1,000 WoARDrdsS **目標**　　**現在~~1 2 5 2~~** ~~WARDS~~1,252 Words　Title～Conclusion

Title

Undiagnosed diabetes has worse profiles for cardiovascular and metabolic markers than known diabetes

Summary

We compared cardiovascular and metabolic markers between undiagnosed and known diabetes. We used a dataset of 34,282 subjects who voluntarily attended at health check-up. Subjects with undiagnosed diabetes had worse profiles of these markers than those with known diabetes. Undiagnosed diabetes should be recognized as a condition with these risks.

Introduction

In type 2 diabetes, early detection and intervention is necessary to prevent complications such as cardiovascular disease.

It has been reported, however, that the prevalence rate of 'undiagnosed' diabetes patients is an increasingly important public health issue[1]. Undiagnosed diabetes is defined as unknowingly having an elevated glucose level that meets the definition of diabetes.

For example, there are an estimated 7.0 million persons with undiagnosed diabetes in the U.S. (2.2% of the whole population) [ref]. Samely, it has been reported that the prevalence of undiagnosed diabetes in the adult population of Manitoba was 2.2% in a Canadian study. If patients with diabetes are not diagnosed and are untreated, they may not have a chance to prevent future diabetes-related complications. Accordingly, risk factors or markers relevant to such complication may ~~remaine~~remain~~d~~ to be high in individuals of undiagnosed

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コメント [Ci4]: 1. . Young TK, Mustard CA. Undiagnosed diabetes: does it matter? CMAJ Canadian Medical Association Journal 2001;164:24-8.

BACKGROUND: The 1998 Canadian clinical practice guidelines for the management of diabetes lowered the cutoff point for diagnosing diabetes mellitus from a fasting plasma glucose (FPG) level of 7.8 to 7.0 mmol/L. We studied the prevalence and clinical outcomes of undiagnosed and diagnosed diabetes within specific ranges of FPG among a cohort of subjects recruited in 1990. METHODS: In 1990 a representative sample of 2792 adult residents of Manitoba participated in the Manitoba Heart Health Survey, which included measurement of FPG and a question about each participant's past history of diabetes. Individuals who would now be classified as having undiagnosed diabetes under the new criteria were not considered as such in 1990. Through data linkage with the provincial health care utilization database, the use of health care by these individuals was tracked and compared with that of individuals whose diabetes had been diagnosed and with that of normoglycemic individuals over an 8-year period subsequent to the survey. RESULTS: The prevalence of undiagnosed diabetes in the adult population of Manitoba was 2.2%. Undiagnosed cases accounted for about one-third of all diabetes cases. Individuals with undiagnosed diabetes had an unfavourable lipid profile and higher blood pressure and obesity indices than normoglycemic individuals. Individuals who satisfied the new criteria for diabetes but remained undiagnosed had an additional 1.35 physician visits per year (95% confidence interval [95% CI] 0.93-1.96) and were more likely to be admitted to hospital at least once (odds ratio 1.23, 95% CI 0.40-3.79), compared with normoglycemic individuals. INTERPRETATION: Undiagnosed ... [1]

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diabetes.

In our previous study[2], we conducted just a simple comparison between undiagnosed and diagnosed diabetes, which revealed that some risk indicators for lifestyle-related diseases were higher in subjects with undiagnosed diabetes than those with known diabetes. Therefore, in this study we compared cardiovascular and metabolic markers between ~~subujects~~subjects with undiagnosed and known diabetes, adjusting for major confounders such as age, sex and body mass index in a large Japanese population.

Methods

We used a dataset derived from the health screening program performed by the Yuport Medical Checkup Center in Tokyo from April 1998 to 2006. The details of this program has been reported elsewhere[3,4,5]. In total 97,585 persons (aged 25-64 years) participated in this health check-up. For repeat participants, the first-visit data was used for the study. The finally dataset comprised 34,282 persons for the analysis. According to the diagnostic criteria of diabetes by the Japan Diabetes Society[6,~~7~~] and American Diabetes Association~~(ref)~~ [7]. We distributed these subjects into four separate groups; normal fasting plasma (NFG, <5.6 mmol/l) , impaired fasting glucose (IFG, 5.6-6.9 mmol/l), known diabetes and undiagnosed diabetes(Figure 1). Known diabetes was identified when the participants reported irrespective of their fasting plasma glucose (FPG) levels. Undiagnosed diabetes was defined when FPG >= 7.0 mmol/l and the subjects did not report to have diabetes.

