Title
Undiagnosed diabetes has poorer 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 poorer profiles of these markers than those with known diabetes. Undiagnosed diabetes should be recognized as a condition with these risks.

コメント [F1]: Summary OK

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. 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]. 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 remained to be high in individuals of undiagnosed diabetes.

コメント [F2]: Yiduo Zhang, Timothy M. Dall, Sarah E. Mann, Yaozhu Chen, Jaana Martin, Victoria Moore, Alan Baldwin, Viviana A. Reidel, and William W. Quick. Population Health Management. April 2009, 12(2): 95-101.

コメント [F3]: When considering interventions such as changing patients' lifestyle, thus, it may be beneficial to focus on undiagnosed diabetes.
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In our previous study[ref], 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 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. –In total 97,585 persons (aged 25-64 years) participated in this health check-up. For repeat participants, 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(ref) and American Diabetes Association(ref) 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.

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,

コメント [F4]: Inoue K, Matsumoto M, Akimoto K. Fasting plasma glucose and HbA_{1c} as risk factors for Type 2 diabetes. Diabet Med. 2008;25(10):1157-63.
Inoue K, Matsumoto M, Akimoto K. The threshold for definition of impaired fasting glucose in a Japanese population. Diabet Med. 2009;26(11):1175-8.
Diabet Med. 2011 Dec 12. doi: 10.1111/j.1464-5491.2011.03536.x. [Epub ahead of print]

コメント [F5]: In follow-up evaluations, diabetes was defined as a follow-up FPG level >=7.0 mmol/l, in accordance with the ADA, JDA criteria [6, 7] or as a diagnosis of diabetes by a physician during the follow-up period.
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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 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 study sample, we classified 23,491(68.5%), 8,786(25.6%) (~~retrieved~~ 795 (2.3%) and 1089 (3.1%) persons with NFG, IFG, known and undiagnosed diabetes, respectively (Table 1). In age and sex-adjusted comparisons of variables at baseline, blood pressure, BMI, triglycerides, total cholesterol, aspartate aminotransferase, alanine aminotransferase, 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.

書式変更: インデント ： 最初の行 ： 7.5 mm, 行間 ： 2 行

コメント [F6]: これを真似して書けよ

書式変更: フォント ：（日）+本文のフォント － 日本語（ＭＳ 明朝）

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. 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).

Discussion

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 have heart disease

show increased mortality rates in comparison with hospitalized diabetes patients who have the same condition [ref]. The prevalence of chronic kidney disease (CKD) in undiagnosed diabetes patients was higher than these with clinical diabetes [ref]. However, few studies have examined cardiovascular and metabolic markers in undiagnosed diabetes. We newly examined metabolic markers such as liver enzymes.

When considering interventions such as changing patients' lifestyle, it may be beneficial to focus on undiagnosed diabetes. As such, these results may have clinical relevance in diabetes prevention. 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. 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.

Conclusion:

Subjects with undiagnosed diabetes had poorer 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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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.