A prediction study for incidence rate of diabetes through 2-years health checkup data

ABSTRACT

Objective The number of people with diabetes in Japan has risen rapidly, which impose a heavy burden on both patients and society. It is therefore important to develop effective strategies for the prevention and management of type 2 diabetes based on individualized estimates of the trend of diabetes in the population. The aim of the present study was to survey the incidence of new-onset diabetes and identify the group of people who will require medical consultation due to hyperglycemia in the near future.

Methods 5,603 men and 4,420 women diagnosed as non-diabetes in the first year and who underwent health checkups in the next year were enrolled. The clinical parameters among the three groups (non-diabetes, subjects under treatment for diabetes, subjects needing medical consultation due to hyperglycemia) were compared.

Results The incidence of new-onset diabetes was 2.14%/year in men and 1.36%/year in women. It is considered a feature of our community that the majority of the subjects who newly developed diabetes were already on treatment at the second visit, probably during treatment for other lifestyle-related diseases. The subjects without treatment and those needing medical consultation due to hyperglycemia showed increased visceral obesity and exacerbation of glycemia.

Conclusion In order to improve diabetes care in the community, it is important to understand the characteristics of subjects who will require medical consultation due to hyperglycemia in the near future and to encourage medical consultation by a doctor explaining the results on the day of the health checkup.

Key words type 2 diabetes, incidence of new-onset diabetes, health checkup system, lifestyle-related disease, diabetes treatment

INTRODUCTION

The number of people with diabetes in Japan has risen from 3,166 thousand in 2014 to 3,289 thousand in 2017, at the highest rate ever. Diabetes is an asymptomatic disease in the early stage, and is often found by health checkups. Diabetes is associated with various complications and increased mortality, which imposes a heavy burden on both patients and society. Japan is already a super-aging society and the proportion of elderly people is steadily increasing year by year, which will lead to a great increase in the number of diabetic patients in the future.

In order to improve diabetes care in the community, it is important to develop effective strategies for the prevention and management of type 2 diabetes based on individualized estimates of the trend of diabetes in the population. Tokai University Hospital is located in Isehara city, western Kanagawa. Unlike the eastern Kanagawa area where people have a wider selection of hospitals, there are relatively few core hospitals in the western area. Therefore, residents in and around Isehara city tend to take health checkups repeatedly at Tokai University Hospital. Among a total of 13,766 people who underwent health checkups at Tokai University Hospital in fiscal 2014, 10780 people (78.3%) visited again in 2015, while a repeat rate of over 60% is usually considered reasonable. Such a high repeat rate and large numbers of examinees enable us to estimate the incidence of new-onset diabetes.

We have reported the characteristics of subjects requiring medical consultation due to hyperglycemia and the consultation rate after health checkups at Tokai University Hospital. The prevalence of diabetes was 9.0% for men and 4.2% for women. We then focused on the incidence of new-onset diabetes in our population. Since the prevalence of the disease is determined by incidence and life expectancy, the higher the incidence of new-onset diabetes, the higher the prevalence of diabetes in the population. In this study, we surveyed the incidence of new-onset diabetes using those subjects who were diagnosed as non-diabetes in the first year and who underwent health checkups in the next year. The aim of the study was to survey the incidence of new-onset diabetes and to identify the group of people who will require medical consultation due to hyperglycemia in the near future.
SUBJECTS AND METHODS

1. Subjects
Among 6,157 men and 4,623 women who underwent health checkups successively in fiscal 2014 and 2015, 5,603 men and 4,420 women diagnosed as non-diabetes in 2014 were enrolled. The medical history was obtained using a self-administered questionnaire, asking whether the individual had been on treatment for diabetes, hypertension and/or dyslipidemia. If the subjects without diabetes treatment showed fasting glucose ≥126 mg/dL and HbA1c ≥6.5%, they were considered to need medical consultation due to hyperglycemia. The subjects were categorized at the second visit in 2015 into the following groups: non-diabetes (NonDM), subjects under treatment for diabetes (TxDM), or subjects needing medical consultation due to hyperglycemia (HyperG) (Figure 1).

