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Coronary heart disease and diabetic retinopathy in newly diagnosed diabetes in Da Qing, China: The Da Qing IGT and Diabetes Study

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Abstract. In 1986, 110,660 of 281,589 residents aged 25–74 years in Da Qing, Hei Long Jiang Province of China, were surveyed. Based on the results of a 75-g oral glucose tolerance test, 630 subjects were found to have previously undiagnosed diabetes according to 1985 WHO criteria. Among them, 600 diabetics aged 35–74 years (288 men, 312 women) and 410 non-diabetics of similar age with normal glucose tolerance (207 men, 203 women) were examined to determine the prevalence of retinopathy and coronary heart disease (CHD) and to evaluate associated characteristics. Retinal examinations of 423 newly diagnosed diabetics showed that 15.4% had several microaneurysms and/or small intraretinal haemorrhage, 5.5% soft exudates, 7.1% hard exudates, and 2.3% proliferative retinopathy. Among 220 non-diabetics, 13.6% had one or two microaneurysms and/or small intraretinal haemorrhage, and only 1.4% had a few soft exudates; half of the non-diabetics with retinopathy had hypertension. CHD, according to Minnesota coding (1.1–1.3, 5.1–5.3 and 7.1) of resting electrocardiograms, was ten times more frequent in the diabetics (3.59%) than in the controls (0.32%), after adjusting for age and sex. Multiple regression analysis showed that plasma glucose concentration was a risk factor for retinopathy after adjusting for age, sex, body mass index (BMI), smoking and blood pressure. Two-hour plasma glucose concentration (after adjusting for age, sex, BMI, smoking and blood pressure) and blood pressure (after adjusting for age, sex BMI, smoking and 1-h or 2-h plasma glucose level) were associated with CHD among the diabetics and non-diabetics and among the diabetics alone. Thus, both micro- and macrovascular complications occur frequently in previously undiagnosed Chinese diabetics and the frequency of CHD is markedly increased compared to the low frequency among Chinese non-diabetics.

Key words: Coronary heart disease – Diabetic retinopathy

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Introduction

No population-based study has previously been performed in China to examine the prevalence of and risk factors for coronary heart disease (CHD) and diabetic retinopathy among newly diagnosed diabetics. A cooperative diabetic research group in Beijing and Tiangin, China [1] examined micro- and macrovascular disease in 453 diabetics with various durations of diabetes following the WHO multinational study on the vascular complications of diabetes [2]. The occurrence of diabetic retinopathy in Beijing and Tiangin increased with the duration of diabetes and was similar to the highest incidence found among the 14 countries participating in the WHO study. The prevalence of abnormal Q (0.9%) and ST/T wave (7.7%) abnormalities among Chinese diabetics was similar to that of Japan, and much lower than those of western countries [3, 4]. The degree of hyperglycaemia and duration of diabetes have consistently been associated with diabetic retinopathy (microvascular disease) in studies of many populations; the same relationships have not been consistently demonstrated in the case of CHD (macrovascular disease) [3–5].

In 1986, the population of Da Qing in northern China was surveyed to identify individuals with (IGT). As a result of glucose tolerance testing, a group of individuals was diagnosed as having diabetes. These subjects and normoglycaemic controls were examined to determine the prevalence of retinopathy and CHD and to identify associated characteristics.

Subjects and methods

Da Qing is a new industrial city with a population of 500,000 in Hei Long Jiang province (north-east China) that was built to develop oil exploration and production and to which people from all areas of China have moved since 1960. There were 281,589 persons aged 25 years and over (including workers, retired people and their families) in Da Qing in 1986. All of them receive health care in designated clinics which are located throughout the city. Half of these clinics were randomly selected to participate in the study. These clinics

