Oral Glucose Tolerance Test Results in Pregnancy Can Be Used to Individualize the Risk of Future Maternal Type 2 Diabetes Mellitus in Women With Gestational Diabetes Mellitus

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OBJECTIVE

We aimed to quantify the risk of future maternal type 2 diabetes mellitus (T2DM) in women with gestational diabetes mellitus (GDM) based on the type and number of abnormal 75-g oral glucose tolerance test (OGTT) values and the diagnostic criteria used for the diagnosis of GDM.

RESEARCH DESIGN AND METHODS

We conducted a population-based retrospective cohort study of all nulliparous women with a live singleton birth who underwent testing for GDM using a 75-g OGTT in Ontario, Canada (2007–2017). We estimated the incidence rate (per 1,000 person-years), overall risk (expressed as adjusted hazard ratio [aHR]), and risk at 5 years after the index pregnancy of future maternal T2DM. Estimates were stratified by the type and number of abnormal OGTT values, as well as by the diagnostic criteria for GDM (Diabetes Canada [DC] vs. International Association of the Diabetes and Pregnancy Study Groups [IADPSG] criteria).

RESULTS

A total of 55,361 women met the study criteria. The median duration of follow-up was 4.4 (interquartile range 2.8–6.3; maximum 10.3) years. Using women without GDM as reference (incidence rate 2.18 per 1,000 person-years), women with GDM were at an increased risk of future T2DM; this risk was greater when using the DC compared with the IADPSG criteria (incidence rate 18.74 [95% CI 17.58–19.90] vs. 14.07 [95% CI 13.24–14.91] per 1,000 person-years, respectively). The risk of future maternal T2DM increased with the number of abnormal OGTT values and was highest for women with three abnormal values (incidence rate 49.93 per 1,000 person-years; aHR 24.57 [95% CI 21.26–28.39]). The risk of future T2DM was also affected by the type of OGTT abnormality: women with an abnormal fasting value had the greatest risk, whereas women with an abnormal 2-h value had the lowest risk (aHR 14.09 [95% CI 12.46–15.93] vs. 9.22 [95% CI 8.19–10.37], respectively). Similar findings to those described above were observed when the risk of T2DM at a fixed time point of 5 years after the index pregnancy was considered as the outcome of interest.

CONCLUSIONS

In women with GDM, individualized information regarding the future risk of T2DM can be provided based on the type and number of abnormal OGTT values, as well as the diagnostic criteria used for the diagnosis of GDM.

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Women with gestational diabetes mellitus (GDM) (1–3) are at an increased risk of future type 2 diabetes mellitus (T2DM) (4–8). This association is of major importance, because it allows an opportunity for care providers to identify women at high risk of T2DM, provide proper counseling, initiate preventive lifestyle and medical interventions, and monitor for the development of T2DM (9).

Most available studies quantified the association using the diagnosis of GDM as the exposure or predictor of interest, with the prevalence of T2DM ranging from 15 to 50% at 5 years from delivery (10–12). However, this approach provides a crude measure of the risk of T2DM, because it does not consider the severity or characteristics of maternal dysglycemia during pregnancy (e.g., primarily fasting vs. postprandial elevated glucose levels) among women with GDM and does not consider the diagnostic criteria used for the diagnosis of GDM. We therefore hypothesized that the values of the oral glucose tolerance test (OGTT) may be valuable for the individualization of the risk of future maternal T2DM based on the type and number of abnormal values in women with GDM.

Data on the risk of T2DM associated with abnormal fasting compared with abnormal postload OGTT values are limited and conflicting (13). Furthermore, the interpretation of available studies is limited by sample size (ranging from 71 to 1,262 women) (13) and variation in the doses of glucose load (10,14–21), the OGTT diagnostic criteria used to define GDM and T2DM (10–12,14,15,20,22,23), and the duration of postpartum follow-up (16–19, 21,24,25).

Therefore, we aimed to quantify the risk of future maternal T2DM in women with GDM based on the type and number of abnormal values of the 75-g OGTT performed during pregnancy and the diagnostic criteria used for the diagnosis of GDM.

