



Original Research

Low Vital Capacity Was Associated with Incident Diabetes in a Japanese Health Screening Population in Whom Obesity Was Not Prevalent

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ABSTRACT

Objectives: There have been few studies regarding the relationship between respiratory function and incident diabetes in East Asian populations in whom obesity is not prevalent.

Methods: This is a 6-year follow-up study in a Japanese health-screening population that included 1874 men and 1093 women. Using Cox regression models, hazard ratios (HRs) of incident diabetes for percent vital capacity (%VC) and forced expiratory volume in 1 second divided by forced vital capacity (FEV1/FVC) were calculated. Diabetes was defined as simultaneous fasting plasma glucose (FPG) ≥ 7.0 mmol/L and glycated hemoglobin (A1C) $\geq 6.5\%$ or use of antidiabetic medications.

Results: During the 6-year follow-up period (mean of 4.8 years), 71 men (3.8%) and 18 women (1.7%) developed diabetes. The HRs (95% confidence intervals [CIs]) of incident diabetes for each 1 SD increase in %VC and the lowest tertile of %VC compared with the highest tertile were 0.81 (0.66 to 1.00) ($p=0.045$) and 1.78 (1.01 to 3.16) ($p=0.048$), respectively, adjusted for sex, age, body mass index, antihypertensive drug use and A1C levels. After further adjustment for log high-sensitivity C-reactive protein, the HRs (95% CI) of incident diabetes for each 1 SD increase in %VC and the lowest tertile of %VC were 0.82 (0.67 to 1.01) ($p=0.063$) and 1.69 (0.95 to 3.01) ($p=0.073$), respectively. The association between FEV1/FVC and incident diabetes was not significant.

Conclusions: %VC, but not FEV1/FVC, was significantly associated with incident diabetes in a Japanese health-screening population in whom obesity was not prevalent.

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R É S U M É

Objectifs : Peu d'études portant sur la relation entre la fonction respiratoire et l'incidence du diabète ont été réalisées dans les populations de l'Asie de l'Est où l'obésité n'est pas répandue.

Méthodes : La présente étude de cohorte de 6 ans porte sur une population japonaise sélectionnée en fonction de leur état de santé qui regroupait 1874 hommes et 1093 femmes. À l'aide des modèles de régression de Cox, les rapports de risque (RR) d'incidence du diabète pour la capacité vitale exprimée en pourcentage (CV%) et le volume expiratoire maximal par seconde divisée par la capacité vitale forcée (VEMS/CVF) ont été calculés. Le diabète a été défini par la concomitance d'une glycémie veineuse à jeun (GVJ) $\geq 7,0$ mmol/l et d'une hémoglobine glyquée (A1c) $\geq 6,5\%$ ou de l'utilisation d'antidiabétiques.

Résultats : Durant la période de suivi de 6 ans (moyenne de 4.8 ans), 71 hommes (3.8%) et 18 femmes (1.7%) ont développé le diabète. Les RR (intervalles de confiance [IC] à 95 %) d'incidence du diabète pour chaque augmentation de l'ÉT dans la CV% et le plus faible tertile comparativement au tertile le plus élevé de la CV% ajusté en fonction du sexe, de l'indice de masse corporelle, de l'utilisation d'antihypertenseurs et des concentrations d'A1c ont respectivement été de 0.81 (0.66 à 1.00) ($p=0.045$) et de 1.78 (1.01 à 3.16) ($p=0.048$). Après d'autres ajustements du log de la protéine C réactive à haute sensibilité, les RR (IC à 95 %) de l'incidence du diabète pour chaque augmentation de l'ÉT dans la CV% et le plus faible tertile de la

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CV% ont respectivement été de 0.82 (0.67 à 1.01) ($p=0.063$) et de 1.69 (0.95 à 3.01) ($p=0.073$). L'association entre le ratio VEMS/CVF et l'incidence du diabète n'a pas été significative.

Conclusions : La CV%, mais non le ratio VEMS/CVF, a été significativement associée à l'incidence du diabète au sein d'une population japonaise sélectionnée en fonction de leur état de santé chez qui l'obésité n'était pas répandue.