served 126,715 people over the age of 25. All eligible subjects were given an appointment to attend a central survey site (local hospital) near their home. In all, 110,600 subjects (87.3%; 55,391 men and 55,209 women) participated in the survey and were screened by measurement of plasma glucose concentrations after breakfast containing ≥100 g steam bread (about ≥80 g carbohydrate). The 4209 subjects with 2-h plasma glucose ≥6.67 mmol/l (120 mg/dl), after breakfast, were given an appointment to proceed to the oral glucose tolerance test (OGTT). Of these, 3956 subjects (94%) attended a central survey site for examination. Among the 3956 subjects who underwent an OGTT, 600 subjects aged 35 and over had fasting plasma glucose ≥7.8 mmol/l and/or 2-h plasma glucose ≥11.1 [6] (288 men, 312 women) and had not been previously diagnosed as diabetic. 410 subjects aged 35 and over (207 men, 203 women) had fasting plasma glucose less than 5.8 mmol/l (105 mg/dl), and 2-h glucose less than 6.67 mmol/l (120 mg/dl). These were selected as non-diabetic controls. Their sex ratio and age were approximately similar to those of the newly diagnosed diabetics.

Examination

An OGTT was performed after a 10–12 h overnight fast. Subjects were asked to empty their bladder, and height and mass were measured in light clothing and without shoes. After this, the subjects ingested 75 g glucose monohydrate dissolved in 300 ml water over 2 min. Blood was drawn for measurement of glucose at 0, 60 and 120 min. Fasting total (TC) and HDL cholesterol (HDL-C) and triglyceride (TG) were also measured. Questionnaires were administered to assess past medical history, dietary intake, physical activity and cigarette smoking. Blood pressure was measured and a resting 12-lead electrocardiogram (ECG) was performed.

The methods used for the measurement of blood pressure, height and mass as well as ECG were according to the WHO multinational study of vascular disease in diabetes [2]. A standard mercury sphygmomanometer was used, with the mercury at zero before measurement. The measurement was made with the subject in the sitting position. Diastolic blood pressure was measured as the fourth Korotkoff sound to the nearest 2 mm Hg. Blood for glucose determination was collected into tubes containing ethylenediaminetetraacetic acid and fluoride. These specimens were centrifuged immediately, and plasma glucose was determined in duplicate within 2 h by a glucose oxidase method. Rigorous standard and quality control procedures for glucose measurement were followed throughout the study. Plasma TC and TG were quantified on an auto-analyser using the cholesterol extraction method [7] and the triglyceride enzyme method of Bucols and Davis [8]. HDL-C was determined in the supernatant after precipitation of VLDL and LDL in 1.0 ml plasma with 0.5 ml of 1 M $MnCl_2$ and 0.12 ml sodium heparin [9]. All lipid measurements were made in a single central laboratory with low, medium, and high concentration quantity control pools. Intra- and inner-assay coefficients of variation were 2.1, and 4.4% for plasma glucose; 1.8, and 4.6% for TC; 2.0, and 4.8% for TG; 3.0, and 5.4% for HDL-C, respectively. Plasma TC and HDL-C determinations were standardized under the WHO Monica protocol. Each ECG was read by two trained readers according to the Minnesota code; disagreement was resolved by a cardiologist without knowledge of the clinical data. The occurrence of Minnesota code items 1.1–1.3 (abnormal Q and QS pattern), 5.1–5.3 (T wave abnormalities) and 7.1 (complete left bundle branch block) were taken to signify CHD [10, 11]. Mean blood pressure (MBP) was defined as two-thirds of the diastolic blood pressure (DBP) plus one-third of the systolic blood pressure (SBP). Obesity was assessed by the body mass index [BMI; mass (kg)/hight (m^2)], and was considered present when the BMI was ≥25 kg/m^2. Retinal examinations were performed by two ophthalmologists using direct ophthalmoscopy. Both pupils were dilated and each fundus was photographed. There was a standard assessment chart. The changes found in each eye were recorded separately. Red dots indicated microaneurysms or small intraretinal haemorrhage; white dots showed hard exudates or soft exudates, proliferative changes, neovascularization, vitreous haemorrhage, retinal detachment, and fibrous strands [12].

Statistics

In the cross-sectional analysis, data were expressed as the mean ± SD. Computation was performed on the logarithm of those parameters which were not normally distributed (TG). Multiple logistic regression analysis was used to test several models of the association of ECG abnormality with newly diagnosed diabetes and other variables, and the association of retinopathy with newly diagnosed diabetes and other variables [13]. The results of the parsimonious models are presented.

