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Short-term reproducibility of impaired fasting glycaemia, impaired glucose tolerance and diabetes The ADDITION study, DK

S.S. Rasmussen [a,*], C. Glümer [b], A. Sandbaek [c], T. Lauritzen [c], B. Carstensen [a], K. Borch-Johnsen [a,c]

[a] Steno Diabetes Center, Niels Steensensvej 2, DK-2820 Gentofte, Denmark
[b] Research Centre for Prevention and Health, Glostrup, Denmark
[c] Institution of Public Health, Department of General Practice, University of Aarhus, Denmark

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ABSTRACT

We evaluated variations in glucose measurements and the reproducibility of glucose tolerance classification in a high-risk screening setting in general practice.

Screening for diabetes was performed in persons aged 40–69 years. Based on capillary fasting (FBG) and 2-h blood glucose (2 hBG) individuals with impaired fasting glycaemia (IFG), impaired glucose tolerance (IGT) and diabetes had a second test done after 14 days. Intra-individual coefficients of variation (CV) were estimated in each glucose tolerance class using the approximation $CV^2(x) = \mathrm{var}(\ln(x))$. Bland–Altman plots with limits of agreement were made.

In the total population, the CV_{intra} was 7.9% and 13.8% for FBG and 2 hBG, respectively. Limits of agreement ranged from −1.15 to 1.67 mmol/l for FBG and from − 2.62 to 3.27 mmol/l for 2 hBG. One individual with IFG and 22.5% with IGT had diabetes at the second test, 76.1% with diabetes had this diagnosis confirmed, and about 30% with IFG and IGT had normal glucose tolerance at the second test.

The expected values of repeated capillary blood glucose measurements were about ± 1 and ± 3 mmol/l for FBG and 2 hBG, respectively. Yet, 70% of high-risk prediabetic individuals were persistently classified with abnormal glucose regulation; diabetes was confirmed in 76% of the cases.

1. Introduction

Since 1999, the glucose tolerance classification by the World Health Organization (WHO) includes impaired fasting glycaemia (IFG) as well as impaired glucose tolerance (IGT) defined by fasting glucose and 2-h glucose after an oral glucose tolerance test (OGTT) [1]. The diagnosis of diabetes in asymptomatic individuals requires two diabetic test results on separate days. This is not required for IFG or IGT.

It is known though, that there are considerable intra-individual variations in fasting glucose and after an OGTT; giving rise to misclassification in the abnormal glucose tolerance groups [2–12]. Most studies, though, have used long time intervals between tests and therefore do not represent

* *Corresponding author*. Tel.: +45 44 43 90 77; fax: +45 44 43 07 06.
E-mail address: sssr@steno.dk (S.S. Rasmussen).
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pure reproducibility. They also reflect metabolic progressions and interventions taking place in the time interval between the tests.

Pure reproducibility has to be examined by tests within a short-time interval where progression in glucose intolerance is unlikely to occur. Few studies have evaluated the reproducibility of glucose measurements by two repeated standard OGTTs within a short-time frame (about 2 weeks) [7,9,10,12]. These studies took place in centralised centres or at hospitals and did not evaluate the glucose tolerance categories including IFG. The risk of misclassification of IFG and IGT is greater than of diabetes because IFG and IGT represent intervals of glucose levels while diabetes has an upper ''open end''. In particular, is IFG based on an interval covering a range of only 0.5 mmol/l (blood glucose) or 0.8 mmol/l (plasma glucose) which may be exceeded by the intra-individual variation.

Our aim was to evaluate the Short-term intra-individual variation of fasting and 2-h capillary whole blood glucose by repeating the tests within 14 days for individuals with IFG, IGT and diabetes, and to evaluate the magnitude of misclassification in a high-risk screened population in general practice.