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Introduction

Diabetes has reached epidemic proportions in many populations. Current estimates suggest that the world prevalence of diabetes among adults (aged 20 to 79 years) was 6.4%, affecting 285 million adults in 2010, and that it will increase to 7.7%, affecting 439 million adults by 2030; between 2010 and 2030, there will be a 69% increase in the numbers of adults with diabetes in developing countries, with a 20% increase in such patients in developed countries (1). This diabetes upsurge is concomitant with the global increase in the prevalence of obesity (2). Once thought of as a disease of the West, the prevalence of diabetes is increasing at alarming rates in many other areas of the world (3). Factors such as impaired fasting glucose and/or increased levels of glycated hemoglobin (A1C), known as prediabetes, obesity, sedentary lifestyles and family histories of diabetes are known to be the most important predictors of diabetes. However, it may be useful to identify new predictors of diabetes in order to prevent the development of diabetes. A decreased vital capacity has been reported to be a new predictor of diabetes in Western countries where the prevalence of obesity is high (4–10). Nontraditional risk factors, particularly forced vital capacity (FVC) and serum potassium, are potential mediators of the association between African American race and diabetes risk (11). Decrease in vital capacity is associated with obesity in Westerners (10). However, there have been few reports regarding the relationship between lung function tests and incident diabetes in East Asian populations, in whom the prevalence of obesity is low (12–14). A previous 4-year follow-up study from our centre reported a significant weak association between percent vital capacity (%VC) and incident diabetes in women but not in men. However, the number of subjects was small and the follow-up period was short. Therefore, the association was re-examined using a more precise definition of diabetes.

The aim of this 6-year follow-up study in a historical cohort is to examine the associations between lung function tests and incident diabetes in a health screening population of Japanese men and women, in whom the prevalence of obesity is low.

Methods

Subjects

Between April 2008 and March 2009, 2432 men and 1433 women visited our medical check-up centre for annual general health screenings and gave their written informed consent to provide their data for future studies of cardiovascular risk factors. The demographic backgrounds of the visitors were diverse; they included civil servants, workers engaged in agriculture, fishery, construction, manufacturing, electricity, gas, information and communications, transport and postal activities, wholesale and retail trade, finance and insurance, real estate, scientific research, professional and technical services, accommodations, eating and drinking services, living-related and personal services, amusement services, education and learning support, medical, healthcare and welfare services, housekeepers and retirees who resided in Nagaoka city, the surrounding cities or neighbouring agricultural districts. The visitors were

required to complete a questionnaire that included questions regarding their histories of coronary heart disease and stroke, smoking and drinking status, levels of physical activity and use of antihypertensive, antidiabetic or antihyperlipidemic medications. Physical activity was defined as walking for 1 hour or longer per day or exercising for 30 minutes or longer twice or more per week. Excluding individuals with diabetes at baseline, 2296 men and 1413 women remained as candidate subjects for this study. Among them, 1874 men 24 to 82 (51.6 ± 9.4) years of age and 1093 women 30 to 82 (51.8 ± 9.5) years of age revisited our medical check-up centre between April 2009 and March 2015 and were included in this study. The protocol for the study was approved by the ethics committee of Tachikawa Medical Center, and the study procedures were in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Diabetes was defined as simultaneous fasting plasma glucose (FPG) of ≥ 7.0 mmol/L and A1C levels of $\geq 6.5\%$ or use of antidiabetic medication for both the baseline and the follow-up period.

Measurements

Respiratory function parameters, including %VC and forced expiratory volume (FEV) in 1 second divided by the forced vital capacity (FEV1/FVC), were obtained by trained clinical technicians using the Autospirometer System 7 (Minato Medical Science, Osaka, Japan). The spirometry methods were complied with the guideline for spirometry examinations by the Japanese respiratory society. Slow vital capacity was measured several times. The %VC was calculated as maximal slow vital capacity divided by predicted vital capacity (PVC). PVC was calculated using the equations recommended by the Japanese respiratory society in 2001: $PVC = 0.045 \times \text{height (cm)}^{-0.023} \times \text{age (years)}^{-2.258}$ in men and $0.032 \times \text{height (cm)}^{-0.018} \times \text{age (years)}^{-1.178}$ in women. Blood samples were obtained after an overnight fast to measure the blood levels of routine medical check-up parameters, including FPG, triglycerides, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, A1C levels and high-sensitivity C-reactive protein (hs-CRP). The chemical measurements were all performed at BML Nagaoka (Nagaoka, Japan) according to routine laboratory methods except for those involving the hs-CRP level, which was measured at BML General Laboratory (Tokyo, Japan) with nephelometry using N-latex CRP-2 (Siemens Healthcare Japan, Tokyo, Japan). The measurement limit for the hs-CRP level was 0.02 mg/L and a value of hs-CRP less than the measurement limit was considered to be 0.01 mg/L. The LDL cholesterol levels were measured according to a direct surfactant method using Choletest-LDL (Sekisui Medical Inc, Tokyo, Japan), and the A1C levels were measured using a latex aggregation immunoassay with the Determiner HbA1c (Kyowa Medex, Tokyo, Japan). Blood pressure was automatically measured by MPV-3301 (NIHON KODEN, Tokyo, Japan). Average systolic blood pressure and diastolic blood pressure values were calculated from 2 measurements obtained in the sitting position after 5 minutes of rest. Body weight was measured with the subject wearing light clothes provided by our centre and the weight of the clothes was subtracted from the measured body weight. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in metres.

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