Prevalence of diabetes in Japanese patients with cancer

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INTRODUCTION
In recent years, associations between diabetes mellitus and cancer have been reported in multiple meta-analyses, including reports from Japan1–3. 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 decades4. For instance, cancer accounted for approximately 38% of overall causes of death in diabetes patients in Japan between 2001 and 20105. Cancer patients with diabetes are known to experience a poorer prognosis than those without diabetes6–8, 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, Japan9. 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 Project10.

Cancer cases were classified by sex, 5-year age group and cancer sites that are known to be associated with diabetes in Japanese individuals2 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 Project11,12. We obtained population projections for Japanese individuals with the medium-fertility and medium-mortality assumption from the National Institute of Population and Social Security Research13. 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 exposure2. 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 records15. 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

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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.
The majority of diabetes cases in both studies2,14. 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 diabetes16. 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 point17,18, 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 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%.

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

| Cancer site | ICD-10 | Incidence (overall) | Crude incidence rate |
|-------------|--------|---------------------|----------------------|
|             | No. cases |                     |                      |
| Men, aged ≥20 years | | | |
| All sites | C00–C96 | 564,530 | 1065.6 |
| Colon | C18 | 49,690 | 93.8 |
| Liver | C22 | 28,080 | 53.0 |
| Pancreas | C25 | 19,790 | 37.4 |
| Colon | C18 | 49,690 | 93.8 |
| Liver | C22 | 28,080 | 53.0 |
| Pancreas | C25 | 19,790 | 37.4 |
| Women, aged ≥20 years | | | |
| All sites | C00–C96 | 412,300 | 724.9 |
| Colon | C18 | 14,840 | 26.1 |
| Liver | C22 | 19,450 | 34.2 |
| Pancreas | C25 | 976,830 | 889.2 |
| Colon | C18 | 14,840 | 26.1 |
| Liver | C22 | 19,450 | 34.2 |
| Pancreas | C25 | 976,830 | 889.2 |
| Both sexes, aged ≥20 years | | | |
| All sites | C00–C96 | 976,830 | 889.2 |
| Colon | C18 | 179,380 | 489.4 |
| Liver | C22 | 67,760 | 22.3 |
| Pancreas | C25 | 19,470 | 52.4 |

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

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

| Cancer site | ICD-10 | Prevalent cancer cases (overall) | Prevalent cancer cases with pre-existing diabetes | Prevalence of pre-existing diabetes in cancer patients |
|-------------|--------|-------------------------------|---------------------------------------------|-----------------------------------------------|
|             | No. | Crude incidence rate |
| Men, aged ≥20 years | | | |
| All sites | C00–C96 | 1,728,710 | 377,190 | 21.8% |
| Colon | C18 | 179,380 | 489.4 | 27.3% |
| Liver | C22 | 67,760 | 22.3 | 32.9% |
| Pancreas | C25 | 19,470 | 52.4 | 26.9% |
| Women, aged ≥20 years | | | |
| All sites | C00–C96 | 1,394,820 | 269,970 | 19.4% |
| Colon | C18 | 33,290 | 10,080 | 30.3% |
| Liver | C22 | 17,490 | 6,470 | 37.0% |
| Pancreas | C25 | 3,123,530 | 647,160 | 20.7% |
| Both sexes, aged ≥20 years | | | |
| All sites | C00–C96 | 3,123,530 | 647,160 | 20.7% |
| Colon | C18 | 33,290 | 10,080 | 30.3% |
| Liver | C22 | 17,490 | 6,470 | 37.0% |
| Pancreas | C25 | 3,123,530 | 647,160 | 20.7% |

†Estimated prevalence is expressed in absolute numbers. ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th Revision.
TABLE 3 | Estimated prevalence of cancer* in patients with pre-existing diabetes by age group in Japan, 2019

| Cancer site | ICD-10 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 |
| Men, aged ≥20 years | All sites | 31,300 | 1,860 | 3.6% | 87,400 | 4,600 | 5.3% | 233,000 | 12,400 | 5.3% | 647,160 | 34,700 | 5.3% |
|             | Colon C18 | 31,300 | 1,860 | 3.6% | 87,400 | 4,600 | 5.3% | 233,000 | 12,400 | 5.3% | 647,160 | 34,700 | 5.3% |
|             | Liver C22 | 31,300 | 1,860 | 3.6% | 87,400 | 4,600 | 5.3% | 233,000 | 12,400 | 5.3% | 647,160 | 34,700 | 5.3% |
|             | Pancreas C25 | 31,300 | 1,860 | 3.6% | 87,400 | 4,600 | 5.3% | 233,000 | 12,400 | 5.3% | 647,160 | 34,700 | 5.3% |
| Women, aged ≥20 years | All sites | 31,300 | 1,860 | 3.6% | 87,400 | 4,600 | 5.3% | 233,000 | 12,400 | 5.3% | 647,160 | 34,700 | 5.3% |
|             | Colon C18 | 31,300 | 1,860 | 3.6% | 87,400 | 4,600 | 5.3% | 233,000 | 12,400 | 5.3% | 647,160 | 34,700 | 5.3% |
|             | Liver C22 | 31,300 | 1,860 | 3.6% | 87,400 | 4,600 | 5.3% | 233,000 | 12,400 | 5.3% | 647,160 | 34,700 | 5.3% |
|             | Pancreas C25 | 31,300 | 1,860 | 3.6% | 87,400 | 4,600 | 5.3% | 233,000 | 12,400 | 5.3% | 647,160 | 34,700 | 5.3% |
| Both sexes, aged ≥20 years | All sites | 31,300 | 1,860 | 3.6% | 87,400 | 4,600 | 5.3% | 233,000 | 12,400 | 5.3% | 647,160 | 34,700 | 5.3% |
|             | Colon C18 | 31,300 | 1,860 | 3.6% | 87,400 | 4,600 | 5.3% | 233,000 | 12,400 | 5.3% | 647,160 | 34,700 | 5.3% |
|             | Liver C22 | 31,300 | 1,860 | 3.6% | 87,400 | 4,600 | 5.3% | 233,000 | 12,400 | 5.3% | 647,160 | 34,700 | 5.3% |
|             | Pancreas C25 | 31,300 | 1,860 | 3.6% | 87,400 | 4,600 | 5.3% | 233,000 | 12,400 | 5.3% | 647,160 | 34,700 | 5.3% |

*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 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, 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, 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, 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. As such, our use of overall survival of all cancer patients with and without multimorbidity might have overestimated the prevalence.

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.

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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.