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Letters

Observations

Predictors of the development of impaired fasting glucose versus impaired glucose tolerance are partly different in men: a 6-year follow-up study

To the Editor: Some studies have confirmed that impaired glucose tolerance and Type 2 diabetes share common aetiological factors such as obesity, abdominal obesity, insulin resistance, impaired insulin secretion, family history of diabetes, age and sedentariness [1, 2]. As for IGT, impaired fasting glucose is considered as an intermediate metabolic state between normal and diabetic glucose homeostasis. The aetiology of IFG, however, remains unclear. Several studies have suggested that IGT and IFG are two classes of glucose homeostasis disorders, which could describe two distinct populations with differing cardiovascular risk [2, 3].

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Our aim was to examine factors potentially related to the development of impaired glucose regulation in a sample of men tested over a 6-year follow-up who all had a normal glucose tolerance at baseline. No study has yet documented the respective contribution of regional body-fat distribution as measured by computed tomography (CT) and of indices of plasma glucose-insulin homeostasis to the development of IFG in men. Therefore, as a specific objective, we compared isolated IFG to isolated IGT in terms of their metabolic and anthropometric predictors.

The study was conducted in men (20–62 years of age at baseline) recruited through media advertising in the Quebec City metropolitan area. All subjects were healthy and were not under treatment for coronary heart disease, diabetes, dyslipidaemias or endocrine disorders. At baseline, all men involved in this study had a NGT. At follow-up (mean follow-up: 6.4±1.1 year), some men developed a deteriorated glucose tolerance state whereas others remained with a NGT. A total of 71 men had a NGT at baseline and kept a NGT at follow-up whereas 24 developed an impaired glucose regulation state (did not remain NGT). Among the 24 men who developed impaired glucose regulation, 8 developed isolated IFG and 12 developed isolated IGT. The American Diabetes Association diagnostic criteria (1997) were used to determine the glucose tolerance status [4]. All participants signed an informed consent document before entering the study, which was approved by the Laval University Medical Ethics Committee.

Height, body weight, waist and hip circumferences as well as body fat mass were measured using standardised procedures

Table 1. Baseline characteristics of men with either NGT, isolated IFG or isolated IGT at follow-up

	Remained NGT (*n*=71)	Developed isolated IFG (*n*=8)	Developed isolated IGT (*n*=12)
Physical characteristics			
Age (years)	37.2±12.3	43.4±9.2	41.7±13.4
BMI (kg/m^2)	25.3±3.5	25.9±2.9	27.7±4.7[a]
Body fat mass (kg)	16.7±7.3	18.2±6.9	20.7±9.9
Waist circumference (cm)	88.4±9.8	89.3±10.4	95.8±12.7[a]
Waist-to-hip ratio	0.90±0.06	0.90±0.06	0.95±0.07[a]
Visceral AT (cm^2)	101±54	103±31	134±68
Subcutaneous AT (cm^2)	186±103	230±92	243±145
Insulin-glucose homeostasis			
Fasting plasma glucose (mmol/l)	5.04±0.37	5.46±0.37[a]	5.06±0.25
2-h plasma glucose (mmol/l)	5.09±1.08	5.48±1.43	6.12±1.00[a]
Fasting insulin (pmol/l)	54.5±26.6	52.4±26.3	58.1±36.0
Stumvoll index 1st phase	1946.8±591.4	1500.3±279.1[a]	1707.3±473.2
Cederholm index	19.1±4.1	17.3±3.9	16.5±4.6

Data are means ± SD
[a] Significantly different from men with NGT ($p<0.05$)
CT, computed tomography; AT, adipose tissue
Statistical analyses were done on age-adjusted values

as reported previously [1]. All measurements were done at baseline and at follow-up. Measurements of abdominal adipose tissue (AT) areas were done by CT at baseline and at follow-up with a Siemens Somatom DRH scanner (Erlangen, Germany) as described previously [1]. A 180-min OGTT (75-g) was carried out after an overnight fast at baseline and follow-up visits. Fasting plasma glucose (FPG) concentrations were measured in duplicate. Plasma glucose and insulin were measured as described previously [1]. The coefficients of variation for the glucose and insulin measurements were 1.3% and 7.7% respectively. Beta-cell function was estimated during the OGTT with the Stumvoll 1st phase equation [5]: Stumvoll 1st phase: 700+[1283+(1.829×plasma insulin 30 min)–(138.7×plasma glucose 30 min)+(3.372×fasting insulin)]. The insulin sensitivity was estimated with Cederholm index which required OGTT data [6]: Cederholm index: {[75000+(FPG–plasma glucose 120 min)×1.15×180×0.19×body weight]/[120×log (mean plasma insulin)×(mean plasma glucose)]}.

