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Short Report

Impact of glucose tolerance status on the development of coronary artery disease among working-age men

K. Fujihara[a], R. Igarashi[a], M. Yamamoto[a], M. Ishizawa[b], Y. Matsubayasi[a], S. Matsunaga[a], K. Kato[a], C. Ito[b], M. Koishi[b], N. Yamanaka[b], S. Kodama[a], H. Sone[a,*]

[a] Department of Internal Medicine, Niigata University Faculty of Medicine, Niigata, Japan
[b] Japan Medical Data Center Co., Ltd., Tokyo, Japan

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Abstract

Aims. – To examine the impact of glucose tolerance status on the development of coronary artery disease (CAD) in working-age men in Japan.

Methods. – This population-based retrospective cohort study included 111,621 men aged 31–60 years [63,558 with normal glucose tolerance (NGT); 37,126 with prediabetes; 10,937 with diabetes]. The Cox proportional-hazards regression model was used to identify variables related to the incidence of CAD.

Results. – Multivariate analysis showed that, compared with NGT, diabetes increased the risk of CAD by 17.3 times (95% CI: 6.36–47.0) at ages 31–40 years, by 2.74 times (95% CI: 1.85–4.05) at ages 41–50 years and by 2.47 times (95% CI: 1.69–3.59) at ages 51–60 years. The HRs for CAD in men with diabetes aged 31–40 equaled that of men with NGT aged 51–60 [18.2 (7.15–46.4) and 19.4 (8.28–45.4), respectively].

Conclusion. – The impact of diabetes on CAD was markedly greater in men aged 31–40 years compared with those aged 41–60 years.

Keywords: Coronary artery disease; Glucose tolerance status; Working-age men

1. Introduction

Coronary artery disease (CAD) in working-age people is relevant and urgent not only because of its association with premature death, but also due to its enormous socioeconomic impact. Diabetes mellitus (DM) as well as lipid abnormalities, such as those of low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG), are well known to play major roles in the development of CAD [1–5]. However, longitudinal studies comparing the incidence and risk factors related to CAD in working-age populations by age groups with DM *vs* those with normal glucose tolerance (NGT) are scarce [1,6–8]. Moreover, little is known of the risk of CAD in those with prediabetes [1,6,9]. Therefore, the present study investigated the impact of glucose tolerance status on the development of CAD in a working-age male population.

2. Methods

The study retrospectively reviewed data for male employees in Japan derived from health insurance claims provided by the Japan Medical Data Center Co., Ltd. (JMDC) [10]. Men aged 31–60 years who had been followed for at least 3 years between 1 April 2008 and 31 March 2012 were included and followed up to 31 August 2015. Criteria for inclusion were age 31–60 years and male gender. Excluded were those with CAD at baseline, those not followed for at least 3 years and those with no health examination data including blood tests. Of the 153,278 men who had such available data, 111,621 men without

Abbreviations: CAD, coronary artery disease; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; NGT, normal glucose tolerance; JMDC, Japan Medical Data Center Co., Ltd.; FPG, fasting plasma glucose.

* Corresponding author at: Niigata University Faculty of Medicine, Department of Internal Medicine, 1-754 Asahimachi, Niigata, Niigata 951-8510, Japan. Tel.: +81 25 368 9026; fax: +81 29 368 9300.

E-mail address: sone@med.niigata-u.ac.jp (H. Sone).

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Table 1
Cox regression analysis of variables for the incidence of coronary artery disease (CAD) according to age category in Japanese men.

	All age groups		Age 31–40 years		Age 41–50 years		Age 51–60 years	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
BMI, 5 kg/m^2 increase	0.91 (0.80–1.05)	0.20	0.87 (0.57–1.33)	0.52	1.06 (0.85–1.32)	0.62	1.10 (0.89–1.36)	0.37
SBP, 10 mmHg increase	1.27 (1.20–1.34)	<0.01	1.41 (1.15–1.73)	<0.01	1.13 (1.02–1.25)	0.02	1.23 (1.14–1.33)	<0.01
LDL-C, 1 mmol/L increase	1.69 (1.52–1.88)	<0.01	1.94 (1.38–2.72)	<0.01	1.90 (1.61–2.25)	<0.01	1.47 (1.26–1.71)	<0.01
HDL-C, 1 mmol/L increase	0.34 (0.24–0.47)	<0.01	0.39 (0.11–1.42)	0.16	0.26 (0.15–0.46)	<0.01	0.37 (0.24–0.57)	<0.01
Current smoker	1.58 (1.30–1.91)	<0.01	2.89 (1.04–4.89)	0.03	2.20 (1.60–3.03)	<0.01	1.36 (1.05–1.77)	0.02
Glucose tolerance category								
Normal glucose tolerance	Reference		Reference		Reference		Reference	
Prediabetes	1.74 (1.38–2.23)	<0.01	2.89 (1.02–8.19)	0.046	0.88 (0.61–1.28)	0.52	1.62 (1.16–2.32)	<0.01
Diabetes	4.37 (3.39–5.65)	<0.01	17.3 (6.36–47.0)	<0.01	2.74 (1.85–4.05)	<0.01	2.47 (1.69–3.59)	<0.01
Normal glucose tolerance			Reference		9.11 (3.94–21.0)	<0.01	19.4 (8.28–45.4)	0.02
Prediabetes			3.03 (1.08–8.53)	0.04	8.26 (3.54–19.3)	<0.01	30.8 (13.5–70.4)	<0.01
Diabetes			18.2 (7.15–46.4)	<0.01	25.4 (10.9–59.2)	<0.01	46.7 (20.3–107.3)	<0.01

