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CGM, continuous glucose monitor; GMI, glucose management indicator; NICU, neonatal intensive care unit

ARTICLE HIGHLIGHTS

- The association between continuous glucose monitoring (CGM) metrics and pregnancy outcomes in preexisting diabetes is uncertain.
- The goal was to examine the association of CGM metrics with pregnancy outcomes and to determine the optimal time in range (TIR).
- All CGM metrics, except time below range, were associated with pregnancy outcomes. The statistically optimal TIR was 66–71%.
- Our findings support American Diabetes Association recommendations of >70% TIR. Prospective trials will determine whether higher goals can be safely achieved.

Association of Continuous Glucose Monitoring Metrics With Pregnancy Outcomes in Patients With Preexisting Diabetes

Ayodeji A. Sanusi,[1,2] Yumo Xue,[3] Claire McIlwraith,[4] Hannah Howard,[5] Brian E. Brocato,[1,2] Brian Casey,[1,2] Jeff M. Szychowski,[1,3,4] and Ashley N. Battarbee[1,2]

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OBJECTIVE

Continuous glucose monitoring (CGM) improves maternal glycemic control and neonatal outcomes in type 1 diabetes pregnancies compared with self-monitoring of blood glucose. However, CGM targets for pregnancy are based on expert opinion. We aimed to evaluate the association between CGM metrics and perinatal outcomes and identify evidence-based targets to reduce morbidity.

RESEARCH DESIGN AND METHODS

This was a retrospective cohort study of pregnant patients with type 1 or 2 diabetes who used real-time CGM and delivered at a U.S. tertiary center (2018–2021). Multiple gestations, fetal anomalies, and early pregnancy loss were excluded. Exposures included time in range (TIR; 65–140 mg/dL), time above range (TAR), time below range (TBR), glucose variability, average glucose, and glucose management indicator. The primary outcome was a composite of fetal or neonatal mortality, large or small for gestational age at birth, neonatal intensive care unit admission, hypoglycemia, shoulder dystocia or birth trauma, and hyperbilirubinemia. Logistic regression estimated the association between CGM metrics and outcomes, and optimal TIR was calculated.

RESULTS

Of 117 patients, 16 (13.7%) used CGM before pregnancy and 68 (58.1%) had type 1 diabetes. Overall, 98 patients (83.8%) developed the composite neonatal outcome. All CGM metrics, except TBR, were associated with neonatal morbidity. For each 5 percentage-point increase in TIR, there was 28% reduced odds of neonatal morbidity (odds ratio 0.72, 95% CI 0.58–0.89). The statistically optimal TIR was 66–71%.

CONCLUSIONS

Nearly all CGM metrics were associated with adverse neonatal morbidity and mortality and may aid management of preexisting diabetes in pregnancy. Our findings support the American Diabetes Association recommendation of 70% TIR.

Preexisting or pregestational diabetes is present in 1–2% of pregnancies and increases the risks of maternal and fetal complications (1,2). Self-monitoring of capillary blood glucose in pregnancy is recommended by the American Diabetes Association (ADA) and the American College of Obstetricians and Gynecologists (ACOG) for management of diabetes in pregnancy (3,4). However, it only provides snapshots of glycemic control

[1]*Center for Women's Reproductive Health, The University of Alabama at Birmingham, Birmingham, AL*
[2]*Division of Maternal and Fetal Medicine, Department of Obstetrics and Gynecology, The University of Alabama at Birmingham, Birmingham, AL*
[3]*Department of Biostatistics, The University of Alabama at Birmingham, Birmingham, AL*
[4]*Department of Obstetrics and Gynecology, The University of Alabama at Birmingham, Birmingham, AL*
[5]*School of Medicine, The University of Alabama at Birmingham, Birmingham, AL*

Corresponding author: Ayodeji A. Sanusi, aasanusi@uabmc.edu

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at discrete points and may not accurately capture diurnal and nocturnal serum glucose fluctuations (5,6), which are associated with adverse outcomes (7,8). In contrast, continuous glucose monitoring (CGM) measures interstitial glucose continuously and provides a glucose value as frequently as every 1–5 min to aid in diet and lifestyle choices as well as pharmacotherapy.

A recent randomized controlled trial in pregnant patients with type 1 diabetes found that CGM use compared with self-monitoring of blood glucose improved maternal glycemic control with more time in range (TIR) on CGM (68% vs. 61%) and reduced the risk of large for gestational age neonates, neonatal intensive care unit (NICU) admission >24 h, and neonatal hypoglycemia (9,10). Currently, the ADA recommends that pregnant individuals with type 1 diabetes spend >70% TIR (pregnancy target range 63–140 mg/dL), <25% time above range (TAR), and <4% time below range (TBR) (11). However, there are no pregnancy-specific guidelines for glycemic variability (GV), average glucose, and glucose management indicator (GMI), and no recommendations for management of type 2 diabetes in pregnancy. Additionally, it is unclear which of these CGM metrics are associated with adverse maternal and neonatal outcomes and what the optimal TIR is that lowers the risk of adverse pregnancy outcomes (12–14).