2. Methods and statistics
All measurements were included in the routine health checkup examinations. Data is expressed as mean ± standard deviation (SD) or standard error (SE). SPSS Statistics (Version 22.0; SPSS Inc.) was used for the statistical analyses. Comparisons of the clinical parameters (age, body weight, BMI, waist circumference, systolic blood pressure, LDL cholesterol (LDL-C), HDL cholesterol (HDL-C), triglycerides, fasting glucose and HbA1c) among the three groups were made using analysis of variance (ANOVA) followed by Scheffé’s multiple comparison test. All p-values were two-tailed, and p < 0.05 was considered significant.

3. Ethical considerations
Participants were recruited by the opt-out method. All of the data including medical history, anthropometric measurements and blood tests were collected from health records at Tokai University Hospital. Anonymized data were used for the analysis by separate researchers at Tokai University Tokyo Hospital. The privacy of participants was completely protected by unlinkable anonymization. This study was approved by the Ethics Committee of Tokai University (17R-221) and was conducted in accordance with the Declaration of Helsinki.

RESULTS
The average age ± standard deviation of the subjects was 58.6 ± 10.9 for men and 57.7 ± 10.5 for women. Incidence of new-onset diabetes is shown in Figure 2. In men, those who
remained non-diabetes (NonDM) at the second visit were 5,483 (97.9%). Eighty-nine men (1.59%) were under diabetes treatment (TxDM) and 31 men (0.55%) were considered to need medical consultation due to hyperglycemia (HyperG); thus, 120 men were recognized as new-onset diabetes (2.14%). In women, NonDM were 4,360 (98.6%), TxDM were 49 (1.11%) and HyperG were 11 (0.25%). The rate of new-onset diabetes in women was determined as 1.36%.

The clinical parameters (age, body weight, BMI, waist circumference, systolic blood pressure, LDL-C, HDL-C, triglycerides, fasting glucose and HbA1c) among the three groups were compared. The TxDM group was significantly older than the NonDM group in both men and women (Tables 1, 2). In men, compared with NonDM, the HyperG group showed significantly higher body weight, BMI, waist circumference, systolic blood pressure and triglycerides, and significantly lower HDL-C, both in 2014 and 2015 (Table 1). The TxDM men showed significantly higher BMI and waist circumference than NonDM in the second year (Table 1). In women, the HyperG group showed significantly higher BMI, waist circumference and triglycerides, and significantly lower HDL-C, although there was no significant difference in body weight (Table 2). In both men and women, levels of fasting glucose and HbA1c became significantly higher in the order of NonDM, TxDM to HyperG (Table 1, 2). Although fasting glucose and HbA1c remained almost the same in the TxDM group, those in the HyperG group worsened in the next year (Tables 1, 2).

Next, changes in clinical parameters were compared among the three groups. The HyperG group showed the largest changes in body weight, BMI and waist circumference, and the difference in waist circumference between the NonDM group and the HyperG group was statistically significant in men (Figure 3). With regard to fasting glucose and HbA1c, there was no difference between NonDM and TxDM in men (Figure 4). The differences in fasting glucose and HbA1c changes between NonDM and HyperG were 15.4 mg/dL and 0.64%, respectively. In women, the HyperG group showed the largest changes in body weight, BMI and waist circumference, although the differences were not significant compared to the other groups (Figure 5). The changes in fasting glucose and HbA1c between NonDM and HyperG were 18.0 mg/dL and 0.52%, which were statistically significant (Figure 6).

### Table 1  Comparison of the clinical parameters among the three groups in the first year (2014) and the second year (2015) in men.

