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Brief report

Association of fasting and post-prandial hyperglycemia on the risk of cardiovascular and all-cause death among non-diabetic Chinese

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ABSTRACT

The role of post-prandial glucose on cardiovascular risk among Chinese adults without diabetes was investigated. In a median follow-up of 3.5 years on 16,590 participants, 95 cardiovascular deaths were found. The relative risk in the highest quintile post-prandial glucose was 1.61 (*P* for trend, 0.05) for cardiovascular death.

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1. Introduction

Fasting hyperglycemia and post-prandial hyperglycemia, indicators for abnormal glucose homeostasis, are related to diabetes incidence and cardiovascular risk [1,2]. Fasting hyperglycemia, with elevated fasting glucose level, is represented as an elevated hepatic glucose output and/or defect in early insulin secretion [3,4]. In contrast, post-prandial hyperglycemia, a marker for impaired glucose tolerance, is an indicator for peripheral insulin resistance [5]. Although both glucose markers are considered as important risk factors for cardiovascular disease (CVD) endpoints, different effects have been proposed due to laboratory and observational evidence [4,6]. Furthermore, data on the difference between fasting and post-prandial glucose levels are limited. This prospective study was, thus, conducted to examine the roles

of fasting and post-prandial glucose levels and their difference in predicting CVD incidence among ethnic non-diabetic Chinese.

2. Patients and methods

This is a prospective cohort study design involving participants who undertook health examinations at a tertiary hospital [7]. Diagnosed cases of diabetes (defined by fasting glucose ≥ 126 mg/dL or on hypoglycemic medication, $n = 1413$) and missing glucose data were excluded. A total of 16,590 participants (average 51.9 ± 13.1 years, 40% women) without diabetes were included and their fasting and post-prandial blood samples were obtained. Post-prandial blood sampling was taken in 2 h after a standard 650 kcal meal in the noon.

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Table 1 – Median levels, incidence rates (/1,000 person-year), relative risks (95% confidence intervals) of CVD events and death on follow-up (per quintile of fasting and post-prandial glucose levels and their difference).

Quintile	1	2	3			4			5			P for trend		
CVD death														
Fasting glucose (mg/dL)														
Range	<85	85–88.9	89–92.9			93–98.9			99–126					
Median	82	88	91			96			105					
Cases	24	14	14			16			27					
Rate/1000	11.6	8.6	9.1			9.4			17.5					
Model 1	1	0.73	0.38	1.42	0.77	0.40	1.50	0.78	0.41	1.47	1.09	0.62	1.89	0.61
Model 2	1	0.71	0.37	1.38	0.74	0.38	1.44	0.69	0.36	1.34	0.96	0.53	1.72	0.94
Model 3	1	0.64	0.32	1.26	0.61	0.30	1.23	0.59	0.30	1.16	0.84	0.47	1.51	0.77
Postprandial glucose (mg/dL)														
Range	<93	93–103.9	104–115.9			116–134.9			≥134					
Median	85	99	110			124			157					
Cases	15	8	10			16			41					
Rate/1000	7.9	5.7	6.8			10.2			21.7					
Model 1	1	0.88	0.37	2.09	0.96	0.43	2.14	1.23	0.61	2.50	1.86	1.03	3.37	0.007
Model 2	1	0.95	0.40	2.27	1.01	0.45	2.29	1.25	0.61	2.57	1.78	0.96	3.29	0.020
Model 3	1	0.94	0.39	2.24	0.99	0.44	2.24	1.17	0.57	2.42	1.61	0.86	2.99	0.053
Difference between post-prandial and fasting glucose (mg/dL)														
Range	<2	2–12.9	13–24.9			25–41.9			≥42					
Median	–6	8	19			32			62					
Cases	15	9	12			13			41					
Rate/1000	8.1	6.2	8			8.7			21.1					
Model 1	1	0.90	0.40	2.07	1.17	0.55	2.51	1.03	0.49	2.17	1.83	1.01	3.32	0.012
Model 2	1	0.94	0.41	2.17	1.21	0.56	2.62	1.06	0.50	2.25	1.75	0.96	3.20	0.027
Model 3	1	0.89	0.39	2.05	1.17	0.54	2.53	0.98	0.46	2.09	1.57	0.86	2.90	0.063
Total death														
Fasting glucose (mg/dL)														
Range	<85	85–88.9	89–92.9			93–98.9			99–126					
Median	82	88	91			96			105					
Cases	109	71	64			74			114					
Rate/1000	52.6	43.7	41.5			43.5			73.9					
Model 1	1	0.81	0.60	1.09	0.76	0.56	1.04	0.77	0.57	1.03	1.01	0.78	1.32	0.76
Model 2	1	0.83	0.62	1.13	0.79	0.58	1.08	0.81	0.60	1.09	1.08	0.82	1.42	0.45
Model 3	1	0.83	0.61	1.12	0.76	0.55	1.05	0.78	0.58	1.06	1.04	0.78	1.37	0.62
Post-prandial glucose (mg/dL)														
Range	<93	93–103.9	104–115.9			116–134.9			≥134					
Median	85	99	110			124			157					
Cases	78	53	55			62			178					
Rate/1000	40.9	37.5	37.3			39.6			94.4					
Model 1	1	1.06	0.75	1.51	0.96	0.68	1.36	0.89	0.64	1.25	1.61	1.23	2.10	<.0001
Model 2	1	1.12	0.79	1.60	1.05	0.74	1.49	0.95	0.68	1.34	1.74	1.32	2.29	<.0001
Model 3	1	1.12	0.78	1.59	1.01	0.71	1.44	0.89	0.63	1.25	1.58	1.20	2.09	0.0002