RESEARCH DESIGN AND METHODS

Study Design and Participants

This was a population-based retrospective cohort study of all nulliparous women aged 18–45 years with a live singleton hospital birth who underwent testing for GDM using a 75-g OGTT in Ontario, Canada, from 1 April 2007 to 31 December 2017.

The following cases were excluded: *1*) women with T1DM or T2DM at the time of the index pregnancy *2*) pregnancies complicated by stillbirth *3*) missing values for 75-g OGTT or missing neonatal record *4*) cases where the OGTT was performed at ≤23 weeks or ≥31 weeks of gestation, and *5*) non-Ontario residents.

Data Source

Data were obtained from provincial health care administrative databases from the Ministry of Health and the Ministry of Long-Term Care, which are held at the Institute for Clinical Evaluative Sciences. These databases detail various aspects of health service use by residents of the province and include the Registered Persons Database, which records demographic information for all residents of Ontario; the Discharge Abstracts Database, which provides detailed information about all hospital admissions in Ontario; and the Ontario Health Insurance Plan provider service claims database, which records all fee-for-service billing and shadow billing claims submitted by Ontario physicians for in-patient or ambulatory consultations, assessments, and diagnostic or therapeutic procedures. Because Ontario has a single-payer universal health care system, these data capture virtually all care delivered to Ontario residents.

The Ontario Diabetes Database (ODD) is a validated registry of physician-diagnosed nongestational diabetes that is derived using these data (26). The MOMBABY database is derived from hospitalization data and links hospitalization records of delivering mothers with those of their newborn babies. Glucose test results came from the Ontario Laboratory Information Service, which includes data on laboratory test orders and results from community, hospital, and public health laboratories across Ontario. Laboratories have gradually enrolled in the Ontario Laboratory Information Service to contribute their data since in 2007.

These data sets were linked using unique encoded identifiers and analyzed at the Institute for Clinical Evaluative Sciences. The use of data in this project is authorized under section 45 of the Ontario Personal Health Information Protection Act, which does not require review by a research ethics board.

Diagnosis of GDM

The 2013 Diabetes Canada (DC) recommendations (27) support two options for screening and testing for GDM, typically performed between 24 and 28 weeks of gestation. The preferred (two-step) approach involves screening for GDM using a 50-g glucose challenge test (GCT), and when positive (7.8–11.0 mmol/L [140–199 mg/dL]), a 75-g OGTT is administered (cutoff values: fasting ≥5.3 mmol/L [95 mg/dL]; 1 h ≥10.6 mmol [190 mg/dL]; 2 h ≥9.0 mmol/L [162 mg/dL]). GDM is defined as one or more abnormal OGTT values or a GCT result of ≥11.1 mmol/L (200 mg/dL). The alternative nonpreferred approach includes a one-step screening for GDM using a 75-g OGTT without a prior 50-g GCT.

The criteria used for screening and diagnosis of GDM up until April 2013 were similar to the 2013 DC recommendations, with the minor exceptions that the 2-h cutoff value was 8.9 mmol/L [160.0 mg/dL] instead of 9.0 mmol/L [162.0 mg/dL] and that the diagnostic cutoff of the 50-g GCT was lower (≥10.3 mmol/L [185.4 mg/dL] instead of ≥11.1 mmol/L [200 mg/dL]) (28).

The International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria recommend a one-step approach using a 75-g OGTT with lower thresholds compared with the 2013 DC recommended thresholds (cutoff values: fasting ≥5.1 mmol/L [92 mg/dL]; 1 h ≥10.0 mmol [180 mg/dL]; 2 h ≥8.5 mmol/L [153 mg/dL]). GDM is defined as one or more abnormal OGTT values (29).

Exposures

The primary exposures were the type (fasting, 1 h, or 2 h) and number (zero, one, two, or three) of abnormal antepartum 75-g OGTT values according to the 2013 DC or the IADPSG thresholds.

Outcome

The primary outcome was future maternal T2DM following the index pregnancy, based on diagnostic codes in the ODD.

