The Sensitivity and Specificity of the Glucose Challenge Test in a Universal Two-Step Screening Strategy for Gestational Diabetes Mellitus Using the 2013 World Health Organization Criteria

Diabetes Care 2018;41:e111–e112 | https://doi.org/10.2337/dc18-0556

Katrien Benhalima,[1] Paul Van Crombrugge,[2] Carolien Moyson,[1] Johan Verhaeghe,[3] Sofie Vandeginste,[4] Hilde Verlaenen,[4] Chris Vercammen,[5] Toon Maes,[5] Els Dufraimont,[6] Christophe De Block,[7] Yves Jacquemyn,[8] Farah Mekahli,[9] Katrien De Clippel,[10] Annick Van Den Bruel,[11] Anne Loccufier,[12] Annouschka Laenen,[13] Roland Devlieger,[3] and Chantal Mathieu[1]

The International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommends a universal one-step screening strategy with the 75-g oral glucose tolerance test (OGTT) for gestational diabetes mellitus (GDM) (1). Since the adoption of the IADPSG recommendation by the World Health Organization (WHO), the IADPSG criteria are commonly referred to as the 2013 WHO criteria (2). The IADPSG recommendation remains controversial due to the significant increase in GDM prevalence, increased workload, the need for a fasting test, and the risk for increased medicalization of care (3). Several professional associations therefore still recommend a universal two-step screening strategy, using a nonfasting 50-g glucose challenge test (GCT) to determine whether an OGTT should be performed (3). The GCT is easier to perform and is generally better tolerated than an OGTT. In addition, a two-step screening strategy with a GCT could limit the number of OGTTs. The GCT has been used in combination with the 100-g OGTT or the 75-g OGTT with various diagnostic criteria, but data are lacking on the sensitivity and specificity of the GCT in conjunction with the 2013 WHO criteria for GDM.

We performed a multicentric prospective cohort study, the Belgian Diabetes in Pregnancy Study (BEDIP-N), between 2014 and 2017, enrolling 2,006 women between 6 and 14 weeks of pregnancy (4). Participants without prediabetes or diabetes in early pregnancy (defined by the American Diabetes Association criteria) received both a GCT and 75-g OGTT between 24 and 28 weeks of pregnancy. Participants and health care providers were blinded for the result of the GCT (4). The GCTs were analyzed centrally at the laboratory of the university hospital of Leuven. Because the GCT has not yet been validated in conjunction with the 2013 WHO criteria and the result of the GCT was not used to treat patients, GCT thresholds were not prespecified. The diagnosis of GDM was based on the 2013 WHO criteria (1,2). Of all participants, 1,811 (90.3%) received both a GCT and OGTT between 24 and 28 weeks of pregnancy. The receiver operating characteristic curve showed an area under the curve of 0.77 (95% CI 0.74–0.81) for the GCT. Based on the 75-g OGTT, GDM prevalence was 12.5% ($n = 231$). By using a universal two-step screening strategy with the commonly used GCT thresholds 140 mg/dL (7.8 mmol/L) and 130 mg/dL (7.2 mmol/L), GDM prevalence varied from 7.5 to 9.1% (Table 1). The GCT threshold of 140 mg/dL (7.8 mmol/L) only had a sensitivity of 59.6%. To achieve sensitivity rates ≥70%, the threshold of the GCT would need to be reduced to at least 130 mg/dL