Men who developed isolated IFG had at baseline body composition and body-fat distribution variables that were not significantly different from men who remained NGT throughout the follow-up (Table 1). In contrast, men who developed isolated IGT during the follow-up had significantly higher BMI, waist circumference and waist-to-hip ratio than men who remained NGT and tended (p=0.09) to have higher visceral AT accumulation.

Men who developed isolated IFG during the follow-up had, at baseline, higher FPG concentrations and lower insulin secretion as evaluated by Stumvoll 1st phase index than men who maintained a NGT (Table 1, p<0.05). At baseline, 2-h plasma glucose (2-h PG) was significantly higher in men who developed isolated IGT than in men who maintained a NGT throughout follow-up (Table 1) whereas insulin sensitivity, as expressed with the Cederholm index, tended to be lower in men who developed isolated IGT compared with men who remained NGT (p=0.07).

In comparison with observations made at baseline, we found at follow-up that men who developed isolated IFG had a significantly lower insulin sensitivity than men who kept a NGT (p<0.05) but had higher insulin sensitivity than men who developed isolated IGT (p<0.05). Differences in early insulin secretion that were observed at baseline still tended to be present at follow-up between men who developed isolated IFG and men who maintained a NGT (p=0.053).

In agreement with previous observations, men who developed isolated IGT were characterised at baseline by increased BMI and waist circumference, and also tended to have higher visceral AT areas than men who remained NGT over the follow-up. From a clinical standpoint, these results suggest that the measurement of waist circumference can help identify subjects at risk for developing isolated IGT. However, our results indicate that measuring waist circumference or BMI would not be helpful to identify men at risk of developing IFG because no significant differences in body composition and body-fat distribution indices were observed at baseline between men who developed isolated IFG and men who remained NGT.

Men who developed isolated IFG were characterised at baseline by higher FPG concentration than men who remained NGT. From a clinical perspective, these results suggest that a marginally increased FPG (≈5.5 mmol/l) could be an indicator of further risk of IFG development and could be used as a predictive measure. In contrast, men who developed isolated IGT during the follow-up were characterised at baseline by higher 2-h PG concentrations but similar FPG than men who maintained NGT. Therefore, results showing an increased FPG at baseline in men who subsequently developed isolated IFG and increased 2-h PG in men who developed isolated IGT, support the notion of a progressive deterioration in glucose homeostasis from normal to marginally increased and to clinically relevant increase.

At baseline, men who eventually developed isolated IGT showed a tendency for a higher degree of insulin resistance than men who kept a NGT (p=0.07). Insulin resistance found in men who further developed isolated IGT is consistent with the increased adiposity found in these men and is concordant with other studies [7, 8]. In contrast, men who developed isolated IFG were not characterised by increased insulin resistance at baseline but rather by decreased early insulin secretion. These results suggest that reduction in the first-phase insulin secretion could be an early event in the development of isolated IFG. Presence of reduced early insulin secretion could explain the fact that at baseline, men who developed isolated IFG were already characterised by marginally increased FPG concentrations. A recent study has reported that the normal control of FPG depends on the ability of the beta cell to maintain adequate early insulin secretion [3].

Our results suggest that some risk factors for IFG and IGT could be different. For men who developed isolated IGT, increased adiposity associated with insulin resistance and increased 2-h PG can be suggested as predictive of an increased IGT risk. In contrast, in men who eventually developed IFG, increased FPG and decreased insulin secretion appeared to be the most important features at baseline.