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A blood sample was obtained after overnight fasting and measured at the Center's

laboratory. For the measurements of fasting plasma glucose and hemoglobin A1c levels, a Toshiba TBA-40FR Autoanalyzer (Toshiba Medical Systems, Tokyo, Japan) was used. Plasma glucose level was measured via the hexokinase-G6PD method (Denka Seiken, Niigata, Japan) with an inter-assay coefficient of covariation (CV) of 3.0% or less. HbA1c level was measured by the latex immuno-agglutinin method (Determiner hemoglobin A1c, Kyowa Medex, Tokyo, Japan), with an inter-assay CV of 1.7-2.1%, which was comparable to that of plasma glucose and aligned to the Japan Diabetes Society (JDS) assigned values. The JDS value of hemoglobin A1c were converted into NGSP units in this study by adding 0.4%{Seino, 2010 #2471}.

Other blood tests included serum levels of lipids and hepatic enzymes, and white blood cell count. Triglycerides, and total and HDL cholesterol were measured using enzymatic methods (reagents supplied by Daiichi Pure Chemicals, Tokyo, Japan). Aspartate aminotransferase and alanine aminotransferase were measured using enzymatic methods (reagents supplied by Denka Seiken, Niigata, Japan), as were gamma-glutamyltranspeptidase levels (Wako Junyaku, Osaka, Japan). White blood cell count was measured using the DC detection method (reagents supplied by Sysmex, Kobe, Japan).

All the evaluation procedures were performed in the same manner, both during the baseline and follow-up periods, including blood measurements. Height and weight were measured to calculate body mass index (BMI), which was defined as weight divided by height squared (kg/m2). All analyses were performed using the SAS9.2 for Windows. Analysis of variance (ANOVA) tests adjusted for age and sex were used to compare the mean values at baseline among the four categorized groups according to FPG and HbA1c levels. Because of their skewed distributions, serum levels of triglycerides, hepatic enzymes and white blood cell count were log-transformed for statistical analysis. For the four group comparisons, a p value of 0.005 was used to determine statistical significance since a Bonferroni correction was needed. A cut-off p value of 0.05 was used for all the other statistical tests. A cut-off p-value <0.05 was used to determine statistical significance.

In accordance with the Private Information Protection Law, information that might identify subjects was kept private by the Center. Informed consent for anonymous participation in epidemiological research was obtained at every check-up.

Results

From the 34,282 study ~~sample~~subjects, we classified 23,491(68.5%), 8,786(25.6%) (795 (2.3%) and 1089 (3.2~~1~~%) persons with NFG, IFG, known and undiagnosed diabetes, respectively ~~(Table 1)~~. Among the 795 with known diabetes, 493 (54.0%) met the new criteria for diabetes.

Table 1 shows the comparisons of variables among the four groups, and between known and undiagnosed diabetes. In simple comparisons, age, BMI and the proportion of male were likely to increase across the four groups. In age, sex and BMI -adjusted comparisons of variables ~~at baseline~~, systolic/diastolic blood pressures, ~~BMI,~~ triglycerides, total cholesterol, aspartate aminotransferase, alanine aminotransferase, and gamma-glutamyltranspeptidase~~, and white blood cell count~~ were more likely to increase across the four subject groups. Conversely, HDL cholesterol was likely to decrease across the four subject groups.

（上下のパラグラフの表現を再度合わしてください。グループ数が違うだけで同じ比較です。下に合わしたらいいところが多いです。）

~~Among the 795 with known diabetes, 493 (54.0%) met the new criteria for diabetes.~~ There was no significant difference in sex distribution between the two groups. In age, sex and BMI -adjusted comparisons of variables ~~After controlling for age, sex and BMI~~, subjects with undiagnosed diabetes had higher FPG, HbA1c, body mass index, systolic/diastolic blood pressures, serum levels of liver enzymes (alanine aminotransferase and gamma-glutamyl transpeptidase) and serum lipids (total cholesterol and triglycerides) than those with known diabetes(Table1).

Accordingly, the prevalence of an abnormal range of these markers was higher in subjects with undiagnosed diabetes than those with known diabetes (Figure1).

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コメント [Ci8]: 要チェック、HbA1c と Age も

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Discussion

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This study indicated that cardiovascular and metabolic markers such as blood pressure, serum lipids, and liver enzymes are higher in individuals with undiagnosed than those with known diabetes, even after adjusting for major confounders.