[1]*Department of Endocrinology, University Hospital Gasthuisberg, KU Leuven, Leuven, Belgium*
[2]*Department of Endocrinology, Onze-Lieve-Vrouwziekenhuis Aalst-Asse-Ninove, Aalst, Belgium*
[3]*Department of Gynaecology and Obstetrics, University Hospital Gasthuisberg, KU Leuven, Leuven, Belgium*
[4]*Department of Obstetrics and Gynecology, Onze-Lieve-Vrouwziekenhuis Aalst-Asse-Ninove, Aalst, Belgium*
[5]*Department of Endocrinology, Imelda Ziekenhuis, Bonheiden, Belgium*
[6]*Department of Obstetrics and Gynecology, Imelda Ziekenhuis, Bonheiden, Belgium*
[7]*Department of Endocrinology-Diabetology and Metabolic Diseases, Antwerp University Hospital, Edegem, Belgium*
[8]*Department of Gynaecology, Obstetrics and Fertility, Antwerp University Hospital, Edegem, Belgium*
[9]*Department of Endocrinology, Kliniek Sint-Jan, Brussels, Belgium*
[10]*Department of Obstetrics and Gynecology, Kliniek Sint-Jan, Brussels, Belgium*
[11]*Department of Endocrinology, AZ Sint-Jan, Brugge, Belgium*
[12]*Department of Obstetrics and Gynecology, AZ Sint-Jan, Brugge, Belgium*
[13]*Leuven Biostatistics and Statistical Bioinformatics Centre, KU Leuven, Leuven, Belgium*

Corresponding author: Katrien Benhalima, katrien.benhalima@uzleuven.be.

Received 13 March 2018 and accepted 27 March 2018.

© 2018 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. More information is available at http://www.diabetesjournals.org/content/license.

See accompanying articles, pp. 1337, 1339, 1343, 1346, 1362, 1370, 1378, 1385, and 1391.

Table 1—Sensitivity and specificity of the GCT across different thresholds

Threshold GCT	Abnormal GCTs, % (*n*)	Prevalence of GDM, % (*n*)	Sensitivity, % (95% CI), *n/N*	Specificity, % (95% CI), *n/N*	LR+ (95% CI)	LR− (95% CI)	Positive posttest probability, % (95% CI)	Negative posttest probability, % (95% CI)
≥140 mg/dL	23.9 (441)	7.5 (136)	59.6 (53.0–66.1), 136/228	81.0 (79.0–82.9), 1,282/1,583	3.1 (2.7–3.6)	0.50 (0.42–0.58)	31.7 (26.1–37.5)	6.9 (5.7–8.2)
≥135 mg/dL	29.1 (537)	8.3 (151)	66.2 (59.7–72.3), 151/228	76.1 (73.9–78.1), 1,204/1,583	2.8 (2.4–3.1)	0.44 (0.37–0.53)	29.1 (23.9–34.3)	6.2 (5.1–7.4)
≥130 mg/dL	34.9 (645)	9.1 (165)	72.4 (66.1–78.1), 165/228	70.2 (67.9–72.4), 1,111/1,583	2.4 (2.2–2.7)	0.39 (0.32–0.49)	26.4 (21.7–31.2)	5.5 (5.6–6.6)
≥125 mg/dL	40.8 (754)	9.8 (177)	77.6 (71.7–82.9), 177/228	64.2 (61.8–66.5), 1,016/1,583	2.2 (2.0–2.4)	0.35 (0.27–0.45)	24.3 (20.0–28.7)	4.9 (4.0–6.0)
≥120 mg/dL	48.4 (895)	10.3 (187)	82.0 (76.4–86.8), 187/228	56.0 (53.5–58.4), 886/1,583	1.9 (1.7–2.0)	0.32 (0.24–0.43)	21.6 (17.8–25.6)	4.5 (3.7–5.5)

Sensitivity: *n* = number with GCT ≥cut-off; *N* = number with GDM. Specificity: *n* = number with GCT <cut-off; *N* = number without GDM. LR+: positive likelihood ratio; LR−: negative likelihood ratio. Conversion factor for SI units for glucose in mmol/L: × 0.05551.

(7.2 mmol/L), and applying lower thresholds to the GCT would increase sensitivity rates to ≥77% but would lead to low specificity rates varying from 64.2 to 56.0% for a GCT threshold of 125 mg/dL (6.9 mmol/L) and 120 mg/dL (6.7 mmol/L), respectively (Table 1). For a GCT threshold of 130 mg/dL (7.2 mmol/L), the positive posttest probability was 26.4%, the negative posttest probability was 5.5%, and 65.1% of all OGTTs could be avoided compared with a universal one-step screening strategy with the 75-g OGTT (Table 1).