Results

Comparisons between newly diagnosed diabetics and non-diabetics

A total of 630 individuals (296 men, 334 women) aged 25 years and over were newly diagnosed as having diabetes. This represents a prevalence rate of 6/1000. Since 1.7/1000 already reported having diabetes, the total prevalence of diabetes was 7.7‰.

When those with newly diagnosed diabetes aged 35–74 years were compared with controls of similar age and sex ratio, diabetics had higher BMI, SBP, DBP, plasma fasting (FPG) 1-h (PG1h) and 2-h (PG2h) plasma glucose concentrations, TC, TG and lower HDL-C concentrations (Table 1). The prevalence of obesity (54%), hypertension (26%) and hyperlipidaemia (43%) in diabetics was about twice that in the controls (obesity, 31%; hypertension, 14%; and hyperlipidaemia, 17.5%) after adjusting for age and sex (Fig. 1).

Among 220 control subjects who had retinal examinations, 23 (10.5%) had one or two microaneurysms and/or two small intraretinal haemorrhages. Three (1.4%) had a

Table 1. Clinical and laboratory data of non-diabetics and newly diagnosed diabetics aged 35–74 years

Variable	Non-diabetics		Diabetics		
	n	Mean ± SD	*n*	Mean ± SD	*P*
Age	410	47.0 ± 7.2	600	49.1 ± 8.2	<0.001
BMI	410	13.9 ± 3.5	600	25.6 ± 3.6	<0.001
SBP	409	124.7 ± 22.0	600	136.5 ± 23.8	<0.001
DBP	409	83.3 ± 14.6	600	88.6 ± 14.3	<0.001
FPG	410	4.8 ± 0.5	600	8.7 ± 3.1	<0.001
PG1h	409	6.8 ± 1.4	596	16.0 ± 3.4	<0.001
PG2h	410	5.0 ± 0.8	596	15.3 ± 3.6	<0.001
TC	356	4.9 ± 1.1	447	5.3 ± 1.6	<0.001
TG	322	1.4 ± 1.1	395	2.1 ± 1.9	<0.001
HDL-C	354	1.40 ± 0.31	442	1.35 ± 0.34	<0.005

Non-diabetics were subjects with normal glucose tolerance.
BMI, Body mass index kg/m^2; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; PG1h, 1-h plasma glucose after 75 g glucose load; TC, plasma cholesterol (mmol/l); TG, plasma triglyceride (mmol/l)

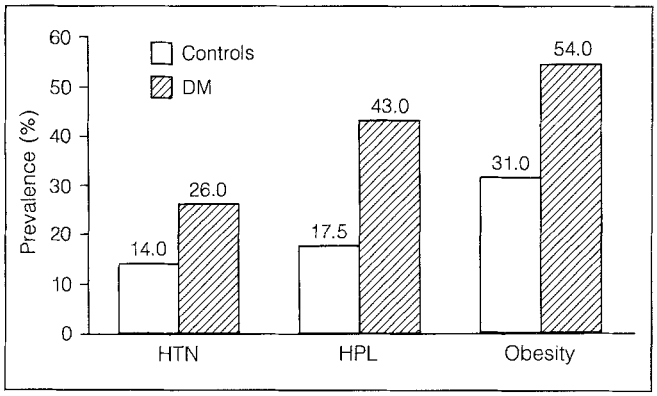

Fig. 1. Prevalence of hypertension (*HTN*), hyperlipidaemia and obesity adjusting for age and sex. *HTN*, systolic blood pressure ≥160/diastolic blood pressure = 95 mm HG; *HPL*, plasma cholesterol ≥6.45 mm/l and/or triglyceride ≥2.26 mm/l; obesity, body mass index ≥25 kg/m^2; DM, diabetes mellitus