| Parameter                  | First Year | Second Year |
|----------------------------|------------|-------------|
| **Age**                   |            |             |
| NonDM                     | 58.5 ± 10.9| ** vs NonDM |
| TxDM                      | 64.0 ± 9.9 | ** vs NonDM |
| HyperG                    | 61.3 ± 9.8 |             |
| **Body weight (kg)**      |            |             |
| NonDM                     | 66.6 ± 9.8 | 66.6 ± 9.9  |
| TxDM                      | 67.9 ± 12.0| 68.0 ± 12.0 |
| HyperG                    | 71.0 ± 12.9| ** vs NonDM |
|                           |            | 71.7 ± 13.3 |
| **BMI**                   |            |             |
| NonDM                     | 23.3 ± 2.9 | 23.4 ± 3.0  |
| TxDM                      | 24.2 ± 3.5 | ** vs NonDM |
| HyperG                    | 24.4 ± 3.4 |             |
|                           |            | ** vs NonDM |
| **Waist circumference (cm)**|          |             |
| NonDM                     | 81.9 ± 7.6 | 82.5 ± 7.7  |
| TxDM                      | 84.6 ± 8.2 | 85.2 ± 8.7  |
| HyperG                    | 84.9 ± 8.4 |             |
|                           |            | ** vs NonDM |
| **Systolic BP (mmHg)**    |            |             |
| NonDM                     | 119.5 ± 16.5| 123.4 ± 16.9|
| TxDM                      | 123.4 ± 16.6| 127.2 ± 18.8|
| HyperG                    | 128.6 ± 14.7| ** vs NonDM |
|                           |            | 132.5 ± 20.3| ** vs NonDM |
| **LDL-C (mg/dL)**         |            |             |
| NonDM                     | 127.1 ± 29.0| 126.3 ± 29.7|
| TxDM                      | 117.9 ± 28.9| 116.7 ± 33.0|
| HyperG                    | 137.6 ± 31.1| ** vs TxDM  |
|                           |            | 135.8 ± 42.8| ** vs TxDM  |
| **HDL-C (mg/dL)**         |            |             |
| NonDM                     | 62.3 ± 15.8| 61.5 ± 15.7 |
| TxDM                      | 61.7 ± 16.3| 61.4 ± 17.6 |
| HyperG                    | 56.0 ± 16.1|             |
|                           |            | ** vs NonDM |
| **Triglycerides (%)**     |            |             |
| NonDM                     | 118.4 ± 79.0| 115.9 ± 73.8|
| TxDM                      | 128.1 ± 100.2| 120.9 ± 74.0|
| HyperG                    | 163.4 ± 100.1| ** vs NonDM |
|                           |            | 169.6 ± 113.9| ** vs NonDM |
| **Fasting glucose (mg/dL)**|         |             |
| NonDM                     | 99.5 ± 9.4 | 99.7 ± 9.8  |
| TxDM                      | 117.7 ± 20.2| ** vs NonDM |
| HyperG                    | 126.0 ± 21.7| ** vs NonDM |
|                           |            | ** vs NonDM |
| **HbA1c (%)**             |            |             |
| NonDM                     | 5.5 ± 0.3  | 5.5 ± 0.3   |
| TxDM                      | 6.1 ± 0.4  | ** vs NonDM |
| HyperG                    | 6.2 ± 0.2  | ** vs NonDM |

Mean ± SD. *p<0.05, **p<0.01.
Table 2  Comparison of the clinical parameters among the three groups in the first year (2014) and the second year (2015) in women.

|                  | First year | Second year |
|------------------|------------|-------------|
|                  | NonDM      | TxDM        | HyperG       | NonDM      | TxDM        | HyperG       | NonDM      | TxDM        | HyperG       |
| **Age** (years)  | 57.6 ± 10.5 | 63.1 ± 7.5  | ** vs NonDM  | 60.4 ± 10.0 |             |             | 63.1 ± 7.5  | 65.9 ± 10.4 | ** vs NonDM  |
| **Body weight**  |            |             |              | 53.3 ± 8.4  | 54.4 ± 10.9 | 57.5 ± 13.6 |            | 54.4 ± 10.9 | 56.1 ± 14.2  |
| (kg)             | NonDM      | TxDM        | HyperG       | NonDM      | TxDM        | HyperG       | NonDM      | TxDM        | HyperG       |
| **BMI** (kg/m²)  |            |             |              | 21.9 ± 3.2  | 23.3 ± 4.3  | 24.2 ± 5.4  | * vs NonDM  | 22.0 ± 3.3  | 23.4 ± 4.9  |
| **Waist circumference** (cm) | NonDM      | TxDM        | HyperG       | NonDM      | TxDM        | HyperG       | NonDM      | TxDM        | HyperG       |
| Body weight      |            |             |              | 77.3 ± 8.5  | 80.3 ± 10.8 | 83.2 ± 11.1 | * vs NonDM  | 77.4 ± 8.6  | 80.7 ± 11.9 | * vs NonDM  |
| **Systolic BP**  |            |             |              | 114.8 ± 17.8| 120.1 ± 20.1| 115.9 ± 17.6|            | 117.9 ± 18.5| 123.8 ± 18.4| * vs NonDM  |
| (mmHg)           | NonDM      | TxDM        | HyperG       | NonDM      | TxDM        | HyperG       | NonDM      | TxDM        | HyperG       |
| **LDL-C** (mg/dL) |            |             |              | 127.7 ± 28.8| 129.4 ± 28.6| 122.7 ± 36.6|            | 126.7 ± 28.9| 124.9 ± 26.2| * vs NonDM  |
| **HDL-C** (mg/dL) |            |             |              | 73.9 ± 17.0  | 71.7 ± 17.5  | 60.8 ± 14.1  | ** vs NonDM | 72.7 ± 16.8  | 69.1 ± 16.8  | * vs NonDM  |
| **Triglycerides** (%) | NonDM      | TxDM        | HyperG       | NonDM      | TxDM        | HyperG       | NonDM      | TxDM        | HyperG       |
| BMI              |            |             | 68.3 ± 41.1  |            | 96.1 ± 52.7  | 126.7 ± 95.1 | * vs NonDM  | 87.1 ± 42.8  | 101.8 ± 59.2 | ** vs NonDM |
| **Waist circumference** (cm) | NonDM      | TxDM        | HyperG       | NonDM      | TxDM        | HyperG       | NonDM      | TxDM        | HyperG       |
| Triglycerides    |            |             |              | 95.0 ± 9.3  | 108.1 ± 13.1 | 124.2 ± 6.8  | ** vs NonDM | 95.3 ± 9.5  | 117.0 ± 34.0 | ** vs NonDM |
| **Fasting glucose** (mg/dL) | NonDM      | TxDM        | HyperG       | NonDM      | TxDM        | HyperG       | NonDM      | TxDM        | HyperG       |
| **HbA1c** (%)    |            |             | 5.5 ± 0.3    |            | 6.0 ± 0.4    | 6.5 ± 0.5    | ** vs NonDM | 5.5 ± 0.3    | 6.1 ± 0.9    | ** vs NonDM |

