Lack of Concordance between the 75-g and 100-g Glucose Load Tests for the Diagnosis of Gestational Diabetes Mellitus

Giorgio Mello,1 Parretti Elena,1 Agostino Ognibene,2* Riccardo Cioni,1 Filippo Tondi,1 Paola Pezzati,2 Monica Pratesi,3 Gianfranco Scarselli,1 and Gianni Messeri2

Background: Gestational diabetes mellitus (GDM) is common and can have a substantial impact on fetal growth, birth weight, and morbidity. The American Diabetes Association recommends GDM testing with either a 3-h, 100-g glucose load (100g) (criteria according to *Am J Obstet Gynecol* 1982;144:768–73) or a 2-h, 75-g glucose load (75g). We investigated the comparability of the 75g and the 100g tests in the diagnosis of GDM.

Methods: From January 1997 to December 1999, in 1061 consecutive Caucasian nonobese and nondiabetic pregnant women who attended the Maternal-Fetal Medicine Unit, we performed GDM testing with a 75-g load during 2 periods of pregnancy: early (16–20 weeks) and late (26–30 weeks). Because we assumed there would be few GDM cases in women with a 1-h plasma glucose <1300 mg/L in the 75g test, we did not retest these women. We retested the remaining women with possible or diagnosed GDM with a 100-g load within a week.

Results: GDM was diagnosed in 41 of 227 women with the 100-g load and 15 of 227 with the 75-g load (11 concordant); the κ index was 0.21. At 26–31 weeks of pregnancy, 484 of 976 women (49.9%) underwent both tests. GDM was diagnosed in 60 of 484 woman with the 100-g load and in 26 of 484 with the 75-g load (13 concordant); the κ index was 0.18.

Conclusions: Among women with possible GDM in both early and late periods of pregnancy, there was only weak diagnostic agreement between results determined with 75-g and 100-g glucose loads.

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Gestational diabetes mellitus (GDM)4 is a common disturbance that can have a substantial impact on pregnancy outcomes such as fetal growth, birth weight, and morbidity. For this reason, most pregnant women in developed countries undergo GDM testing as part of routine antenatal care. The Clinical Practice Recommendations issued by the American Diabetes Association (ADA) in 2003 (1) state that GDM is diagnosed on the basis of the oral glucose tolerance test (OGTT). The OGTT can consist of either a 3-h, 100-g glucose load (100g) [criteria of Carpenter and Coustan (2)] at fasting and 1, 2, and 3 h after glucose load, or a 2-h, 75-g glucose load (75g), with the same criteria at fasting and 1 and 2 h after glucose load. This recommendation derives from the conclusions of the ADA Fourth International Workshop Conference on Gestational Diabetes Mellitus, held in March 1997, where it was first suggested that both tests, at the same cutoff values, could be used to diagnose GDM (3).

Despite their supposed equivalence, the 2 tests clearly have many relevant differences and have not been compared thus far as to their usefulness for identifying women with GDM in the same population. The aim of this study was to compare the performance of the 75g and 100g tests in pregnant women with possible or diagnosed GDM according to the 75g test.

1 Department of Gynecology, Perinatology and Human Reproduction, University of Florence, Firenze, Italy.
2 Department of Laboratory, Clinical Chemistry Laboratory, Azienda Ospedaliero–Universitaria Careggi, Firenze, Italy.
3 Department of Statistics and Mathematics Applied to Economics, University of Pisa, Pisa, Italy

*Address correspondence to this author at: Department of Laboratory, Clinical Chemistry Laboratory, Azienda Ospedaliero–Universitaria Careggi, Viale Morgagni 85, 50139 Firenze, Italy. Fax: 39-55-4279390; e-mail: a.ognibene@med.unifi.it.

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4 Nonstandard abbreviations: GDM, gestational diabetes mellitus; ADA, American Diabetes Association; OGTT, oral glucose tolerance test; 100g, 3-h, 100-g glucose load; 75g, 2-h, 75-g glucose load; AUC, area under the curve.
Material and Methods

From January 1997 to December 1999, 1061 consecutive Caucasian nonobese and nondiabetic pregnant women with singleton pregnancy attending the Maternal-Fetal Medicine Unit of the Department of Gynecology, Obstetrics and Gynecology, and Human Reproduction of the University of Florence were tested for GDM with a 75g OGGT performed during 2 periods of pregnancy: early (16–20 weeks) and late (26–30 weeks).

Details of maternal demographic and anthropometric characteristics were obtained from all women at the time of first 75g test (16–20 weeks). Gestational age had been determined by first trimester dating scan.

