

## Metabolic risk factors in southern Taiwanese with impaired fasting glucose of 100 to 109 mg/dL

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### Abstract

This study investigates the influence of changes in impaired fasting glucose (IFG) criteria by the American Diabetes Association in 2003 in estimating the prevalence and cardiovascular risks in Taiwanese with fasting plasma glucose (FPG) between 100 and 109 mg/dL. Data came from a cross-sectional study on 1411 participants aged 30 years and older without known diabetes in southern Taiwan. Besides collection of anthropometric and biochemistry data, a 75-g oral glucose tolerance test was performed. The new IFG criteria additionally identified 14.2% of all participants as having IFG100, with FPG between 100 and 109 mg/dL, among which the percentage of normal glucose tolerance (NGT), impaired glucose tolerance (IGT), and diabetes mellitus were 7.7%, 5.0%, and 1.5%, respectively. Mean body weight, body mass index, abdominal girth, systolic blood pressure, diastolic blood pressure (DBP), 2-hour glucose, and triglyceride were significantly higher in the IFG100 group than in normal fasting glucose (NFG) group (FPG, <100 mg/dL). Moreover, body weight, body mass index, systolic blood pressure, DBP, and 2-hour glucose were statistically higher in subgroups of IFG100/IGT than in NFG/NGT. In contrast, only DBP and 2-hour glucose were significantly higher in the IFG100/NGT group than in the NFG/NGT group. The 2003 criteria increased the prevalence of IFG and identified more IGT and diabetes. However, the increase of cardiovascular risks among newly identified IFG100 subjects came from those who concomitantly had IGT.

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### 1. Introduction

Impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), as defined by the World Health Organization in 1985 [1] and by the American Diabetes Association (ADA) in 1997 [2], respectively, have been found to predict both diabetes and cardiovascular diseases. Over the years, however, there have been debates over different aspects of IFG and IGT [3–5]. The prevalence of IGT in the general population is higher than that of IFG [3]. The association between IGT and the development of diabetes, cardiovascular events, and related mortality is stronger than that for IFG [6,7]. Attempting to adjust for these differences and

improve the agreement between the 2 measures, the ADA recommended that the cutoff point for IFG be lowered from 110 to 100 mg/dL in 2003 [8]. Some commentators, however, have questioned the need for this adjustment [9,10]. Several studies from different countries, including Denmark [11], France [12], Italy [13], India [14], and the United States [15], have confirmed that the revised diagnostic criterion actually led to a dramatic increase in the prevalence of IFG, although the consistency between IFG and IGT remained low [16]. One study has shown that the additional IFG individuals identified by the 2003 ADA criteria had a significantly lower cardiovascular risk when compared with IFG subjects with fasting plasma glucose (FPG) of 110 to 125 mg/dL [16]. In this study, we evaluate the impact of lowering the IFG diagnostic criteria for the concordance between IFG and IGT with regard to prevalence and cardiovascular risks in Taiwanese with FPG levels

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between 100 and 109 mg/dL. We attempted to compare the different cardiovascular risk factors between the additionally identified IFG subjects (FPG, 100–109 mg/dL), those with normal fasting glucose (NFG) (FPG, <100 mg/dL), and also those with the originally defined IFG (FPG, 110–125 mg/dL). Thus, the clinical significance of applying the 2003 criteria to the indigenous Taiwanese population will be determined.

## 2. Study design and methods

A total of 1411 volunteer subjects without known diabetes, aged 30 years and older, were recruited for this study. The sample consisted of 602 men and 809 women with a mean age of  $54.51 \pm 10.73$  years. Written informed consent was obtained from each participant at the time of enrollment, and the protocol for this study was approved by the institutional review board at Kaohsiung Medical University Hospital. Anthropometric data, including body weight (BW), height, abdominal girth (AG), and blood pressure (BP), were measured using standardized techniques. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. All subjects underwent an overnight fast of 12 hours before blood tests for FPG, cholesterol (Chol), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). Study subjects further received the 75-g oral glucose tolerance test (OGTT). The 2-hour postload plasma glucose (2-hour PG) was then measured. The prevalence of IFG and IGT was calculated twice: first according to the 1997 [2] and then according to the 2003 [8] ADA criteria.