Some studies have reported information concerning undiagnosed diabetes. For example, among those 70-years-old and over, undiagnosed diabetes patients who had heart disease show increased mortality rates in comparison with hospitalized diabetes patients who have the same condition [8]. The prevalence of chronic kidney disease in undiagnosed diabetes patients was higher than these with clinical diabetes [9]. However, few studies have examined cardiovascular and metabolic markers in undiagnosed diabetes. Comparing with our previous report[2], we newly examined metabolic markers such as liver enzymes.

The results of our study may have clinical relevance in diabetes prevention. When considering interventions to change patients' lifestyle such as body weight and blood pressure reduction , it may be beneficial to focus on individuals with undiagnosed diabetes since they might remain at worse profiles than those with unknown diabetes.

Some issues deserve to be mentioned as possible limitations. First, Since the study subjects participated on a voluntary basis, they may be healthier than the general population, causing a selection bias. Second, we used a single fasting plasma glucose to diagnose diabetes, and did not utilize other diagnostic methods such as an oral glucose tolerance test. However, it is considered acceptable to base our analysis upon a single fasting glucose measurement for epidemiological estimates of diabetes prevalence and incidence [10, 11],. Third, This study was a cross-sectional study. Therefore, the factor that causes undiagnosed diabetes is unknown. Diabetes at the time of diagnosis should have therapeutic intervention and should not be left as undiagnosed. Thus, a cross-sectional design is appropriate for this study.

In summary, subjects with undiagnosed diabetes had worse profiles of cardiovascular and metabolic predictors than those with known diabetes. Undiagnosed diabetes should be

recognized as a condition with these risks.

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Declaration of Competing Interests

Nothing to declare

Acknowledgments

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Reference

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［5］印刷中 Diabet Med. 2011 Dec 12. doi: 10.1111/j.1464-5491.2011.03536.x. [Epub ahead of print]

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A , Bruguera J , Cano-Perez JF　Prevalence of chronic kidney disease in US adults with undiagnosed diabetes or prediabetes.ClinJAmSoc Nephrol2010;5:673-82

［10］Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 1997; 20: 1183-1197.

［11］Report of the Japan Diabetes Society Committee on the Classification and Diagnostic Criteria of Diabetes Mellitus [in Japanese]. J Japan Diab Soc 1999; 42: 385-404.

Table1. Subject Characteristics

Characteristics	NFG	IFG	Known Diabetes	Undiagnosed Diabetes	*P* value adjusted by sex, age and BMI	
	n＝23,491	n＝8,786	n＝916	n＝1,089	4 groups	2groups Known vs. Undiagnosed
Fasting plasma glucose (mmol/l)	5.0±0.32	5.9±0.3	8.0±2.4	8.9±2.3	<.0001	<.0001
HbA1c (%)	4.8±0.4	5.2±0.5	6.9±1.6	7.1±1.8	<.0001	<.0001
Age (years)	49.8 ±13.3	55.3±11.6	60.3±8.0	58.6±10.4	<.0001	<.0001
Male sex, n (%)	9879〈42.1)	5779(65.8)	650(71.3)	781(71.7)	<.0001	<.0001
Body Mass Index (kg/m^2)	22.3±2.9	24.0±3.1	23.9±3.1	24.9±3.5	<.0001	<.0001
Systolic blood pressure (mmHg)	120±17	131±18	131±17	137±19	<.0001	<.0001
Diastolic blood pressure (mmHg)	73±11	80±11	78±10	83±11	<.0001	<.0001
Triglycerides (mmol/l)	0.93(0.67-1.35)	1.24(0.89-1.79)	1.33(0.92-1.85)	1.54(1.07-2.30)	<.0001	<.0001
Total cholesterol (mmol/l)	199.6±35.1	208.1±35.4	202.0±34.4	214.0±38.1	<.0001	<.0001
HDL cholesterol (mmol/l)	59.1±14.8	54.5±14.0	52.3±13.8	51.1±12.7	<.0001	<.0001
Aspartate aminotransferase (U/l)	20.0(17-24)	22.0(19-27)	22(18-27)	24(19-31)	<.0001	<.0001
Alanine aminotransferase (U/l)	17(13-23)	21(16-32)	22(16-32)	26(19-39)	<.0001	<.0001
γ -Glutamyltranspeptidase (U/l)	17(11-28)	26(16-47)	25(15-46)	38(23-72)	<.0001	<.0001
Uric acid (mg/dl)	5.1±1.3	5.8±1.4	5.4±1.3	5.6±1.4	<.0001	<.0001

Data are expressed as mean ± SD, median (25th percentile, 75th percentile) or number (%). Probability values are for comparison of cartegories of means (analysis of variance for age and body mass index and analysis of variance adjusted by sex, age and body mass index for the other variables) or percentages (chi-square test). For comparison of means, of triglycerides, aspartate aminotransferase, alanine

aminotransferase and γ-glutamyltranspeptidase were log-transformed for their skewed distributions.