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References

1. Pascot A, Després JP, Lemieux I et al. (2000) Contribution of visceral obesity to the deterioration of the metabolic risk profile in men with impaired glucose tolerance. Diabetologia 43:1126–1135
2. Tominaga M, Eguchi H, Manaka H, Igarashi K, Kato T, Sekikawa A (1999) Impaired glucose tolerance is a risk factor for cardiovascular disease, but not impaired fasting glucose. The Funagata diabetes study. Diabetes Care 22:920–924
3. Unwin N, Shaw J, Zimmet P, Alberti KG (2002) Impaired glucose tolerance and impaired fasting glycaemia: the current status on definition and intervention. Diabet Med 19:708–723
4. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (1997) Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 20:1183–1197
5. Stumvoll M, Mitrakou A, Pimenta W et al. (2000) Use of the oral glucose tolerance test to assess insulin release and insulin sensitivity. Diabetes Care 23:295–301
6. Cederholm J, Wibell L (1990) Insulin release and peripheral sensitivity at the oral glucose tolerance test. Diabetes Res Clin Pract 10:167–175
7. Haffner SM, Miettinen H, Gaskill SP, Stern MP (1996) Decreased insulin action and insulin secretion predict the development of impaired glucose tolerance. Diabetologia 39: 1201–1207
8. Tripathy D, Carlsson M, Almgren P et al. (2000) Insulin secretion and insulin sensitivity in relation to glucose tolerance. Lessons from the Botnia Study. Diabetes 49:975–980

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Abbreviations: AT, Adipose tissue · CT, computed tomography · FPG, fasting plasma glucose · 2-h PG, 2-h plasma glucose

Acute metabolic cataract as a first manifestation of diabetes mellitus in a 12-year-old girl

Keywords Juvenile cataract · Mitochondrial diabetes · 3243 mitochondrial tRNA mutation · Oxidative stress · MELAS

To the Editor: We report a case of juvenile cataract and Type 2 diabetes in a 26-year-old female (154 cm, 51 kg). A sibling of her mother had impaired glucose tolerance. Polydipsia and leg paresthesia were apparent in this patient with cataract since the age of 10, and she was diagnosed with diabetes at the age of 12. On her first visit, her intelligence and physical examination results were normal, except for bilateral cataracts (an unusual manifestation in a 12-year-old girl). Ptosis, ophthalmoplegia and hearing loss were not observed. Her fasting plasma glucose concentration was 25.3 mmol/l, and her HbA_{1c} was 20.1%. Other laboratory examination data were normal. She began intensive insulin treatment and 4 months later her HbA_{1c} rapidly decreased to 5.9%, and the leg paresthesia disappeared. She underwent successful bilateral cataract extraction with intraocular lens implantation. Four years later, she stopped insulin therapy and has been under excellent control (HbA_{1c} 6.0%) with oral hypoglycaemic agents, and she has been free of symptoms.

Neuroimaging findings at the globus pallidus are a sign of MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes) or mitochondrial diabetes. In this patient, high intensity areas in the bilateral globus pallidus were noted on T1-weighted magnetic resonance imaging at the age of 18 (Fig. 1). However, she was not recognised as showing signs of mitochondrial disease, because the results of detecting mitochondrial DNA (*mtDNA*) mutation at position ***3243*** were negative in the laboratories, where the cut-off degree of heteroplasmy ranged from 0.2 to 1%. Informed consent was obtained and the study was approved by the local ethics committee of Saiseikai Central Hospital. Other important data, as to whether other family members had considerable mitochondrial *DNA* mutation, were not available.

A new technology using real-time PCR with a TaqMan Probe was introduced in *Diabetologia* [1], which can quantify as little as 0.001% of the *3243 mtDNA* mutation in blood cells.

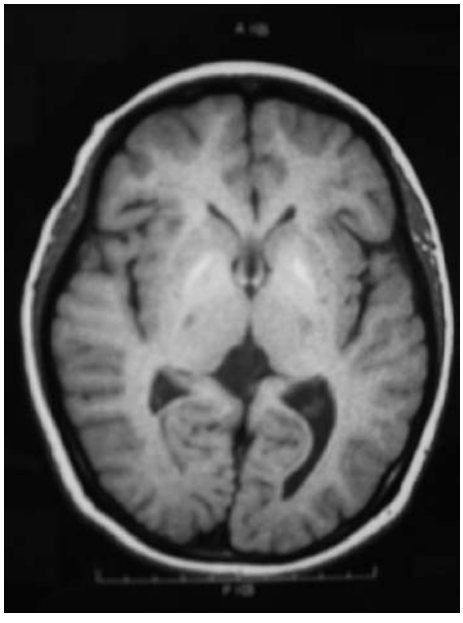

Fig. 1. High intensity areas in the bilateral globus pallidus were noted on T1-weighted magnetic resonance imaging

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