Early pregnancy (16–21 weeks). All pregnant woman underwent a 75g test at 16–20 weeks of pregnancy. To identify and treat women with gestational diabetes as soon as possible, as recently described (4), we chose to begin screening for GDM at a time different from the ADA recommendation of 24–28 weeks.

We collected venous blood samples into iodofluoride vacutainer tubes (Becton Dickinson and Company) and measured plasma glucose at fasting and at 60 and 120 min after the 75-g load. We assumed that there were few GDM cases among the women with a 1-h result <1300 mg/L on the 75g test; accordingly, for all women with a plasma glucose concentration ≥1300 mg/L after 1 h, we performed a 100g test within 1 week. Carpenter and Coustan (2) diagnostic criteria were used for the 100g interpretation. Diagnosis of GDM was made when 2 or more venous plasma glucose concentrations met or exceeded the following concentrations: fasting concentration, 950 mg/L; 1-h results, 1800 mg/L; 2-h, 1550 mg/L; and 3-h, 1400 mg/L. To interpret the results of the 75g test, we used the same criteria without the 3-h value, as recommended by the Fourth International Workshop Conference on Gestational Diabetes Mellitus Recommendations.

Our study design is comparable to the study design adopted by Pettitt et al. (5), in which a 75-g glucose load was administered to nonfasting women during pregnancy for the diagnosis of impaired glucose tolerance and diabetes. They tested women with a 1-h plasma glucose of ≥7.8 mmol/L with a 100-g load after an overnight fast. Because the glucose load makes little difference in the glucose concentration at 1 h in persons with typical glucose tolerance (5), this cutoff point is comparable to a glucose concentration of 7.8 mmol/L after a 50-g load, the concentration above which the 100g test is recommended according to National Diabetes Data Group criteria.

Late pregnancy (26–31 weeks). All women without GDM according to 75g or 100g tests at 16–21 weeks of pregnancy were retested at 26–30 weeks with a 75-g glucose load. Assuming that very few GDM cases would be found among the women with a 1-h result of <1300 mg/L on the 75g test, we performed a 100g test within 1 week only in women with a plasma glucose concentration ≥1300 mg/L after 1 h for the 75g test.

We performed data analysis on results obtained from women who underwent both 75g and 100g tests (Fig. 1). Forty-four of 1061 women (4.1%) were excluded from the study; of these, 28 of 44 discontinued the GDM screening/diagnosis program, and 16 did not perform the 100g test according to the schedule.

We measured plasma glucose with an automated enzymatic assay performed by Aeroset (Abbott Laboratories).

The study was approved by the Institutional Review Board Project of the Department of Gynecology, Obstetrics and Gynecology, and Human Reproduction of the University of Florence, Italy, and the participants gave written informed consent.

Statistical Analysis

We used the Cohen κ index to assess the overall reliability of the 2 glucose load tests. Values for κ ranged from 0 to 1.00, with higher values indicating better reliability. A κ index of 0–0.2 suggested weak agreement, 0.2–0.4 fair agreement, 0.4–0.8 good agreement, and 0.8–1.0 perfect agreement; 0 values suggested disagreement (6). We also performed analysis with a McNemar test (7) to compare the performance of the 75-g and 100-g glucose loads in the detection of the GDM.

We considered p <0.05 to be statistically significant.

The area under the curve (AUC) was calculated by $\Delta Y \cdot (Y_1 + Y_2)/2$; we used this formula repeatedly for each adjacent pair of points defining the curve. Finally, we summarized the results to obtain the complete area. The curve was defined by the time points 0, 60, and 120 min after glucose load for both the 75g and 100g tests. We performed Bland-Altman analysis to assess the degree of agreement of AUCs for the 75g and 100g tests. We used the Wilcoxon rank-sum test to assess the significance of continuous data and calculated Spearman correlation coefficients for paired responses at each testing interval of the oral glucose load. Statistical analysis was performed with the Statistical Package for the Social Sciences for Windows, version 6.

Results

Maternal demographic and anthropometric characteristics of the women who underwent both the 75g and the 100g tests in early and late periods of pregnancy are reported in Table 1, A and B, respectively.

During the early period, 227 of 1017 women (22.3%) underwent both the 75g and the 100g tests. At this stage, the 100g test was diagnostic for GDM in 41 women (41 of 227, 18.1%), the 75g test in 15 women (15 of 227, 6.7%), and both tests in 11 women. The κ index was 0.21.