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Figure 2. Frequencies of subjects with worse profiles of cardiovascular and metabolic markers per four categories

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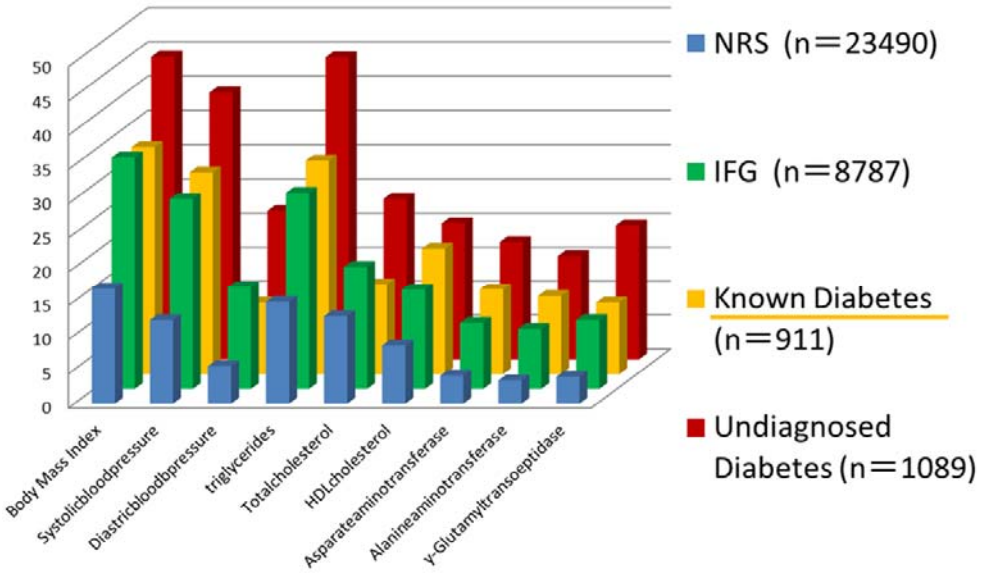

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As such, these results may have clinical relevance in diabetes prevention. We examined cardiovascular and metabolic risk factors in individuals with undiagnosed (unknown and newly diagnosed) diabetes using current diagnostic criteria to compare to individuals with

known diabetes.

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When considering interventions such as changing patients' lifestyle, thus, it may be beneficial to focus on undiagnosed diabetes.

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1. Young TK, Mustard CA. Undiagnosed diabetes: does it matter? CMAJ Canadian Medical Association Journal 2001;164:24-8.

BACKGROUND: The 1998 Canadian clinical practice guidelines for the management of diabetes lowered the cutoff point for diagnosing diabetes mellitus from a fasting plasma glucose (FPG) level of 7.8 to 7.0 mmol/L. We studied the prevalence and clinical outcomes of undiagnosed and diagnosed diabetes within specific ranges of FPG among a cohort of subjects recruited in 1990. METHODS: In 1990 a representative sample of 2792 adult residents of Manitoba participated in the Manitoba Heart Health Survey, which included measurement of FPG and a question about each participant's past history of diabetes. Individuals who would now be classified as having undiagnosed diabetes under the new criteria were not considered as such in 1990. Through data linkage with the provincial health care utilization database, the use of health care by these individuals was tracked and compared with that of individuals whose diabetes had been diagnosed and with that of normoglycemic individuals over an 8-year period subsequent to the survey. RESULTS: The prevalence of undiagnosed diabetes in the adult population of Manitoba was 2.2%. Undiagnosed cases accounted for about one-third of all diabetes cases. Individuals with undiagnosed diabetes had an unfavourable lipid profile and higher blood pressure and obesity indices than normoglycemic individuals. Individuals who satisfied the new criteria for diabetes but remained undiagnosed had an additional 1.35 physician visits per year (95% confidence interval [95% CI] 0.93-1.96) and were more likely to be admitted to hospital at least once (odds ratio 1.23, 95% CI 0.40-3.79), compared with normoglycemic individuals. INTERPRETATION: Undiagnosed cases represent the unseen but clinically important burden of diabetes, with significant concurrent metabolic derangements and a long-term impact on health care use.