Therefore, our objectives were to examine the association between CGM metrics and maternal and neonatal outcomes and determine the optimal TIR threshold to reduce adverse pregnancy outcomes.

RESEARCH DESIGN AND METHODS

We performed a retrospective cohort study of patients with preexisting type 1 or type 2 diabetes receiving prenatal care (at two prenatal clinics, where management of diabetes follows a standardized protocol) and delivering at a tertiary U.S. center from 2018 to 2022. Included patients had a singleton gestation and used a real-time Dexcom G6 CGM in pregnancy. We excluded patients with fetal anomalies or pregnancy loss prior to 20 weeks' gestation.

The exposures of interest for this analysis were CGM metrics of TIR, TAR, TBR, average glucose, GV, and GMI. TIR was defined as the proportion of time a patient spent within the target pregnancy range (65–140 mg/dL). A lower limit of 65 mg/dL was chosen for this analysis because the cutoff of 63 mg/dL cannot be selected using the Dexcom G6 CGM device. TAR was the proportion of TAR (>140 mg/dL), and TBR was the proportion of TBR (<65 mg/dL). Average glucose was the mean glucose reading on CGM, and GV was calculated by dividing the average glucose by the SD; GV reflects fluctuations around the average glucose. The associations between all CGM metrics and outcomes were evaluated per 5 percentage point change, except for average glucose, which was assessed per 5 mg/dL change, and GMI, which was assessed per 0.5-unit change. Five-unit increments were selected, consistent with data from prior studies indicating 5 percentage point changes in metrics in the second and third trimesters are associated with pregnancy outcomes and to ease comparison/aggregation of results with other studies (15). The GMI was calculated using GMI (%) = 3.31 + 0.02392 × [mean glucose in mg/dL] (16), to approximate the expected glycated hemoglobin (HbA_{1c}) based on the average glucose from CGM. Percentage of time CGM was in use was calculated as the proportion of time the CGM was in use in the preceding period prior to data upload. These metrics were calculated using raw CGM data downloaded from patients' CGM devices at prenatal visits and uploaded to a password-secured online database, Dexcom Clarity. CGM devices are recommended to be worn throughout pregnancy for 24 h a day, with glucose readings measured continuously and transmitted every 5 min. CGM data were reviewed every 1–2 weeks after automatic upload to the online portal or manual upload at prenatal care visits with the assistance of registered dietitian and certified diabetes care and education specialists. Medication adjustments were made following the ADA-recommended CGM guidelines (11), with all patients seen at two dedicated prenatal clinics with trained clinical providers who have experience reviewing CGM reports and expertise in the management of diabetes in pregnancy.

The primary outcome was a composite of adverse neonatal outcomes, including fetal or neonatal mortality, large or small for gestational age at birth, NICU admission, hypoglycemia, shoulder dystocia or other birth trauma, and hyperbilirubinemia. Fetal or neonatal mortality, defined as death after 20 weeks' gestation or before hospital discharge, was included in the composite as it precluded development of the other adverse outcomes. The Fenton growth chart was used to classify neonates as small (<10th percentile of birth weight) or large (≥90th percentile for birth weight) for gestational age (17). The Fenton growth chart was selected due to its improved accuracy in identifying small for gestational age among preterm neonates, a common outcome in patients with preexisting diabetes in pregnancy (17). For example, among preterm infants, compared with the World Health Organization growth chart, fewer infants are classified as small for gestational age by the Fenton growth chart (18). Hypoglycemia was defined as neonatal glucose <40 mg/dL within first 24 h of life, and hyperbilirubinemia was defined as neonates requiring phototherapy.

Secondary outcomes were preeclampsia, defined as at least two elevated blood pressures ≥140/90 mmHg and proteinuria or clinical or laboratory evidence of end-organ dysfunction (19), cesarean delivery, preterm birth <37 weeks, gestational age at delivery, and individual components of the primary outcome. Race and ethnicity were self-reported by study participants and represent a social construct rather than biological differences and were not included in multivariable regression models.