To compare the distributions of cardiovascular risks, we divided our sample into NFG (FPG, <100 mg/dL), IFG100 (FPG, 100–109 mg/dL), IFG110 (FPG, 110–125 mg/dL), and diabetes mellitus (DM) (FPG,  $\geq 126$  mg/dL). To focus on those subjects with NFG and IFG, 82 participants with FPG of at least 126 mg/dL were excluded from the following statistical analyses. Comparisons for NFG, IFG100, and IFG110 were done first. Then, based on the results of the OGTT, NFG and IFG100 groups were subdivided into NFG/NGT (normal glucose tolerance), NFG/IGT, IFG100/NGT, and IFG100/IGT for further analyses.

Statistical analyses with post hoc Scheffe tests of analysis of variance were used to compare each variable between groups and subgroups. The SPSS software package (version 10.0; SPSS, Chicago, IL) was used for all analyses.  $P < .05$  (2-sided) was considered statistically significant.

## 3. Results

In total, this study included 1411 people without known diabetes. We compared the results based on 1997 and 2003 ADA criteria (Table 1). Based on the 1997 ADA criteria, 74 subjects (5.2% of all participants) were identified as having IFG (FPG, 110–125 mg/dL). Twenty-four (1.7%) were identified as having NGT, 28 (1.9%) IGT, and 22 (1.6%) DM, using OGTT to further study these IFG participants. Based on the ADA 2003 criteria, 275 (19.4%) were diagnosed as having IFG (FPG, 100–125 mg/dL). Oral glucose tolerance test results indicated that of the participants with IFG, 133 (9.4%) had NGT, 99 (6.9%) IGT, and 43 (3.1%) DM. Of the 275 participants with IFG, 201 (14.2%) had FPG levels ranging between 100 and 109 mg/dL. When OGTT was performed on these 201 subjects, 109 (7.7%) were identified as having NGT, 71 (5.0%) IGT, and 21 (1.5%) DM.

Of the 1255 participants identified by the 1997 ADA criteria as having NFG, 45 (3.2%) were identified by OGTT as having DM and 250 (17.7%) as having IGT. Of the 1054 participants identified by the 2003 ADA criteria as having NFG, 24 (1.7%) were identified by OGTT as having DM and 179 (12.7%) as having IGT (Table 1).

When using 2003 IFG criteria revised by the ADA, the percentages of IGT ( $n = 71$ , 35.3%) and DM ( $n = 21$ , 10.5%) in the additionally identified IFG subjects ( $n = 201$ ) were significantly higher than the percentages of IGT ( $n = 179$ , 17%) and DM ( $n = 24$ , 2.3%) in the 1054 participants with NFG ( $\chi^2 = 17.86$ ,  $P < .001$ ).

We compared the demographic data and cardiovascular risks of the subjects with NFG, IFG100 (FPG, 100–109 mg/dL), and IFG110 (FPG, 110–125 mg/dL) (Table 2). The mean values of BW, BMI, AG, systolic BP (SBP), diastolic BP (DBP), 2-hour PG, and TG in IFG100 and IFG110 groups were significantly higher than they were in the NFG group. The IFG100 group also had a significantly lower HDL-C value than the NFG group. Comparing the

Table 1  
Distribution of the study population based on the 1997 and the 2003 criteria

		FPG						
2-h PG	n	ADA 1997			ADA 2003			
		NFG	IFG	Diabetes	NFG	IFG	Diabetes	
		(<110 mg/dL)	(110-125 mg/dL)	(≥ 126 mg/dL)	(<100 mg/dL)	(100-109 mg/dL)	(110-125 mg/dL)	(≥ 126 mg/dL)
NGT	992	960 (68.0)	24 (1.7)	8 (0.6)	851 (60.3)	109 (7.7)	24 (1.7)	8 (0.6)
IGT	290	250 (17.7)	28 (1.9)	12 (0.9)	179 (12.7)	71 (5.0)	28 (1.9)	12 (0.9)
DM	129	45 (3.2)	22 (1.6)	62 (4.4)	24 (1.7)	21 (1.5)	22 (1.6)	62 (4.4)
Total	1411	1255 (88.9)	74 (5.2)	82 (5.9)	1054 (74.7)	201 (14.2)	74 (5.2)	82 (5.9)

Data are expressed as n (%). Percentages are calculated with the study population of 1411 as the denominator.