The BEDIP-N study is, to our knowledge, the first study that has prospectively evaluated the sensitivity and specificity of the GCT in a universal two-step screening strategy for GDM using the 2013 WHO criteria. The GCT has been used in combination with the 100-g OGTT or the 75-g OGTT with various diagnostic criteria such as the Carpenter and Coustan criteria, the National Diabetes Data Group criteria, the 1999 WHO criteria, or the Canadian Diabetes Association criteria and has shown variable sensitivity rates between 70 and 88% and specificity rates between 69 and 89% when using a GCT threshold of 140 mg/dL (7.8 mmol/L) and sensitivity rates between 88 and 99% and specificity rates between 66 and 77% when using a GCT threshold of 130 mg/dL (7.2 mmol/L) (5). However, many studies had a high or unclear bias because the result of the screening test was used to determine whether further testing was needed for GDM and not all patients received a confirmatory OGTT if the GCT was below a certain threshold (5). Our study avoided these limitations as both health care providers and participants were blinded for the GCT, thus avoiding any bias in screening.

In conclusion, we show now that the GCT has a moderate diagnostic accuracy in a universal two-step screening strategy for GDM using the 2013 WHO criteria. A GCT threshold of 140 mg/dL (7.8 mmol/L) had only a sensitivity of 59.6% and can therefore not be recommended in a two-step approach for GDM using the 2013 WHO criteria. To achieve sensitivity rates ≥70%, the threshold of the GCT would need to be reduced to at least 130 mg/dL (7.2 mmol/L).

Acknowledgments. The authors thank Inge Beckstedde from the Antwerp University Hospital site and Sylva Van Imschoot from the AZ Sint-Jan site for their help with the recruitment and study assessments. The authors thank the research assistants, paramedics, and physicians of all the participating centers for their support and all the women who participated in the study.

Funding. This investigator-initiated study was funded by the Belgian National Lottery, the Fund of Academic Studies of UZ Leuven, and the Fund Yvonne and Jacques François-de Meurs of the King Baudouin Foundation. K.B. is the recipient of a Clinical Doctoral Scholarship of the Fund of Academic Studies of UZ Leuven. R.D. is the recipient of a Fundamenteel Klinisch Navorserschap Fonds Wetenschappelijk Onderzoek Vlaanderen.

The sponsors of the study had no role in the design of the study; in the collection, handling, analysis, or interpretation of the data; or in the decision to write and submit the manuscript for publication.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. K.B., P.V.C., and C.M. conceived the project. K.B. performed the literature review. K.B. and C.M. wrote the first draft of the manuscript. C.M. prepared the data. A.La. performed the statistical analysis. All authors contributed to the study design, including data collection, data interpretation, and manuscript revision. K.B. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. Metzger BE, Gabbe SG, Persson B, et al.; International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 2010;33:676–682

2. World Health Organization. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy: a World Health Organization guideline. Diabetes Res Clin Pract 2014;103:341–363

3. Benhalima K, Mathieu C, Damm P, et al. A proposal for the use of uniform diagnostic criteria for gestational diabetes in Europe: an opinion paper by the European Board & College of Obstetrics and Gynaecology (EBCOG). Diabetologia 2015;58:1422–1429

4. Benhalima K, Van Crombrugge P, Verhaeghe J, et al. The Belgian Diabetes in Pregnancy Study (BEDIP-N), a multi-centric prospective cohort study on screening for diabetes in pregnancy and gestational diabetes: methodology and design. BMC Pregnancy Childbirth 2014;14:226

5. Donovan L, Hartling L, Muise M, Guthrie A, Vandermeer B, Dryden DM. Screening tests for gestational diabetes: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med 2013;159:115–122