We used summary statistics to describe baseline characteristics of included patients and reported mean (±SD) for normally distributed variables, median (interquartile range [IQR]) for nonnormally distributed continuous variables, and number (proportion) for categorical variables. Multivariable logistic and linear regression models were used to estimate the association between all CGM metrics and the primary outcome and between TIR and the primary and secondary outcomes. These results were reported as odds ratios (ORs) with 95% CIs and β-coefficients with 95% CIs, as appropriate. Adjusted models included prepregnancy HbA_{1c} and diabetes type (type 1 vs. type 2), which were chosen a priori based on known associations with perinatal outcomes. Receiver operating characteristic curves were constructed, and areas under the curves (AUC) were calculated and compared using a nonparametric test described by DeLong et al. (20) to assess the association of each CGM metric as continuous variables with the primary outcome. The optimal cut point for the TIR was identified for the primary outcome using the Youden index (sensitivity + specificity − 1) and Liu method (product of sensitivity and specificity) (21,22). Supplemental

analyses were performed stratifying by pregnancy trimester and diabetes type. All analyses were performed using SAS 9.4 software, with level of significance set at $P < 0.05$. There was no adjustment for multiple comparisons or imputation for missing data. The study was approved by The University of Alabama at Birmingham Institutional Review Board.

Data and Resource Availability

The data sets generated during and/or analyzed in the current study are available from the corresponding author upon reasonable request.

RESULTS

Of 117 included participants, the mean maternal age was 28.8 ± 6.0 years, 51% had obesity, and 58% had type 1 diabetes. Sixteen patients (13.7%) used CGM prior to pregnancy, and the median gestational age at CGM initiation was 19.3 weeks' gestation (IQR 13.6–24.7). Overall, 19 (16.2%) used an insulin pump during pregnancy. With regards to obstetric characteristics, 42% were nulliparous, and the median gestational age at prenatal care initiation was 10.1 weeks' gestation (IQR 8.1–15.3) (Table 1).

Overall, the mean percentage of time CGM was in use was 83.6% ± 17.1. The mean TIR was 53.2% ± 17.8, and 22.2% achieved TIR ≥70%. The mean GV was 47.0 ± 14.8 mg/dL, and the mean average glucose was 143.1 ± 23.4 mg/dL. On average, 16.6 weeks of glycemic control data were captured after initiation of CGM during pregnancy. With advancing gestational age across trimesters, TAR, GV, average glucose, and GMI decreased while TIR increased ($P < 0.05$ for all) (Supplementary Table 1). TBR and percentage time CGM were not significantly different, although generally improved across pregnancy trimesters (Supplementary Table 1).

The primary outcome of composite neonatal morbidity and mortality occurred in 98 patients (83.8%). Overall, 30 patients (25.6%) had large for gestational age neonates at birth, 66 (57.4%) required NICU admission, 42 (36.5%) had hyperbilirubinemia, 28 (24.4%) had neonatal hypoglycemia, 21 (18.0%) were small for gestational age, 9 (7.7%) had a shoulder dystocia or birth trauma, and 8 (6.8%) had fetal or neonatal mortality. Among secondary maternal outcomes, 55 (47.0%) developed preeclampsia, 51 (43.6%) were delivered at <37 weeks' gestation, and 71 (60.7%) had a cesarean delivery. Individuals with the primary composite neonatal morbidity had lower TIR and higher TAR, average glucose, GV, and GMI compared with those without the primary composite (Table 2).

Table 1—Baseline demographics of patients with preexisting diabetes and CGM use in pregnancy

Characteristics	All (N = 117)
Maternal age at delivery (years)	28.8 ± 6.0
Race	
White	52 (44.5)
African American	59 (50.4)
Asian	4 (3.4)
Other	2 (1.7)
Hispanic ethnicity	4 (3.5)
Prepregnancy BMI (kg/m^2)	30.8 (24.5–35.7)
Prepregnancy obesity	60 (51.3)
Nulliparous	49 (41.9)
Government-assisted insurance	77 (65.8)
Aspirin use†	88 (76.5)
Pregnancy weight gain (kg)†	13.2 ± 7.3
Tobacco use in pregnancy†	7 (6.2)
Spontaneous conception	113 (96.6)
Gestational age at first prenatal visit (weeks)	10.1 (8.1–15.3)
Gestational age at initiation of CGM	19.3 (13.6–24.7)
Prepregnancy CGM use	16 (13.7)
Type of diabetes	
Type 1	68 (58.1)
Type 2	49 (41.9)
Diabetes class	
B	23 (19.6)
C	38 (32.5)
D	41 (35.0)
R	1 (0.9)
F	13 (11.1)
H	1 (0.9)
Prepregnancy or 1st trimester HbA_{1c} (%)†	8.6 (7.0–10.3)
Metformin use†	23 (19.8)
Insulin use	116 (99.2)
Subcutaneous insulin use†	97 (85.1)
Insulin pump use	19 (16.2)
Medical comorbidities	69 (59.0)
Asthma requiring medications	6 (5.1)
Chronic hypertension	40 (34.2)
Chronic kidney disease	8 (6.8)
Cardiac disease	1 (0.9)
Prior hypertensive disorder of pregnancy	26 (22.2)
Previous preterm delivery	36 (30.8)
Seizure disorder	5 (4.3)
Thyroid disease	14 (12.0)
Male fetus	51 (43.6)
Antenatal betamethasone receipt during pregnancy	24 (20.5)