The diagnostic criteria for T2DM (outside of pregnancy) in Canada during the study period included any of the following: *1*) fasting glucose ≥7.0 mmol/L (126 mg/dL), *2*) 2-h result in a 75-g OGTT ≥11.1 mmol/L (200 mg/dL), *3*) random glucose ≥11.1 mmol/L (200

mg/dL), or *4*) glycosylated hemoglobin (HbA_{1c}) ≥6.5% (starting from 2013). In the absence of symptoms of hyperglycemia, a repeat confirmatory test (fasting glucose, HbA_{1c}, or 75-g OGTT) should be performed on another day (30).

Statistical Analysis

The incidence rate of future maternal T2DM (per 1,000 person-years) was estimated for women without and with GDM and was further stratified by the type and number of abnormal OGTT values.

Cox proportional hazards models were used to estimate the association of abnormal OGTT (as defined using either the DC or the IADPSG criteria) with future T2DM, with censoring on death, migration from the province, or arrival at the end of the study period of 31 March 2017. Models were adjusted for the following variables that were determined a priori: maternal age at the time of index birth, ethnicity, income quintile, and fetal sex. The associations were presented as adjusted hazard ratio (aHR) with 95% CI and were stratified by the type and number of abnormal OGTT values, using women without GDM as reference. Kaplan-Meier curves were used to present the cumulative probability of T2DM by the type and number of abnormal OGTT values. The cumulative probability curves were compared between women diagnosed with GDM using the DC versus IADPSG criteria using the log-rank test. To determine the independent association of each OGTT value (fasting, 1 h, and 2 h) with future T2DM, we developed a second prediction model for T2DM in women with GDM that was adjusted for all three OGTT values in addition to the covariates included in the previous model described above.

We also calculated the proportion of women diagnosed with T2DM at a fixed time point of 5 years after the index pregnancy. Modified Poisson regression models were used to estimate the risk of T2DM at 5 years after the index pregnancy by the type and number of abnormal OGTT values, using women without GDM as reference. Models were adjusted for the same variables described above (maternal age at the time of index birth, ethnicity, income quintile, and fetal sex), and the associations were presented as adjusted relative risk (aRR) with 95% CI.

Data were analyzed using SAS statistical software (version 9.4).

RESULTS

Characteristics of the study cohort

We identified 162,622 women who underwent 75-g OGTT during the study period, of whom 55,361 met the study criteria (Fig. 1). The characteristics of the study cohort are presented in Supplementary Table 1. The mean gestational age at the time of 75-g OGTT was 27.5 ± 1.7 weeks. The median duration of follow-up was 4.4 (interquartile range 2.8–6.3; maximum 10.3) years.

GDM and the Risk of Future Maternal T2DM by Type and Number of Abnormal OGTT Values

Time-to-Event Analysis

We estimated the association of GDM with future maternal T2DM using the 2013 DC and the IADPSG thresholds based on the type and number of abnormal OGTT values (Table 1). Using women without GDM (zero abnormal OGTT values) as reference (incidence rate 2.18 per 1,000 person-years), women with GDM (one or more abnormal values) were at an increased risk of future T2DM, irrespective of whether the diagnosis of GDM was based on the 2013 DC (incidence rate 18.74 per 1,000 person-years; aHR 8.22 [95% CI 7.38–9.16]) or the IADPSG criteria (incidence rate 14.07 per 1,000 person-years; aHR 7.45 [95% CI 6.59–8.42]) (Table 1). The cumulative probability curves were steeper when GDM was diagnosed using the 2013 DC compared with the IADPSG criteria (Fig. 2*A*).

For women with GDM, the risk of future maternal T2DM increased with the number of abnormal OGTT values. The risk was lowest for women with only one abnormal value (incidence rate 12.08 per 1,000 person-years; aHR 4.92 [95% CI 4.31–5.62]). Women with three abnormal values had a more than fourfold higher risk of T2DM (incidence rate 49.93 per 1,000 person-years; aHR 24.57 [95% CI 21.26–28.39]), as well as a shorter interval from pregnancy to diagnosis of T2DM, compared with women with one or two abnormal values (Table 2 and Fig. 2*B*). For each given number of abnormal values, the cumulative probability curves were steeper when the abnormal values were defined based on the 2013 DC compared with the IADPSG criteria (Fig. 2*B*).