Table 2  
Demographic characteristics among groups of NFG, IFG100, and IFG110

Group	NFG	IFG100	IFG110
FPG (mg/dL)	<100	100–109	110–125
n	1054	201	74
Age	53.92 ± 10.28	54.92 ± 11.60	56.64 ± 11.61
BW (kg)	60.71 ± 9.64	63.12 ± 10.48**	66.26 ± 10.38***
BMI (kg/m <sup>2</sup> )	24.01 ± 3.18	24.80 ± 3.86**	25.65 ± 3.30***
AG (cm)	80.27 ± 9.47	82.40 ± 10.85*	85.69 ± 9.26***†
SBP (mmHg)	127.62 ± 18.64	132.86 ± 20.16**	138.68 ± 20.98***
DBP (mmHg)	83.03 ± 11.15	86.60 ± 11.50***	88.21 ± 13.89**
2-h PG (mg/dL)	115.12 ± 33.26	142.22 ± 44.12***	172.01 ± 54.24***††
Chol (mg/dL)	214.68 ± 40.05	214.05 ± 41.03	223.86 ± 44.25
TG (mg/dL)	132.72 ± 93.87	152.10 ± 138.14*	156.05 ± 77.93*
HDL (mg/dL)	56.24 ± 14.97	53.25 ± 13.22*	54.30 ± 15.55
LDL (mg/dL)	132.00 ± 36.52	130.97 ± 39.43	138.35 ± 36.14

Data are expressed as mean ± SD. Chol indicates cholesterol.

\*  $P < .05$  vs NFG.

\*\*  $P < .01$  vs NFG.

\*\*\*  $P < .001$  vs NFG.

†  $P < .05$  vs IFG100.

††  $P < .001$  vs IFG100.

IFG100 group with the IFG110 group, we only found significant differences in mean AG and 2-hour PG values.

To weigh the influence of glucose intolerance on demographic and cardiovascular factors in participants with NFG and IFG100, we subdivided the 2 groups into NFG/NGT, NFG/IGT, IFG100/NGT, and IFG100/IGT (Table 3). Body weight, BMI, SBP, DBP, and 2-hour PG values in the IFG100/IGT group were significantly higher than they were in the NFG/NGT group, whereas the IFG100/NGT group had significantly higher DBP and 2-hour PG values than the NFG/NGT group. Most importantly, the NFG/IGT group had significantly higher BMI, AG, SBP, DBP, 2-hour PG, and TG values and significantly lower HDL-C values than the NFG/NGT group. Comparing the data for NFG/IGT, IFG100/NGT, and IFG100/IGT groups, except for the

2-hour PG value, there was no significant difference found in demographic and cardiovascular risk data.

#### 4. Discussion

In this study, we found that lowering the diagnostic cutoff point for IFG from 110 to 100 mg/dL markedly increased the prevalence of IFG and identified more people with IGT and DM. However, 53% (24/45) of the participants with DM and 73% (179/250) of those with IGT in the 1997 NFG group maintained their NFG status when the 2003 criteria was applied. The new IFG participants with FPG levels between 100 and 109 mg/dL (IFG100) were found to be at greater risk for cardiovascular disease than those in NFG group. In fact, increased risk of cardiovascular disease was found mainly in IFG100 subjects with concomitant IGT. These additional individuals with IFG100/IGT who were at increased risk for cardiovascular disease would have been overlooked by the 1997 IFG criteria. Lowering the cutoff point for IFG had identified more people at increased risk for diabetes and for cardiovascular disease, no matter what comparisons were made with the old criteria. So, an FPG of less than 110 mg/dL was not normal.