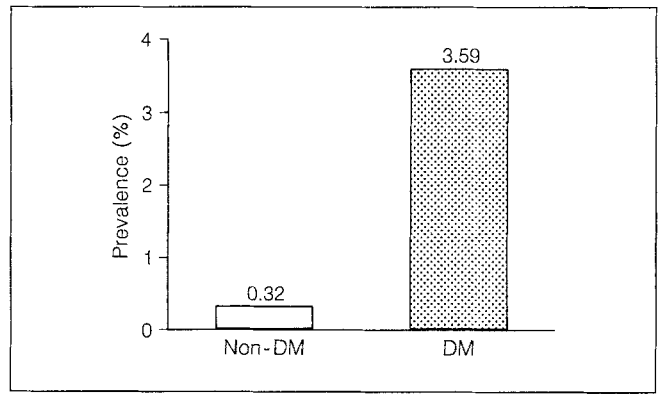

Fig. 2. Prevalence of coronary heart disease (CHD) adjusted for age and sex. CHD, Minnesota Code 1.1–1.3, 5.1–5.3, 7.1

Table 2. Retinopathy of newly diagnosed diabetics and non-diabetics aged 35–74 years

	Non-diabetics (n=220)		Diabetics (n=423)	
	n	%	n	%
No retinopathy	194	88.1	294	69.5
Red dots[a]	23	10.5	65	15.4
White dots[b]	3	1.4	54	12.8
Proliferative[c]	0	0	10	2.8
Change				

[a] Included microaneurysm and/or small intraretinal haemorrhage
[b] Included hard or soft exudates
[c] Included neovascularization or fibrous strands

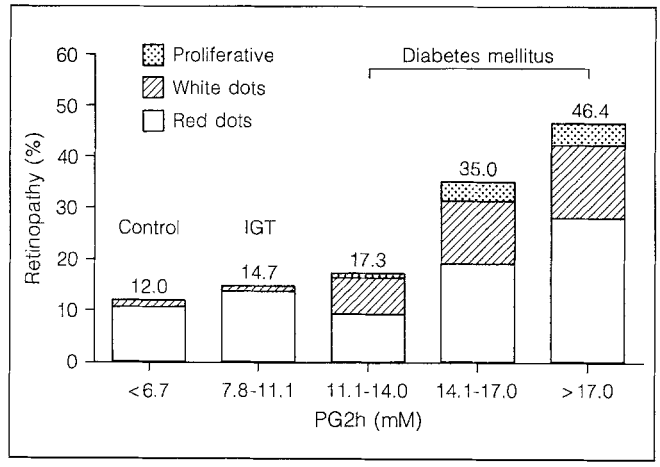

Fig. 3. Prevalence of retinopathy adjusted for age, sex and mean blood pressure

few soft exudates with one or two intraretinal haemorrhages confirmed by fluorescein angiography. Of the controls with retinal changes 40% had hypertension (≥140/or ≥90 mm Hg); among 423 diabetics who had retinal examinations, 65 (15.4%) had several microaneurysms and/or small intraretinal haemorrhages, 44 (12.8%) had soft or hard exudates, and 10 (2.4%) had proliferative retinopathy (7 with new vessels, 3 with fibrous strands). Of the diabetics with retinopathy 58% had hypertension (Table 2).

Among 600 diabetics aged 35–74 years, there were 8 subjects (4 men, 4 women) with Minnesota code abnormalities 1.1, 1.2, 2 men with 1.3, 17 subjects (11 men, 6 women) with 5.1–5.3, and 1 man with 7.1. Among 410 non-diabetics, 1 subject had 1.2, and 1 had 5.2 (both women). ECG evidence of CHD was seen ten times more frequently in diabetics (3.59%) than in controls (0.32%) after adjusting for age and sex (Fig. 2).

Association with retinopathy

To explore the possible determinants of retinopathy, a multiple logistic regression analysis was performed. The independent variables included age, sex, BMI, MBP, smoking and PG2h (or FPG or PG1h). PG2h (FPG or PG1h) was significantly related to retinopathy after adjusting for age, sex, BMI, MBP and smoking (Table 3, Fig. 3). Retinopathy was not significantly associated with any measure of blood pressure.

Associations with ECG abnormalities

To explore the possible determinants of ECG abnormalities, a forward stepwise multiple logistic regression analysis was performed. Since plasma TC, TG and HDL-C did not enter the model, the independent variables included age, sex, BMI, smoking, MBP (or SBP) and diabetic state (or FPG, or PG1h, or PG2h). Included in this analysis were 1006 subjects with normal glucose tolerance (non-diabetics) and newly diagnosed diabetics in whom all the variables were measured. The presence of diabetes (or PG1h or PG2h) and MBP (or SBP) was always significantly associated with ECG abnormalities after controlling for other variables (Table 4).