Mean ± SD. * p<0.05, ** p<0.01. Systolic BP, systolic blood pressure; LDL-C, LDL cholesterol; HDL-C, HDL cholesterol.

Fig. 3  Changes in body weight, BMI and waist circumference in men.
* p<0.05.
Fig. 4  Glycemic changes in men.

** p<0.01.

Fig. 5  Changes in body weight, BMI and waist circumference in women.

Fig. 6  Glycemic changes in women.

** p<0.01.
The distribution of the treatment status for hypertension and dyslipidemia is shown in Table 3. The percentages of the subjects under treatment were higher in the TxDM group in both men and women. Development of diabetes might be detected and treated before the next health checkup during treatment for other lifestyle-related diseases by doctors.

**DISCUSSION**

In the present study, we surveyed the incidence of new-onset diabetes using non-diabetes subjects who underwent health checkups for two successive years, and found that it was 2.14%/year in men and 1.36%/year in women. The subjects without diabetes treatment and needing medical consultation due to hyperglycemia (HyperG) showed increased visceral obesity and exacerbation of glycemic status. Although the majority of the subjects who newly developed diabetes were already on treatment at the second visit, it was found that other subjects required medical consultation due to hyperglycemia.

The incidence of new-onset diabetes varies depending on factors such as participants' background and diagnosis criteria. The risk of diabetes is significantly higher among Asians than among whites. Therefore, we compared the incidence of new-onset diabetes with that reported in previous Japanese studies. The National Health and Nutrition Survey of Japan only used a diabetes with that reported in previous Japanese studies. The other methods. According to the Hisayama Study, one of the most famous studies using community-dwelling people, the subjects aged 40–69 who had been diagnosed as non-diabetes in 1988 underwent the 75 g OGTT after 5 years in 1993. As a result, the incidence of new-onset diabetes was determined to be 1.28%/year for men and 0.57%/year for women. The Hisayama Study is considered of great value because of the high participation rate of the whole population and the diagnosis of diabetes by the OGTT. One report states that the five-year incidence of diabetes was 4% (0.8%/year) by a study conducted at a single health management center in central Tokyo. Another study using subjects who underwent health screening at the Niigata Association of Occupational Health reported that 4.46% of the subjects developed diabetes in 6 years (0.74%/year). Compared with community-dwelling people with a low risk of lifestyle-related diseases, the incidence of new-onset diabetes in our study subjects seems to be slightly higher.