The mean glucose load values at each time point for the 227 women during the early period of pregnancy is shown in Table 2A.
Mean glucose concentrations differed significantly between the 2 tests at the 2-h time point but were not significantly higher in the 100g test than the 75g test at the fasting and 1-h time points. A significant correlation between the glucose concentrations for the 2 tests at parallel time points between was found only at 60 min.

In the late period, 484 of 976 women (49.6%) underwent both the 75g and the 100g tests. At this stage, the 100g test was diagnostic for GDM in 60 women (60/484, 12.4%), the 75g test in 26 women (26/484, 4.4%), and both tests in 11 women. The $\kappa$ index was 0.18.

The mean glucose load values at each time point for the 484 women during the late period of pregnancy are shown in Table 2B. Mean glucose concentrations differed significantly between the 2 tests at the 2-h time point, and a significant correlation existed between the 2 tests for 1-h and 2-h values.

The differences between the AUCs for the 100g and 75g tests, originating from the same time points (0, 60, and 120 min), were plotted vs the 100g AUC data for the early and late pregnancy period according to the Bland-Altmann method (Fig. 2).
We performed the McNemar test during the early period (16–21 weeks); of 227 women tested, 41 had positive 100g test results, 15 had positive on 75g test results, and 11 had positive results for both tests. Thus GDM was diagnosed in 4 women by the 75g test but not the 100g test and 30 by the 100g test but not the 75g test. The McNemar test results were highly significant \((P < 0.001)\), which may indicate that GDM diagnosis was more likely with the 100g than the 75g test, but in some cases, diagnosis was made by only the 75g test. At the later time point, GDM was diagnosed in 15 women by the 75g test but not the 100g test and in 49 by the 100g test but not the 75g test; the McNemar test results again were highly significant \((P < 0.001)\). Nevertheless, a substantial number of women \((15)\) had positive results only for the 75g test.

### Discussion

In 1997, the Fourth International Workshop Conference on Gestational Diabetes Mellitus issued recommendations for the diagnosis of GDM that are accepted worldwide. It was suggested that the diagnosis of GDM can be made on the basis of an OGTT performed with either a 1-step or a 2-step strategy. The selected cutoff values for the 100g test \((2)\) had been extrapolated from the O'Sullivan and Mahan data and were originally intended to predict the likelihood of maternal overt diabetes later in life, rather than adverse pregnancy outcome and/or GDM-related perinatal morbidity \((8)\).

In the absence of conclusive data relating the test to perinatal outcome, cutoff values for the 75-g glucose load in pregnancy are arbitrary. The same cutoff values were adopted for the 75g and 100g tests, but the 75g test is considered positive when 2 of 3 values are abnormal instead of the 2 of 4 abnormal values required for a positive 100g test \((1)\). The decision to use the same cutoff values was based on previous studies \((5, 9, 10)\).

To date, the 75-g glucose load in pregnancy has been used to a lesser extent than the more traditional 100-g load, probably because the 75g test was developed to diagnose diabetes in nonpregnant persons and has had little validation in pregnant women \((1)\). As Weiss et al. \((11)\) have observed, generalized use of the 75g test recommended by the ADA has been impeded by the lack of data directly comparing this test with the established 100g test. In addition, those studies that have applied both tests have done so to investigate the incidence of adverse pregnancy outcomes successfully predicted by each test \((5, 10, 12)\). The relationship between glucose concentration results from a 75g test and the risk of abnormal neonatal anthropometric features has been explored in a previous investigation by our group performed on 829 glucose-tolerant pregnant women \((4)\). In that study, which was performed with the same study population of 1061 women reported here, we used the 75-g load glucose challenge test with a threshold of 1350 mg/L, prompted by the observation that in glucose-tolerant women, there are no differences between 1-h glucose values after a 50-g load and after a 75-g load. In the current study, we also defined, at the 1-h time point for the 75-g load, threshold glucose values above which there is an increased risk for abnormal neonatal anthropometric characteristics; inter-

### Table 1. Maternal demographic and anthropometric characteristics.

<table>
<thead>
<tr>
<th>Test</th>
<th>75g</th>
<th>100g</th>
<th>(P)</th>
<th>(r)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>79.1 (16)</td>
<td>80.8 (15)</td>
<td>0.56</td>
<td>0.19</td>
<td>0.59</td>
</tr>
<tr>
<td>1 h</td>
<td>156.1 (33)</td>
<td>159.7 (36)</td>
<td>0.11</td>
<td>0.32</td>
<td>0.023</td>
</tr>
<tr>
<td>2 h</td>
<td>129.2 (28)</td>
<td>136.4 (29)</td>
<td>0.0019</td>
<td>0.12</td>
<td>0.66</td>
</tr>
<tr>
<td>3 h</td>
<td>115.4 (26)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Mean glucose values at each time point (75g and 100g).