When stratified by the type of abnormal OGTT values, the risk of future maternal T2DM was higher and the interval to onset of T2DM was shorter in women who had an abnormal fasting value (incidence rate 31.58 per 1,000 person-years; aHR 14.09 [95% CI 12.46–15.93]) compared with women with an abnormal 1-h value (incidence rate 22.77 per 1,000 person-years; aHR 10.22 [95% CI 9.13–11.43]) and women with an abnormal 2-h value (incidence rate 19.97 per 1,000 person-years; aHR 9.22 [95% CI 8.19–10.37]) (Table 2 and Fig. 2*C*). For each type of OGTT value, the cumulative probability curves were steeper when the abnormal values were defined based on the 2013 DC compared with the IADPSG criteria (Fig. 2*C*). This analysis, however, did not provide information on the independent association of each OGTT value with future maternal T2DM, because it included women who had more than one abnormal value (e.g., some of the women in the abnormal fasting value group may have also had an abnormal 1- or 2-h value). Therefore, to better understand the independent association of each of the three OGTT values with the risk of future maternal T2DM, we developed a

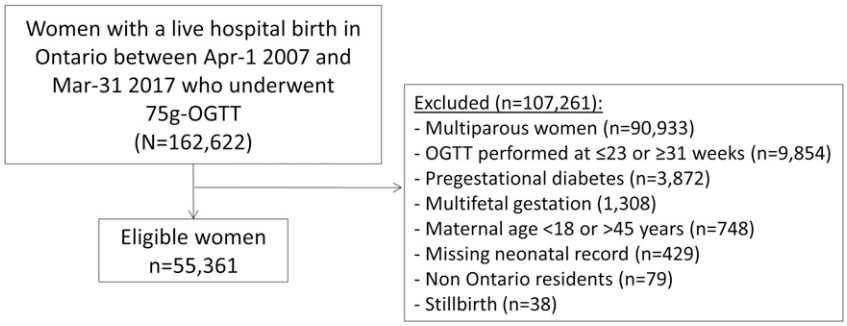

Figure 1—Selection of the study group. OGTT indicates 2-h 75-g OGTT. Of note, most women in our cohort underwent the OGTT as part of a two-step approach for the diagnosis of GDM following an abnormal 50-g GCT.

Table 1—Risk of future T2DM by number and type of abnormal OGTT values: time-to-event analysis

Abnormal OGTT value	Proportion of women with OGTT abnormality, *n* (%)	T2DM per 1,000 person-y, incidence rate (95% CI)	Risk of T2DM in women meeting criteria vs. women without GDM (no abnormal values)	
			Crude HR (95% CI)	aHR[a] (95% CI)
2013 DC OGTT criteria				
Abnormal values, *n*				
0	41,507 (75.0)	2.18 (1.96–2.41)	Reference	Reference
≥1 (GDM)	13,854 (25.0)	18.74 (17.58–19.90)	**8.31 (7.47–9.25)**	**8.22 (7.38–9.16)**
1	8,202 (14.8)	12.08 (10.81–13.35)	**4.98 (4.37–5.67)**	**4.92 (4.31–5.62)**
2	4,270 (7.7)	21.44 (19.28–23.59)	**10.19 (8.95–11.61)**	**10.05 (8.79–11.48)**
3	1,382 (2.5)	49.93 (44.36–55.50)	**25.59 (22.20–29.49)**	**24.57 (21.26–28.39)**
Abnormal values, type				
Fasting (≥5.3 mmol/L [95 mg/dL])	4,058 (7.2)	31.58 (28.87–34.30)	**14.62 (12.95–16.49)**	**14.09 (12.46–15.93)**
1 h (≥10.6 mmol [190 mg/dL])	8,852 (15.7)	22.77 (21.20–24.35)	**10.29 (9.21–11.49)**	**10.22 (9.13–11.43)**
2 h (≥9.0 mmol/L [162 mg/dL])	7,978 (14.2)	19.97 (18.42–21.53)	**9.26 (8.25–10.40)**	**9.22 (8.19–10.37)**
IADPSG OGTT criteria				
Abnormal values, *n*				
0	34,848 (62.9)	1.77 (1.55–1.98)[b]	Reference	Reference
≥1 (GDM)	20,513 (37.1)	14.07 (13.24–14.91)[c]	**7.56 (6.69–8.53)**	**7.45 (6.59–8.42)**
1	10,898 (19.7)	7.06 (6.23–7.89)[c]	**3.60 (3.09–4.18)**	**3.55 (3.05–4.14)**
2	7,194 (13.0)	15.98 (14.50–17.46)[c]	**8.86 (7.72–10.18)**	**8.86 (7.70–10.20)**
3	2,421 (4.4)	39.99 (36.11–43.87)[d]	**24.24 (21.01–27.97)**	**23.49 (20.30–27.18)**
Abnormal values, type				
Fasting (≥5.1 mmol/L [92 mg/dL])	6,376 (11.3)	24.66 (22.74–26.57)[c]	**14.05 (12.33–16.00)**	**13.59 (11.90–15.51)**
1 h (≥10.0 mmol [180 mg/dL])	14,238 (25.3)	16.91 (15.82–18.00)[c]	**9.13 (8.07–10.33)**	**9.03 (7.97–10.23)**
2 h (≥8.5 mmol/L [153 mg/dL])	11,935 (21.2)	16.70 (15.51–17.89)[c]	**9.16 (8.07–10.40)**	**9.18 (8.07–10.44)**