Diabetes, hypertension and dyslipidemia are well-known lifestyle-related diseases, which sometimes overlap in one individual. As it has been shown that some drugs for hypertension and dyslipidemia can affect glucose homeostasis, recent large trials of these drugs often include the incidence of new-onset diabetes as one of the endpoints. The antihypertensive drugs that block the renin-angiotensin system are associated with lower incidence of new-onset diabetes on account of the insulin sensitizing property than other antihypertensive agents. Lipid lowering drugs, especially statins, are associated with higher incidence of new-onset diabetes, although the benefits of treating hyperlipidemia far exceed the risk of diabetes. According to reports using Japanese hypertensive patients, the incidence of new-onset diabetes was 0.8–0.9%/year in patients treated with candesartan (angiotensin receptor blocker) and 1.1–1.3%/year in those with amlodipine (calcium channel blocker). Furthermore, new-onset diabetes occurred more frequently up to 2.3%/year in those treated with amlodipine as BMI increased. As to statins, the incidence of new-onset diabetes was reported to be 12.5%/year in statin users whereas it was 2.3% in non-users. Among various statins, high-potency statins significantly increased the risk of new-onset diabetes compared with low-potency ones. These studies show that the incidence of new-onset diabetes is higher in

| Table 3 The distribution of the treatment status for hypertension and dyslipidemia in the first year (2014) and the second year (2015). |
|-----------------------------------------------|
| **First year** | **Men** | **Women** | **Second year** | **Men** | **Women** |
| Hypertension | NonDM | 1,216 | 22.2% | 678 | 15.6% | NonDM | 1,124 | 20.5% | 663 | 15.2% |
| | TxDM | 30 | 33.7% | 12 | 24.5% | | | 27 | 30.3% | 19 | 38.8% |
| | HyperG | 7 | 22.6% | 3 | 27.3% | | | 7 | 22.6% | 3 | 27.3% |
| Dyslipidemia | NonDM | 235 | 4.3% | 254 | 5.8% | NonDM | 353 | 6.4% | 348 | 8% |
| | TxDM | 7 | 7.9% | 3 | 6.1% | | | 14 | 15.7% | 7 | 14.3% |
| | HyperG | 1 | 3.2% | 0 | 0.0% | | | 4 | 12.9% | 1 | 9.1% |
subjects with other lifestyle-related diseases than in community-dwelling people. Since our study contains a certain number of people with lifestyle-related diseases, who are at higher risk for type 2 diabetes, the incidence of new-onset diabetes in this study might become close to those in other studies.

Another interesting finding is that the majority of the subjects who newly developed diabetes were already on treatment at the second visit, probably during treatment for other lifestyle-related diseases. TxDM people were older in age and showed higher treatment rates for hypertension and dyslipidemia compared with the NonDM or HyperG groups. It is particularly important to detect and treat diabetes as early as possible to stop it from worsening. Owing to earlier treatment, the glycemic status of the TxDM group prevented deterioration of diabetes. On the other hand, the HyperG group showed increased obesity and worse glycemic status in the next year, and it was reported that high-normal BMI occurred before or at the onset of diabetes. Still, it is not too late to start treatment for HyperG people, and we must do our best to encourage medical consultation through doctors explaining the results on the day of the health checkup.

Our study has some limitations. Two-year observation period may not be long enough to make a definite conclusion. We might have underestimated the incidence of diabetes, because the diagnosis of diabetes was made without the OGTT. Also, the treatment status for hypertension and dyslipidemia might be underestimated because the participants were not vigorously tested for the presence of the diseases; rather, we relied on the self-reported history (recall bias). Our subjects, who undergo health checkups at Tokai University Hospital, might be more health-conscious than those who do not take such examinations, and we cannot deny the possibility of selection bias.

In conclusion, the present study shows that the incidence of new-onset diabetes was 2.14%/year in men and 1.36%/year in women, and also shows that the people with lifestyle-related diseases are at higher risk for type 2 diabetes and are more likely to require medical consultation due to hyperglycemia in the near future. It is considered a feature of our community that the majority of the subjects who newly developed diabetes were already on treatment at the second visit, probably during treatment for other lifestyle-related diseases. In order to improve diabetes care in the community, it is important to understand the characteristics of subjects who will require medical consultation due to hyperglycemia in the near future and to do our best to encourage medical consultation through doctors explaining the results on the day of the health checkup.

ACKNOWLEDGEMENTS

The authors state that they have no conflicts of interest (COI).

This study was supported by scientific grant aid from Japan Society of Health Evaluation and Promotion in 2015.

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