Difference between post-prandial and fasting glucose (mg/dL)									
	<2	2–12.9	13–24.9	25–41.9	≥42				
Range	<2	2–12.9	13–24.9	25–41.9	≥42				
Median	–6	8	19	32	62				
Cases	78	51	64	54	179				
Rate/1000	42	35.1	42.8	36.2	91.9				
Model 1	1	0.95	0.67	1.36	1.36	0.82	1.58	0.57	1.15
Model 2	1	0.95	0.67	1.36	1.36	0.83	1.62	0.59	1.20
Model 3	1	0.90	0.63	1.29	1.29	0.80	1.57	0.55	1.11

Incidence rates presented as per 1000 person years.

Model 1: adjusted for age groups (35–44, 45–54, 55–64, 65–74, ≥75 years old) and gender.

Model 2: Model 1 covariates plus period, body mass index (<18, 18–20.9, 21–22.9, 23–24.9, or ≥25 kg/m²), smoking (yes/no or abstinence) and current alcohol drinking (regular/no).

Model 3: Model 2 covariates plus systolic blood pressure, LDL and HDL cholesterol.

The procedure of glucose measurement was the following: after centrifugation by $1500 \times g$ for 10 min, glucose levels were measured on supernatant by enzymatic assay (Merck 3389 commercial kit, Darmstadt, Germany) in a Eppendorf 5060 autoanalyzer (Eppendorf Corp., Hamburg, Germany). All of the sample measurements were carried out in a single hospital and their coefficients of variation were around 5%. The protocol was approved by the IRB of National Taiwan University.

Information on the mortality and causes of death were obtained by linking the identification numbers of the study subjects to a national databank provided by the National Health Administration, which was updated to the end of 2005. CVD mortality was defined by the death codes 390–459 from the 9th version of the International Classification of Diseases (ICD).

The incidence rates for cardiovascular and all-cause death were specified by quintiles of fasting and post-prandial hyperglycemia. Multivariate adjusted Cox models were used to evaluate the relative risk (RR) and 95% confidence interval (CI), treating the first quintile as reference. Adjustments were made for multiple confounding factors as follows: entry periods (1995, 1996, 2001, and 2002 cohort), age (20–39, 40–49, 50–59, 60–69, and ≥70 years old), body mass index (<18, 18–19.9, 20–21.9, 22–23.9, 24–25.9, 26–27.9 and ≥28 kg/m²), smoking (yes/no), alcohol drinking habits (regular/no), and systolic blood pressure. HDL and LDL cholesterol were treated as continuous covariates. To test for linear trend across different glucose categories, the median levels within quintiles were used as a continuous variable. All analyses were performed with SAS version 9.1 (SAS Institute, Cary, NC).