OGTT refers to 2-h 75-g OGTT unless otherwise indicated. Bold font indicates significant association. [a]Values reflect the results of Cox proportional hazards model including women without GDM (no abnormal values) as reference and adjusted for the following variables: maternal age at the time of index birth, ethnicity, income quintile, and fetal sex. [b]$P = 0.009$ for the comparison of this incidence rate with the incidence rate associated with the corresponding predictor under the 2013 DC criteria. [c]$P < 0.001$ for the comparison of this incidence rate with the incidence rate associated with the corresponding predictor under the 2013 DC criteria. [d]$P = 0.003$ for the comparison of this incidence rate with the incidence rate associated with the corresponding predictor under the 2013 DC criteria.

second prediction model for T2DM that included all three OGTT values as well as maternal age at the time of index birth, ethnicity, income quintile, and fetal sex (Table 2). Overall, we found that women with an abnormal fasting value had the greatest risk, whereas women with an abnormal 2-h value had the lowest risk of future T2DM (Table 2).

Five Years After Index Pregnancy

We finally estimated risk of T2DM at a fixed time point of 5 years after the index pregnancy (Supplementary Table 2). When using the DC criteria, the rate of T2DM at 5 years after the index pregnancy was 0.86% in women without GDM compared with 7.37% in women with GDM (aRR 8.58 [95% CI 7.27–10.11]). The risk increased with the number of abnormal OGTT values and was 20.41% for women with three abnormal values (aRR 23.12 [95% CI 20.34–26.27]). The risk was also greater for women with an abnormal fasting value (12.67%; aRR 14.36 [95% CI 12.63–16.33]) compared with women with an abnormal 1- (9.06%) or 2-h (8.07%) value (Supplementary Table 2). The corresponding associations of abnormal OGTT values with the risk of T2DM at 5 years after the index pregnancy were lower when the OGTT was interpreted using the IADPSG criteria compared with the DC criteria (Supplementary Table 2).

CONCLUSIONS

Principal Findings

In the current study, we aimed to quantify the risk of future maternal T2DM in women with GDM based on the type and number of abnormal 75-g OGTT values during pregnancy and the diagnostic criteria used for the diagnosis of GDM. Our main findings were that among women with GDM, *1*) the risk of future maternal T2DM is affected by the diagnostic criteria used for the diagnosis of GDM, *2*) an increasing number of abnormal OGTT values is associated with a considerable increase in the risk of T2DM and a decrease in the interval to onset of T2DM, and *3*) the risk of future maternal T2DM seems to be greatest for women with an abnormal fasting value and lowest for women with an abnormal 2-h value.