Our data showed that the 2003 ADA criteria increased the prevalence of IFG from 5.2% to 19.4%, a finding that is consistent with several studies [13,17,18]. Impaired fasting glucose prevalence increased from 3.2% to 9.7% in Italy [13], from 9.5% to 32.3% in Singapore [17], and from 20.4% to 31.9% in the United States [18], using the new diagnostic threshold. Moreover, our study showed that the new IFG criteria identified more people as having IGT and DM, increasing from 3.5% to 10.0% of all participants. We also found the percentage of IGT and DM in the IFG100 group (FPG, 100–109 mg/dL) to be significantly higher than that found in the NFG group. Therefore, the new 2003

Table 3  
Demographic characteristics among subgroups of NFG/NGT, NFG/IGT, IFG100/NGT, and IFG100/IGT

Subgroup	NFG/NGT	NFG/IGT	IFG100/NGT	IFG100/IGT
FPG (mg/dL)	<100	<100	100–109	100–109
2-h PG (mg/dL)	<140	140–199	<140	140–199
n	851	179	109	71
Age	53.42 ± 10.12	55.87 ± 10.96	53.02 ± 11.17	56.01 ± 11.49
BW (kg)	60.35 ± 9.46	62.44 ± 10.12	62.25 ± 9.74	63.83 ± 11.99*
BMI (kg/m <sup>2</sup> )	23.84 ± 3.15	24.81 ± 3.14**	24.23 ± 3.64	25.22 ± 4.08**
AG (cm)	79.82 ± 9.32	82.15 ± 9.63*	81.54 ± 9.94	83.09 ± 12.55
SBP (mm Hg)	126.33 ± 17.86	132.36 ± 19.30**	130.72 ± 21.10	135.37 ± 19.73**
DBP (mm Hg)	82.40 ± 11.01	85.31 ± 10.53*	85.73 ± 12.46*	87.37 ± 10.22**
2-h PG (mg/dL)	102.97 ± 19.98	158.06 ± 15.68***	109.93 ± 17.76**	165.79 ± 15.90***
Chol (mg/dL)	213.68 ± 39.22	216.62 ± 41.94	207.14 ± 36.74	217.08 ± 39.66
TG (mg/dL)	125.47 ± 89.64	161.79 ± 103.27***	145.19 ± 161.69	156.35 ± 109.44
HDL (mg/dL)	56.88 ± 15.04	53.23 ± 13.57*	53.75 ± 13.89	52.04 ± 12.14
LDL (mg/dL)	131.82 ± 36.02	131.03 ± 38.17	125.43 ± 34.74	133.77 ± 40.24

Data are expressed as mean ± SD.

\*  $P < .05$  vs NFG/NGT.

\*\*  $P < .01$  vs NFG/NGT.

\*\*\*  $P < .001$  vs NFG/NGT.

criteria have made it possible to identify more people with DM and IGT than the 1997 criteria.

However, 54.2% (109/201) of newly identified (based on the 2003 criteria) IFG100 subjects were categorized as NGT, whereas only 32.4% (24/74) of those with IFG110 were grouped as NGT according to the 1997 criteria. That is, more people with NGT were labeled as “prediabetes” using the new IFG criteria. As Borch-Johnsen et al [16] and Tai et al [17] pointed out in 2004, this increase in diagnoses could have an enormous impact on the quality of life and finances of the population and affect the cost of health insurance and life insurance as well. On the other hand, 14.4% of all participants, who were found by OGTT to actually have IGT and DM, were diagnosed as having NFG based on the 2003 IFG criteria. Although when the new 2003 IFG cutoff point was used, we found an additional 6.5% of all participants to have IFG100 with OGTT-diagnosed IGT and DM, the new criteria still failed to increase the concordance between IFG and IGT categories. Similar findings were also found in Denmark [16], Italy [13], and the United States [18], in which 40%, 48.5%, and 59.3%, respectively, of the cases of IGT remained undetected using the revised IFG criteria. Our findings, as well as theirs, show that the new IFG criteria identify more cases of IGT and DM and classify more people with NGT as having IFG but fail to completely identify cases of IGT and DM in people with NFG. The failure of the new cutoff point for IFG to identify all cases of IGT may simply mean that IFG and IGT are intrinsically different, although both are labeled “prediabetes.”