All CAD variables adjusted for BMI, SBP, LDL-C, HDL-C, smoking status and glucose tolerance category.
HR: hazard ratio; BMI: body mass index; SBP: systolic blood pressure; LDL-C/HDL-C: low-density lipoprotein/high-density lipoprotein cholesterol.

CAD at baseline were analyzed. Details of the extraction of our study participants are shown in Fig. S1 (see supplementary material associated with this article online). The participating men were classified as having NGT, prediabetes or DM based on their fasting plasma glucose (FPG), HbA_{1c} (as per the National Glycohemoglobin Standardization Program, NGSP) and claims database data. These categories were defined as: NGT, either FPG < 5.6 mmol/L or HbA1c < 5.7% or both and no antidiabetic drug prescription; prediabetes, either FPG 5.6–6.9 mmol/L or HbA_{1c} 5.7–6.4% or both and no antidiabetic drug prescription; and diabetes, FPG $\geq$ 7.0 mmol/L or $HbA_{1c} \geq 6.5\%$ or both without antidiabetic drug prescription or with an antidiabetic drug prescription regardless of FPG or HbA_{1c}.

The presence of CAD was determined according to claims using International Classification of Diseases, 10th Revision (ICD-10) codes for cardiac events, including fatalities, but excluding heart failure and, medical procedures. Data were compared in the three study groups according to 10-year increments in age (31–40 years, 41–50 years, 51–60 years). Unadjusted overall time to development of CAD was derived by Kaplan–Meier analysis and log-rank tests. The Cox proportional-hazards regression model identified variables related to the incidence of CAD. Analyses were performed using SPSS version 19.0 software (IBM SPSS Statistics, Armonk, NY, USA). Statistical significance was considered to be $P < 0.05$. The Ethics Committee of Niigata University approved the study.

3. Results

Baseline characteristics of our study participants according to age category are shown in Table S1 (see supplementary material associated with this article online). Except for the age 51–60 category, there were significant differences in all variables between the groups with CAD (+) and without CAD (−) in all age categories. Median follow-up duration was 4.1 years. During the study period, 33, 172 and 231 CAD events occurred in the 31–40, 41–50 and 51–60 age categories, respectively, while the absolute risks for CAD were 0.09%, 0.33% and 0.94% in the same age categories, respectively. Rates of CAD in those with NGT, prediabetes and DM were 0.06, 0.23 and 1.91 per 1000 person-years, respectively, in those aged 31–40 years. In those aged 41–50 years, CAD rates were 0.52, 0.62 and 2.52 per 1000 person-years with NGT, prediabetes and DM, respectively, and similarly, CAD rates in men aged 51–60 years with NGT, prediabetes and DM were 1.12, 2.24 and 4.14 per 1000 person-years, respectively. The absolute risks of CAD according to glucose tolerance status for each age category are shown in Table S2 (see supplementary material associated with this article online), and the cumulative incidences and Kaplan–Meier curves for CAD in each age group according to glucose tolerance are shown in Fig. S2 (see supplementary material associated with this article online).

The incidence of CAD in those with DM was significantly higher than in those with NGT or prediabetes (all $P < 0.01$ for DM *vs* NGT/prediabetes groups in all age categories). Risk factors for CAD, analyzed by multivariate Cox proportional-hazards models, are shown in Table 1 and Table S3 (see supplementary material associated with this article online). DM was a significant factor for CAD that persisted, on multivariate analysis, in all age categories, whereas prediabetes was associated with a 2.9-fold risk in men aged 31–40 years, 0.9-fold risk in men aged 41–50 years and 1.6-fold risk in men aged 51-60 years. Multivariate analyses showed increased hazard ratios (HRs) for CAD across all glucose tolerance and age categories, using NGT in men aged 31–40 years as the reference. Increased LDL-C levels were associated with an increase in CAD incidence across all age categories, whereas decreased HDL-C levels were associated with an increase in CAD in men aged 41–60 years (Table 1).

4. Discussion

This was the first study to examine the incidence and risk factors of CAD in men of working age in a general population free of DM and/or prediabetes. Compared with those with NGT aged 31–40 years, the risks of CAD in men with NGT