Results of the Study in the Context of Other Observations

The original diagnostic criteria for GDM were based on the future risk of maternal T2DM (31). However, since that landmark study of O'Sullivan and Mahan (31), data on the magnitude of the risk of future maternal T2DM in women with GDM have been inconsistent, which makes proper counseling for women with GDM challenging (32,33). Furthermore, many of the available studies on the future risk of maternal T2DM considered women with GDM as a single homogenous group and provided average risk estimates for women with GDM as a whole, with little consideration of the severity of glucose intolerance in pregnancy. In the current study, we attempted to individualize the

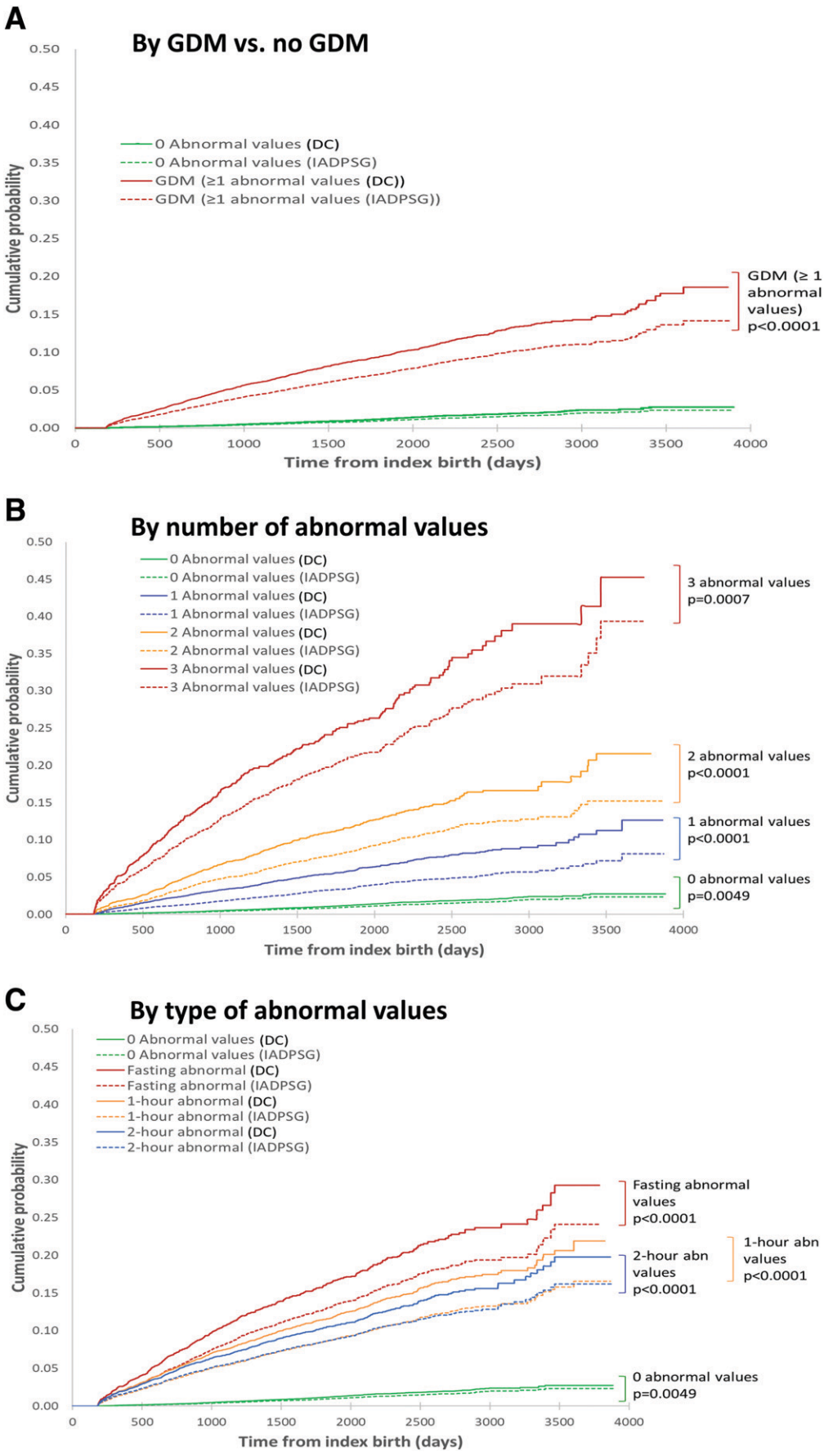

Table 2—Independent association of fasting, 1-h, and 2-h OGTT values with future maternal T2DM in women with GDM: time-to-event analysis