<table>
<thead>
<tr>
<th>Test</th>
<th>75g</th>
<th>100g</th>
<th>(P)</th>
<th>(r)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>81.4 (14)</td>
<td>81.7 (15)</td>
<td>0.77</td>
<td>0.14</td>
<td>0.062</td>
</tr>
<tr>
<td>1 h</td>
<td>159.6 (28)</td>
<td>161.9 (34)</td>
<td>0.34</td>
<td>0.34</td>
<td>0.019</td>
</tr>
<tr>
<td>2 h</td>
<td>131.9 (27)</td>
<td>138.1 (31)</td>
<td>0.009</td>
<td>0.31</td>
<td>0.028</td>
</tr>
<tr>
<td>3 h</td>
<td>116.3 (27)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Interestingly, this association was observed at 16–20 weeks of pregnancy. Our results therefore suggest that a 1-h, 75-g oral glucose load can be used as a single test for the diagnosis of GDM.

The results of our study, performed on the largest sample of Caucasian women studied so far, suggest that when testing is performed according to ADA recommendations, only a weak agreement between the 75g and 100g test results occurs for women with possible or diagnosed GDM in the early stages of pregnancy. In the late period of pregnancy, our results show a weak amount of agreement. Hence, we can state that the 2 tests cannot be used interchangeably and cannot be assumed to share similar diagnostic characteristics. In addition, the prevalence of diagnosed GDM was lower with the 75g test in both early and late periods of pregnancy. Although the ADA suggests that values for the 2 tests are “similar” (1), this claim was not upheld by our study, in which the 2-h values were significantly different for the 2 tests, even when only the mean values obtained from our results were considered. These findings have also been reported for other studies, such as those conducted by Brustman et al. (13) and Weiss et al. (11). Brustman et al. (13) compared the results of a 3-h, 75-g glucose load OGTT with those of a 100g test in 32 pregnant women from high-risk ethnic groups. They found that the 1-, 2-, and 3-h plasma glucose values for the 100g test were significantly higher than the comparable values for the 75g test in women with normal glucose tolerance and with GDM. In addition, the prevalence of results diagnostic for GDM was found to be higher with the 100g test. Weiss et al. (11) compared 75-g and 100-g glucose loads during a 2-h OGTT in 30 women with GDM and 30 healthy pregnant women and found that in healthy women, plasma glucose concentrations at both 1 and 2 h obtained after a 100-g load were significantly higher than those obtained after a 75-g load. Our results, obtained for a much larger sample population, are in agreement with those of these 2 studies.

The previous results are confirmed by the results of the McNemar test, which indicate that the 100g test is more...
powerful in detecting GDM, a finding that may be attributable to the extra time point, which gives an extra opportunity to cross the threshold, although in some women, GDM was detected only by the less powerful 75g test.

Plotting of the 2 tests by use of Bland-Altman analysis revealed that the AUC of the 75g test was very different from that of the standard 100g test. When differences in the AUC data, originating from the same time points after glucose load, were plotted vs the 100g test, noncomparable results were found for data obtained in the early pregnancy period, as well as in the late pregnancy period. The lack of concordance between the 2 tests that was revealed by our results is hardly surprising, because the 2 tests were developed for different purposes. The 100g test, as originated by O’Sullivan and Mahan (8), was initially intended to predict the likelihood of onset of maternal overt diabetes after pregnancy, whereas the 75g test was developed to diagnose diabetes in nonpregnant persons, and only a few reports describe its use in pregnancy. According to our results, the recommendation that either a 100g or a 75g test can be used to diagnose GDM in the same population by use of the same cutoff values is questionable.

Because we did not repeat the 75g or the 100g test for any of our study participants and because the 2 tests were not performed on the same day, but within a week of one another, it is possible that some of the variation revealed could be caused by day-to-day variability in testing or in glycemic response. To our knowledge, however, no previous studies have examined the reproducibility of either test, and those studies that have compared the 2 tests have also done so within a 1–2-week interval (11, 13, 14).

Our study may represent a preliminary step in the diagnostic accuracy evaluation of the 75-g glucose load OGTT. Further studies are needed to establish the appropriate cutoff values for the use of the 75g test in pregnancy.

References