When a similar multiple logistic regression analysis was performed on the 596 newly diagnosed diabetics in

Table 3. Retinopathy: multiple logistic regression model in newly diagnosed diabetics aged 35–74 years ($n=439$)

Variable	β	SE	χ^2	P	OR	95% CI
Dependent variable: retinopathy[a] ($n=131$)						
Age (10 years)	0.285	0.142	4.02	<0.05	1.33	1.01–1.76
Sex (fem.=0, male=1)	−0.0417	0.2513	0.03	>0.05	0.96	0.59–1.57
BMI[b]	−0.0340	0.0337	1.02	>0.05	0.97	0.91–1.04
Smoker	−0.0951	0.2648	0.13	>0.05	0.91	0.54–1.53
MBP[c] (20 mm Hg)	0.0924	0.1434	0.42	>0.05	1.10	0.83–1.45
PG2h[d] (5 mmol/l)	0.7995	0.1555	26.34	<0.001	2.22	1.64–3.01
Intercept	4.3049	1.2299	12.25	<0.001		

[a] Included microaneurysms, intraretinal haemorrhage, soft or hard exudates and neovascularization with haemorrhage
[b] Mass (kg/height cm^2)
[c] 2/3 Diastolic blood pressure (DBP)+1/3 systolic blood pressure (SBP)
[d] 2-h Plasma glucose

Table 4. ECG abnormalities: multiple logistic regression model in diabetics[a] and non-diabetics[b] aged 35–74 years ($n=1006$)

Variable	β	SE	χ^2	P	OR	95% CI
Dependent variable: ECG abnormalities[c] ($n=30$)						
Age (10 years)	0.2380	0.2220	1.14	>0.05	1.27	0.82– 1.96
Sex (fem.=0, male=1)	0.3672	0.4437	0.68	>0.05	1.44	0.60– 3.44
BMI	−0.0044	0.0543	0.01	>0.05	1.00	0.90– 1.11
Smoker	−0.0355	0.4339	0.01	>0.05	0.97	0.41– 2.26
MBP[d] (20 mm Hg)	0.6280	0.0194	10.48	<0.01	1.87	1.80– 1.95
Diabetes[e] (1=yes, 0=no)	2.0977	0.7458	7.91	<0.01	8.15	1.89–35.13
Intercept	9.8367	1.9557	25.30	<0.001		

[a] Newly diagnosed diabetics
[b] Subjects with normal glucose tolerance
[c] The occurrence of Minnesota code 1.1–1.3, 5.1–5.3, 7.1 was taken to signify ECG abnormality
[d] 2/3 DBP+1/3 SBP
[e] PG1h or PG2h instead of presence of diabetes led to similar results

whom all the above variables were measured, MBP (or SBP) and PGh2 were still significantly associated with ECG abnormalities (Table 5).

A forward stepwise multiple logistic regression analysis of the determination of ECG changes ($n=21$) was performed, with BMI, smoking, plasma TC, HDL-C, MBP and PG2h as independent variables, on 442 non-diabetics and newly diagnosed diabetics in whom all the variables were measured, forcing age and sex into the model to adjust for the possible effects of these two variables. The MBP and PG2h were significantly related to

Table 5. ECG abnormalities: multiple logistic regression model in newly diagnosed diabetics aged 35–74 years ($n=596$)

Variable	β	SE	χ^2	P	OR	95% CI
Dependent variable: ECG abnormalities[a] ($n=28$)						
Age (10 years)	0.2050	0.2410	0.72	>0.05	1.23	0.74–1.97
Sex (fem.=0, male=1)	0.6684	0.4725	2.00	>0.05	1.95	0.78–4.90
BMI	0.0370	0.0576	0.41	>0.05	1.04	0.93–1.16
Smoker	0.1151	0.4502	0.07	>0.05	1.12	0.46–2.71
MBP (20 mm Hg)[b]	0.6220	0.214	8.51	<0.01	1.94	1.22–2.83
PG2h (5 mmol/l)	0.6760	0.2515	7.22	<0.01	1.97	1.20–3.20
Intercept	11.0019	2.4217	20.64	<0.001		

[a] The occurrence of Minnesota code 1.1–1.3, 5.1–5.3, 7.1 was taken to signify ECG abnormality
[b] 2/3 DBP+1/3 SBP

ECG abnormalities; odds ratio (OR) and 95% confidence inerval (CI) were 1.89, 1.25–2.85 for MBP and 1.90, 1.17–3.07 for PG2h, respectively. BMI, smoking, plasma TC and HDL-C did not contribute significantly to the model.