Type of abnormal OGTT value	Crude HR (95% CI)	aHR[a] (95% CI)
2013 DC criteria		
Fasting (vs. normal fasting)	**2.50 (2.23–2.80)**	**2.76 (2.46–3.10)**
1 h (vs. normal 1 h)	**2.11 (1.83–2.42)**	**2.33 (2.02–2.67)**
2 h (vs. normal 2 h)	**1.29 (1.15–1.45)**	**1.63 (1.45–1.84)**
IADPSG criteria		
Fasting (≥5.1 mmol/L [92 mg/dL])	**2.92 (2.62–3.25)**	**3.23 (2.89–3.60)**
1 h (≥10.0 mmol [180 mg/dL])	**2.26 (1.96–2.61)**	**2.41 (2.09–2.79)**
2 h (≥8.5 mmol/L [153 mg/dL])	**1.67 (1.49–1.87)**	**2.02 (1.80–2.27)**

OGTT refers to 2-h 75-g OGTT unless otherwise indicated. Bold font indicates significant association. [a]Values reflect the results of Cox proportional hazards model, adjusted for all three OGTT values as well as maternal age at the time of index birth, ethnicity, income quintile, and fetal sex. The reference group for each of the variables is the group of women in whom the corresponding OGTT value was within normal limits.

risk of future maternal T2DM based on the characteristics of the OGTT values.

We found that the risk of T2DM increases in a dose-response manner with the number of abnormal OGTT values, independent of a patient's baseline characteristics. Prior studies reported a positive relationship between the number of abnormal OGTT values and short-term adverse pregnancy outcomes (34,35), but data on the association of the number of abnormal OGTT values with future maternal T2DM are limited (36,37). These findings provide support for the concept that glucose intolerance in pregnancy is a continuum rather than a dichotomous phenomenon (38,39).

There is evidence to suggest that the pathophysiology underlying abnormal fasting glucose levels differs from that associated with abnormal postprandial glucose levels. For example, it has been suggested that women with impaired fasting glycemia are more likely to have stationary β-cell dysfunction and chronic low β-cell mass, reduced hepatic insulin sensitivity, and a genetic predisposition for T2DM, whereas women with impaired glucose tolerance are more likely to have reduced peripheral insulin sensitivity that is more likely to be related to environmental factors such as physical inactivity and unhealthy diet (40–43). In addition, fasting hyperglycemia is likely to indicate a greater degree of β-cell dysfunction such that basal insulin secretion is insufficient to control hepatic glucose output in the fasted state, let alone maintain normoglycemia postchallenge. These observations provide the rationale for the hypothesis that the risk of future T2DM in women with GDM may vary by the type of abnormal OGTT value and may be greater for those with fasting hyperglycemia. However, data on the relative importance of fasting compared with postload OGTT values have been inconsistent (15,23,43–47). In a recent meta-analysis of the association between the antepartum OGTT results and future T2DM, the authors concluded that neither abnormal fasting nor 2-h OGTT values were associated with future T2DM after controlling for potential cofounders (13). In another meta-analysis of the future risk of T2DM in women with GDM, all OGTT values were found to have a similar association with future T2DM (odds ratio 3.05–3.57), although this study reported only unadjusted associations. However, the interpretation of these meta-analyses is limited by the small number and the high heterogeneity of included studies and the lack of information on the independent association of each individual OGTT value (through a simultaneous adjustment for all three or four OGTT values). In addition, individual studies were limited by small sample size, relatively short duration of follow-up periods, and variation in OGTT doses, diagnostic criteria, and reference groups (19,20,24).