3. Results

Compared with those in the first quintile of fasting or post-prandial glucose, participants in the higher quintiles were more likely to have higher age, BMI, systolic and diastolic blood pressure, and higher cholesterol and triglyceride levels, but lower HDL cholesterol level. During a median follow-up of 3.5 years (inter-quartile range, 2.7–7.9 years), 95 cases of cardiovascular deaths and 432 deaths were documented. The incidence rates of the cardiovascular death increased with the second quintile of each of measure of fasting and post-prandial glucose and their disparity, reaching the highest rates in the fifth quintile.

After multivariate adjustment, the RRs of cardiovascular death and all-cause death comparing the highest and lowest quintiles of fasting glucose were 0.84 (95% CI, 0.47–1.51, *P* for trend, 0.77) and 1.04 (95% CI, 0.78–1.32, *P* for trend, 0.62) (Table 1). The RRs comparing individuals in the highest quintile with those in the lowest quintile of post-prandial glucose were 1.61 (95% CI, 0.86–2.99, *P* for trend, 0.05) for cardiovascular death and 1.58 (95% CI, 1.20–2.09, *P* for trend, 0.0002) for all-cause death. For the comparison of the fifth with the first quintile of the disparity between fasting and post-prandial glucose, the multivariate RRs of cardiovascular and all-cause deaths were 1.63 (95% CI, 0.86–2.90, *P* for trend, 0.063) and 1.48 (95% CI, 1.13–1.95, *P* for trend, 0.0005), respectively.

Adjustment for lifestyle, obesity, systolic blood pressure, and HDL, and LDL cholesterol slightly attenuated the RRs for cardiovascular and all-cause death risk.

4. Discussion

In this prospective cohort of adult Chinese without diabetes, higher levels of post-prandial glucose and the disparity between fasting and post-prandial glucose were significantly associated with increased risk of cardiovascular and all-cause death, even after adjustment for established cardiovascular risk factors. However, higher fasting hyperglycemia was not significantly associated with CVD risk.

Post-prandial glucose, similar to post-challenge glucose, was related to CVD than fasting glucose [8–11]. However, the association was not seen in moderately high fasting glucose level from the prospective DECODE study [8]. In an Italian study, post-prandial but not fasting glucose significantly predicted cardiovascular events in diabetic patients in a 5-year follow-up [10]. Previous analyses suggested that fasting hyperglycemia tended to be associated with beta cell dysfunction, whereas post-challenge hyperglycemia tended to be more strongly related to insulin resistance, higher blood pressure, obesity, and dyslipidemia.

The results here support the hypothesis that peripheral tissue insulin resistance (reflected by post-challenge glucose) may provide additional information beyond measuring fasting glucose alone. In clinical practice and in lifestyle and pharmacologic interventions, post-prandial glucose, which is easier measured than post-challenge glucose, should still be emphasized as a target to reduce diabetes incidence and CVD risk [12].

To our knowledge, this is the first extensive investigation on various glucose markers and risk of CVD in non-diabetic Chinese. Studies from other Asian populations have demonstrated that post-prandial and post-challenge glucose may be related to CVD events [13,14], but the head-to-head comparison of post-challenge and fasting glucose is not available. Because of the prospective cohort design, the baseline measurements of all cohort members were unlikely to be affected by storage.

This study had several limitations. First, the number of incident cases of CVD events was relatively small, such that the power is reduced. Second, because glucose and insulin levels were measured only once, the results might be prone to intra-individual variations that might have attenuated the results.

In conclusion, both post-prandial and the disparity value between fasting and post-challenge glucose were associated with the risk of CVD and all-cause death among Chinese without diabetes.

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Conflict of interest

There are no conflicts of interest.

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