Among the 312 women with newly diagnosed diabetes, PG2h was the only variable significantly associated with ECG abnormalities ($n=10$) after controlling for age, BMI, smoking and MBP ($P<0.05$, OR 2.22, 95% CI 1.04–4.71). Among the 288 newly diagnosed male diabetics, MBP was significantly associated with ECG abnormalities ($n=18$) (OR 1.49, 95% CI 1.16–1.91, $P<0.01$), and PG2h was marginally significant (OR 1.13, 95% CI 0.99–1.29, $P=0.06$) after controlling for age, BMI, MBP and smoking.

Discussion

This paper is the first Chinese population-based study of retinopathy and CHD in newly diagnosed diabetes. Compared with non-diabetics, newly diagnosed diabetics had higher prevalence and severity of retinopathy. Multiple logistic regression analysis showed that plasma glucose (FPG, or PG1h or PG2h) was independently associated with retinopathy after controlling for age, sex, BMI, smoking and blood pressure. The cooperative diabetic research group in Beijing and Tiangin studied retinopathy in 411 previously diagnosed diabetics following the WHO multinational study protocol [2]. The prevalence of retinopathy was 25.2%, 75.8% and 76.9% in those with a duration of diabetes of 0–6, 7–13 and ≥14 years, respectively, and was similar to the highest incidence found among the 14 countries participating in the WHO study [4]. The prevalence of retinopathy in newly diagnosed diabetics (30.5%) in Da Qing was similar to that found in Beijing/Tiangin in patients with diabetes of 0–6 years' duration (25.2%) and much lower than that of diabetics in Beijing/Tiangin with longer diabetes dura-

tions. Thus, Chinese data, to date, appear consistent with other reports that both diabetes duration and degree of hyperglycaemia are associated with diabetic retinopathy [2, 14]. However, in contrast to most other studies, there was no association with blood pressure.

In the present study, among the newly diagnosed diabetics aged 35–74 years there were 8 subjects (1.3%) with abnormal Q waves (Minnesota code 1.1–1.2). All EGG-indicated CHD (defined as Minnesota code 1.1–1.3, 5.1–5.3, 7.1) occurred ten times more frequently in the newly diagnosed diabetics (3.59%) than in non-diabetics (0.32%) after adjusting for age and sex. The cooperative diabetic research group in Beijing and Tiangin also examined the cardiovascular complications of 416 previously diagnosed diabetics aged 35–55 years. Four diabetics (0.9%) had Q wave abnormalities (Minnesota code 1.1–1.2). The rate of Q wave abnormalities in diabetics was three times higher than that in 610 age- and sex-matched non-diabetics. Our data and those from Beijing and Tiangin are similar to those reported from Hong Kong and Japan, and the prevalences are much lower than those reported in western countries [3]. These Chinese data suggest that the prevalence of atherosclerosis in Chinese diabetics is lower than that in western diabetics, but that the effect of diabetes on CHD is still significant.

In this study, newly diagnosed diabetics had significantly higher BMI, blood pressure, TC, TG, and lower HDL-C compared with non-diabetics. The prevalence of hypertension, hyperlipidaemia and obesity in newly diagnosed diabetics was about twice that in non-diabetics, after adjusting for age and sex. The increased levels of these risk factors might be expected to increase the risk of atherosclerosis in newly diagnosed diabetics. However, the multiple logistic regression analysis showed that the presence of diabetes (or PG2h in the diabetics) was independently associated with ECG abnormalities after controlling for age, sex, BMI, smoking and MBP (or SBP); and blood pressure was also associated with CHD after controlling for age, sex, BMI, smoking and PG1h or PG2h. Plasma lipid levels were not significantly associated with ECG abnormalities, although our ability to detect such associations is limited by the relatively small number of affected subjects.

