreas	C25	310	20	6.5%	1,220	160	13.1%	3,550	820	23.1%	7,880	2,250	28.6%	6,510	1,990	30.6%
Women, aged ≥20 years																
All sites	C00–C96	125,300	4,790	3.8%	181,430	17,820	9.8%	239,000	42,900	17.9%	383,630	88,680	23.1%	465,450	115,780	24.9%
Liver	C22	440	20	4.5%	650	90	13.8%	3,050	770	25.2%	10,910	3,320	30.4%	18,230	5,880	32.3%
Pancreas	C25	360	30	8.3%	930	180	19.4%	2,640	850	32.2%	5,990	2,320	38.7%	7,570	3,090	40.8%
Both sexes, aged ≥20 years																
All sites	C00–C96	176,600	6,650	3.8%	278,870	28,020	10.0%	511,030	93,320	18.3%	1,024,440	237,440	23.2%	1,132,580	281,730	24.9%
Liver	C22	1,310	90	6.9%	4,260	720	16.9%	14,880	4,120	27.7%	35,930	11,930	33.2%	44,660	15,540	34.8%
Pancreas	C25	670	50	7.5%	2,150	340	15.8%	6,190	1,670	27.0%	13,870	4,570	32.9%	14,080	5,080	36.1%

[†]Estimated prevalence is expressed in absolute numbers. ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th Revision.

DISCUSSION

The present study provides the first evidence of its kind on the incidence and prevalence of cancer in patients with pre-existing diabetes. Our results showed that approximately 647,160 Japanese adults are living with cancer and diabetes, which means that nearly 20% of cancer patients in fact have diabetes. Globally, the American Diabetes Association and American Cancer Society published a consensus report on the biological link between diabetes and cancer risk[3]; to date, however, no previous study has estimated the co-prevalence of the two morbidities. The present findings suggest that healthcare professionals should consider multimorbidity in patients with cancer in the aged population. As cancer patients with coexisting diabetes might have a comparatively poorer life prognosis than their non-diabetic counterparts[6–8], the increased recognition of multimorbidity might lead to better medical management and possibly improve the prognosis of such patients.

The major strength of the present study was its use of the best available data on diabetes prevalence, summary estimates of relative risks and cancer incidence, and survival, all of which are representative of the Japanese population. However, several limitations also warrant mention. First, because of a lack of data on diabetes prevalence by type of treatment that the patient had received, we were unable to consider differences by stage of diabetes. It is known that patients on glucose-lowering medications, such as exogenous insulin, show an elevated cancer risk than those on metformin therapy[19], which might lead to biased estimates. Second, we were unable to differentiate the overall survival of cancer patients with pre-existing diabetes from that of patients with no co-existing morbidity, because of a lack of information on medical history in the cancer registry data. Because it is well known that cancer patients with diabetes experience poorer prognosis than those without diabetes[6–8], the differences in overall survival might operate toward overestimation of the prevalence. Similarly, we were unable to consider other comorbidities that are commonly found in cancer patients, although it has been reported that patients with multiple co-existing diseases are likely to experience higher mortality than patients with a single co-existing disease[6–8]. As such, our use of overall survival of all cancer patients with and without multimorbidity might have overestimated the prevalence. Fourth, the present results show the 5-year prevalence of diabetes in cancer patients, which means that cancer patients beyond 5 years after diagnosis were not included in our estimation. Finally, our estimates do not include the prevalence of diabetes that occurred subsequent to cancer diagnosis and treatment. Considering these points together, the potential biases arising from these limitations might have attenuated towards null. Nonetheless, our estimates provide the first evidence on the number of cancer patients with pre-existing diabetes in Japan and permit national cancer control policy-making to effectively account for the impact of diabetes on cancer, and its implications on the treatment and survival of patients.

In conclusion, the present study found that approximately 20.7% of Japanese cancer patients with any cancer are living with diabetes in 2019. With the growing number of patients with diabetes, prevention and management of multimorbidity in cancer patients warrant further attention by health practitioners and policy-makers.

DISCLOSURE

The other authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix S1 | Supplemental Methods.