The cardiovascular risks in IFG subjects with FPG levels between 100 and 125 mg/dL have been reported to be significantly higher than in those with NFG [13,19]. It is also important to evaluate whether the additionally identified IFG100 subjects were at higher or lower cardiovascular risk than NFG or IFG110. Until now, very few studies have addressed this issue. Borch-Johnsen et al [16] and Wen et al [20] have shown that cardiovascular risk factor profiles in those with IFG100 were markedly lower than in those with IFG110. Our study found that the newly identified IFG100 subjects had higher BMI, AG, BP, and TG, and lower HDL-C than NFG. Compared with the IFG110 group, the IFG100 subjects showed no difference in BP and lipid profiles, although they were found to have greater AG. More recently, Tai et al [17] and Phillips et al [21] reported that IFG100 subjects exhibited a higher percentage of clinical features for metabolic syndrome. In 8-year follow-up study of Tai and colleagues [17], IFG100 subjects were also found to be at greater risks for developing diabetes and ischemic heart diseases than those with NFG and NGT. Based upon these reported findings, IFG100 can be considered an intermediate state that exists between NFG and IFG110. Therefore, identifying people with FPG levels between 100 and 109 mg/dL may be necessary because they have a higher percentage of cardiovascular risk factors, ischemic heart diseases, and related mortality than those with NFG due to their increased risk of developing diabetes.

Although we found the participants who had IFG100 to have more cardiovascular risk factors, increased risk resided mainly in those with IFG100 who also had IGT. We found the IFG100/IGT group to have significantly higher BW, BMI, SBP, and DBP than the NFG/NGT group. The mean TG and LDL-C in the IFG100/IGT group were also higher than in the NFG/NGT group, although not significantly so. In the participants with IFG100/NGT, only DBP was significantly higher than in those with NFG/NGT. In fact, subjects with NFG/IGT had significantly higher BMI, AG, BP, and TG values, and lower HDL-C values than those in the NFG/NGT group. Therefore, IGT was proved in our study to indicate a greater cardiovascular risk not only in those with IFG100 but also those with FPG levels of less than 100 mg/dL, the new diagnostic threshold for IFG in 2003. This is in agreement with many previous studies that compare subjects with IGT with those with IFG110 or IFG100 plus IFG110 [3-5,7,13,16,19,22,23] and emphasizes the stronger associations of cardiovascular risk factors with IGT rather than with IFG. Thus, it is reasonable to assume that IFG and IGT represent distinct phenotypes with different pathophysiologies [24], a postulation that has been supported by many studies [23,25-31]. Individuals with isolated IGT have been found to be more insulin resistant than those with isolated IFG [23,26,28-30], whereas those with IFG have been reported to have a more pronounced defect in early insulin secretion than those with IGT [25,27,31].

The main limitation in our study is that the sample size is small and confined to a certain region in southern Taiwan. In addition, this study was performed on a voluntary basis, and subjects who participated in it were probably more health-conscious than randomly chosen participants would be. Therefore, the actual prevalence of impaired glucose metabolism might be underestimated, and our results may not be extrapolated to general populations. The cross-sectional nature of this study exhibited only the association of FPG with cardiovascular risks rather than causality.

In summary, the 2003 ADA criteria for IFG greatly increased the prevalence of IFG and identified more people with IGT and DM. However, although the new criteria classified more participants with NGT as having IFG, it still left many participants with NFG who also had IGT and diabetes unrecognized. Although the additionally diagnosed IFG subjects with FPG levels from 100 to 109 mg/dL clearly had more cardiovascular risk factors than those with NFG, increases in cardiovascular risks were mainly found in participants who had IFG with concomitant IGT.

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