In the current study, which included a large cohort of women with GDM and tested the independent association of the OGTT values with T2DM, we found that an abnormal fasting OGTT value had the strongest independent association with future T2DM, whereas the association was weakest for the 2-h OGTT value. This observation may be attributed to the differences in pathophysiology and genetic predisposition for elevated fasting compared with postprandial glyecmia, as described above. The greater association of the 1-h compared with the 2-h OGTT value with future T2DM may be attributed to the fact that the 1-h blood glucose levels are thought to reflect the first-phase insulin release, which is believed to be deficient in patients with GDM and T2DM (48).

There is currently no consensus with regard to the screening approach for GDM (27,49,50). However, the IADPSG criteria, based on a 2-h 75-g OGTT, seem to be gaining increasing acceptance in an attempt to move toward a more uniform screening approach for GDM (51–54). Therefore, we chose to interpret our data from women who underwent 2-h 75-g OGTT using the IADPSG criteria in addition to the DC criteria. Unsurprisingly, we found that the OGTT results interpreted using the less strict IADPSG criteria (compared with the DC criteria) were associated with a higher prevalence of GDM and a lower incidence rate of future T2DM. The importance of these data are that they provide risk estimates for future T2DM that are specific to the commonly used IADPSG criteria, as well as emphasize that the risk of future T2DM in women with GDM varies by the OGTT criteria used for the diagnosis of GDM.

Strengths and Limitations

The major strengths of our study are the large sample size, the population-based design in the setting of a single-

Figure 2—Cumulative probability curves of future T2DM are presented for women with GDM (red line) and without GDM (green line) (*A*); women with no abnormal values (green line), a single abnormal value (blue line), two abnormal values (orange line), or three abnormal values (red line) (*B*); and women with no abnormal values (green line), an abnormal fasting value (red line), an abnormal 1-h value (orange line), or an abnormal 2-h value (blue line) (*C*). In each graph, data are presented based on the DC (solid lines) and IADPSG (dashed lines) criteria, and the *P* values refer to comparison of the DC and the corresponding IADPSG curves using the log-rank test. Censoring was done on death, migration from the province, or arrival at the end of the study period on 31 March 2017. Of note, most women in our cohort underwent the OGTT as part of a two-step approach for the diagnosis of GDM following an abnormal 50-g GCT.

payer universal health care system, which allows capture of health care data from virtually all residents of the province of Ontario, and the availability of the OGTT data as opposed to diagnostic ICD codes of GDM (7,32).

There are several limitations to the current study. First, because of the retrospective study design, we did not have information on certain risk factors for T2DM such as maternal BMI (55) and family history of diabetes (56). Therefore, although we attempted to control for several important confounding variables, residual confounding cannot be ruled out. Second, it is possible that postpregnancy preventive interventions and risk reduction measures were undertaken in some of those with a history of GDM, which might have resulted in underestimation of the risk of future T2DM (57). However, at the same time, our findings may reflect the real-world risk of T2DM in the current setting of preventive medicine. Third, our cohort included women who underwent a 75-g OGTT following a positive screening on a 50-g GCT, and thus, our results do not reflect the distribution of the OGTT results in unselected pregnancies. This may be especially relevant in the analysis based on the IADPSG criteria, which are used for the purpose of universal screening. Fourth, the fact that the guidelines for the diagnosis of GDM changed in 2013 (e.g., with respect to the diagnostic cutoff of the 50-g GCT or the introduction of an alternative one-step approach) may have resulted in some differences in the severity of glucose intolerance of the study population between the two time periods. Finally, the definition of the outcome variable was based on the diagnostic code for T2DM in the ODD data set. Thus, possible variation among care providers may have affected the rate of T2DM. However, this approach reflects the real-world variability in practice among care providers.

Conclusion

Women with GDM represent a heterogenous group with regard to the type and severity of the underlying pathophysiology and, consequently, with regard to the future risk of T2DM. This emphasizes the importance of providing women with GDM individualized information regarding their future risk of T2DM, along with individualized recommendations for monitoring and preventive lifestyle and medical interventions. In the current study, we identified several OGTT characteristics that can used for that purpose. Additional studies are needed to develop prediction models that integrate the OGTT results with clinical risk factors such as family history of diabetes and maternal BMI.

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