An earlier analysis of individuals with IGT in Da Qing showed a significantly higher percentage of ECG abnormalities, but not of cases of retinopathy compared to controls. Thus, these data in Da Qing suggest that serious diabetic retinopathy starts after the onset of diabetes, whereas CHD may start before diabetes develops and during the IGT period. These data are consistent with other reports of the atherogenicity of prediabetes [15, 16]. Our data also suggest that hyperglycaemia itself may play a role in the development of CHD, since a relationship to the 2 glucose level was found among the newly diagnosed diabetics, and previously undiagnosed diabetics had higher prevalences of CHD than those with IGT.

This study has several limitations. The results were from a cross-sectional study and the number of subjects with ECG abnormalities was low. Plasma insulin was not measured in diabetics, and some TC, TG and HDL-C values were missing. However, both micro- and macrovascular complications occur frequently in previously undiagnosed Chinese diabetics and the frequency of CHD is markedly increased compared to the low frequency among Chinese non-diabetics. To reduce the rate of cardiovascular disease and prevent diabetic retinopathy, it may be necessary to intervene before the onset of diabetes.

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References

1. Zhi-Sheng Chi, Study of the cardiovascular complications of diabetes mellitus in Beijing and Tiangin, China. Tokoku J Exp Med 141 [Suppl]: 491–493, 1983
2. Jarret RJ, Keen HL, Garabauskas V, The WHO multinational study of vascular disease in diabetes. 1. General description. Diabetes Care 2: 175–186, 1979
3. Keen H, Jarrett RJ, The WHO multinational study of vascular disease in diabetes. 2. Macrovascular disease prevalence. Diabetes Care 2: 187–195, 1979
4. Jarret RJ, Keen H, The WHO multinational study of vascular disease in diabetes. 3. Microvascular disease. Diabetes Care 2: 196–201, 1979
5. Klein R, Klein BEK, Moss SE, Davis MD, Demets DL, Glycosylated hemoglobin predicts the incidence and progression of diabetic retinopathy. JAMA 260: 2864–2871, 1988
6. WHO expert committee on diabetes mellitus: second report, WHO Tech Rep Ser No 646. World Health Organization, Geneva, 1980
7. Rush RL, Leon L, Turrell J, Automated simultaneous cholesterol and triglyceride determination on the auto analyzer. Thurman, Miami, 1970
8. Bucols G, Davis H, Quantitative determination of serum triglycerides by use of enzymes. Clin Chem 19: 475, 1973
9. Warnick R, Albers JJ, Comprehensive evaluation of the heparin manganese precipitation procedure for the estimation of high density lipoprotein cholesterol. J Lipid Res 19: 65–68, 1978
10. Stamler R, Stamler J, A symptomatic hyperglycemia and coronary heart disease. J Chron Dis 32: 829–837, 1979
11. Zimmet P, King H, The epidemiology of diabetes mellitus: recent developments. In: Alberti KGMM, Krall LP (eds) The diabetes annual. Elsevier, Amsterdam, pp 1–15, 1988
12. Bennett PH, Standardization of methods in epidemiology of diabetes mellitus. Tohoku J Exp Med 141 [Suppl]: 29–39, 1983
13. SAS Institute Inc, SAS/STAT user's guide release 6.03 edition. SAS Institute, 1988
14. Diabetes drafting group, Prevalence of small vessel and large vessel disease in diabetic patients form 14 countries: the world health organization multinational study of vascular disease in diabetics. Diabetologia 28: 615–640, 1985
15. Hafner SM, Stern MD, Haguda HP, Mitchell BD, Patterson JK, Cardiovascular risk factors in prediabetic individuals: does the clock for coronary heart disease start ticking before the onset of clinical diabetes? JAMA 263: 2893–2898, 1990
16. McPhillips JB, Barrett-Connor E, Wingard DL, Cardiovascular disease risk factor prior to the diagnosis of impaired glucose tolerance and non-insulin-dependent diabetes mellitus in a community of older adults. Am J Epidemiol 131: 443–453, 1990