2. Subjects and methods

2.1. *Study population and design*

The study population is based on the ADDITION study, DK, which is a population-based, high-risk screening and intervention study for type 2 diabetes in general practice [13,14]. In the present substudy, based on an opportunistic screening approach (Fig. 1), a risk score questionnaire was handed out to patients aged 40–69 years, having an appointment at the participating general practices. This screening step was followed by the diagnostic test, fasting capillary blood glucose (FBG), on another day in individuals who reported high scores. At this second visit, a blood sample for HbA1c measurement was taken and mailed to the central laboratory. An OGTT was performed and the 2-h capillary blood glucose (2 hBG) measured within the same consultation if FBG was elevated or in a subsequent consultation if the FBG was normal but HbA1c $\geq$5.8%. All individuals identified with IFG, IGT or diabetes had a confirmatory test done within approximately 14 days and 2 hBG was measured at each visit if FBG was not in the diabetic range at the respective visit. After the first diagnostic visit, the persons were informed of their glucose tolerance status as they were explained that a second test on another day was indicated. They were instructed to be fasting at both the diagnostic tests. There were no restrictions on diet or physical activity until fasting and no specific instruction was given on lifestyle changes before the second test.

Because of the high-risk screening approach, individuals considered at low risk at the initial steps did not proceed for the diagnostic tests. Individuals with normal glucose tolerance (NGT) were therefore to a large extend not identified. Only few had normal glucose tolerance at the diagnostic step and it was impractical to have these few persons recruited for a confirmatory test.

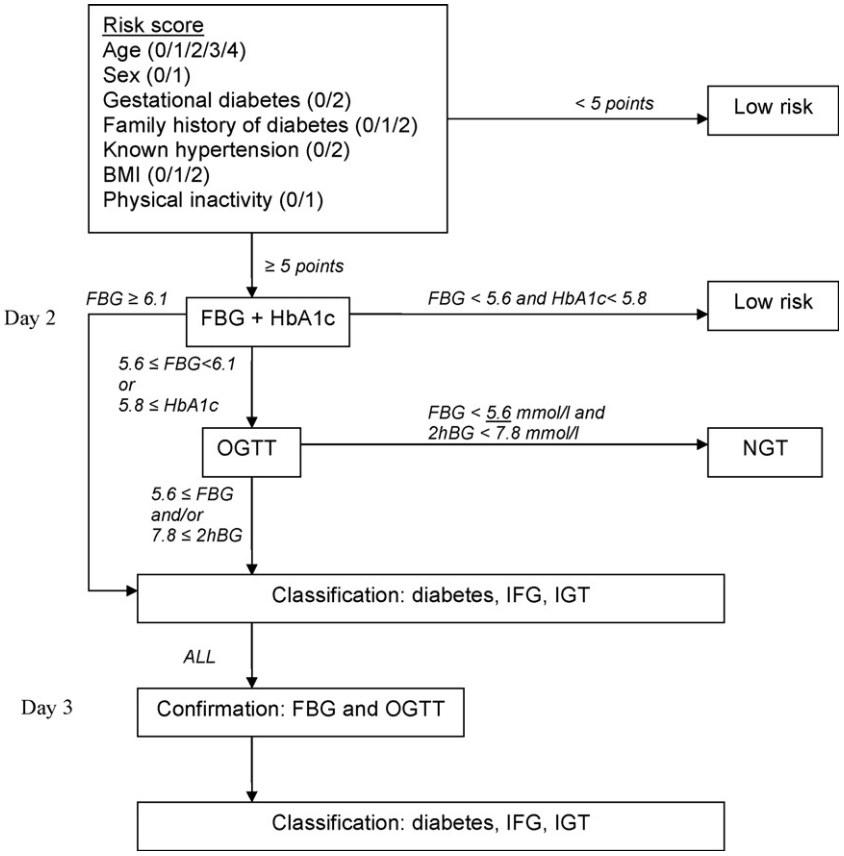

Fig. 1 – The modified screening algorithm in the ADDITION study, DK – the opportunistic screening substudy.