Data are mean ± SD, n (%), or median (IQR), as appropriate. †Missing data: aspirin use missing = 2; pregnancy weight gain missing = 3; tobacco use in pregnancy missing = 4; prepregnancy or 1st trimester HbA_{1c} (%) missing = 8; metformin use missing = 1; subcutaneous insulin use missing = 3.

Table 2—CGM metrics among individuals with and without composite neonatal morbidity

CGM metric	Composite neonatal morbidity (n = 98)	No composite neonatal morbidity (n = 19)	P value
TIR	50.6 ± 16.5	66.7 ± 18.7	<0.001
TAR	47.3 ± 16.5	29.9 ± 18.4	<0.001
TBR	2.1 ± 2.6	3.4 ± 3.4	0.06
GV	48.5 ± 14.5	39.6 ± 14.3	0.02
Average glucose	146.5 ± 22.4	125.8 ± 20.8	<0.001
GMI	6.8 ± 0.5	6.3 ± 0.5	<0.001

Data presented as mean ± SD.

All CGM metrics, except TBR, were associated with the primary composite outcome (Table 3). For every 5-percentage point increase in TIR, there was an associated 28% decrease in the odds of the primary outcome (adjusted OR [aOR] 0.72, 95% CI 0.58–0.89) (Table 3). There was an increased odds of the primary outcome for every 5-percentage point increase in TAR (aOR 1.42, 95% CI 1.14–1.78), 5-percentage point increase in GV (aOR 1.36, 95% CI 1.03–1.79), and 5 mg/dL increase in average glucose (aOR 1.35, 95% CI 1.11–1.65). A 0.5-unit increase in the GMI was associated with an increase in odds of the primary outcome (aOR 3.52, 95% CI 1.52–8.13). TBR was not significantly associated with the primary outcome (Table 3).

Among secondary outcomes, a 5-percentage point increase in TIR was independently associated with a lower odds of cesarean delivery (aOR 0.87, 95% CI 0.76–0.99), large for gestational age neonate (aOR 0.79, 95% CI 0.69–0.92), NICU admission (aOR 0.82, 95% CI 0.71–0.94), and neonatal hypoglycemia (aOR 0.82, 95% CI 0.71–0.95). The association between TAR and pregnancy outcomes was consistent with that for TIR (Table 3). Higher GV was associated with increased odds of NICU admission, preeclampsia, preterm birth, and lower gestational age at delivery (Table 3). Further, increased average glucose and GMI were both associated with increased odds of a large for gestational age neonate, NICU admission, hypoglycemia, cesarean delivery, and earlier gestational age at delivery (Table 3). TBR was not significantly associated with any of the secondary outcomes (Table 3).

Nearly all CGM metrics were modestly good predictors of the primary outcome, with an AUC >0.70 for all metrics except for TBR and GV (Fig. 1). For example, the AUC for TIR was 0.75 (95% CI 0.61–0.88). Compared with TIR, the TAR, TBR, and GV were not significantly different in predicting the primary outcome ($P > 0.05$), while average glucose and GMI were marginally better predictors of the primary outcome compared with TIR ($P < 0.05$ for both). The statistically optimal TIR to reduce the primary outcome was 71.1% (87.8% sensitivity and 57.9% specificity) using the Youden index and 66% (81.6% sensitivity and 63.2% specificity) using the Liu method (21,22).

When evaluated by diabetes type, pregnant individuals with type 2 diabetes were noted to be older, had higher prepregnancy BMI, were more likely to be African American, were less likely to have used CGM before pregnancy, and initiated CGM use later in pregnancy. They also had less pregnancy weight gain, were less likely to use an insulin pump, and were more likely to use metformin and have chronic hypertension (Supplementary Table 2). With respect to CGM metrics, patients with type 2 diabetes had a higher TIR (58.7 ± 20.2 vs. 49.3 ± 14.8) and lower TAR, TBR, and GV. The mean percentage time of CGM in use, average glucose, and GMI were similar between groups ($P > 0.05$) (Supplementary Table 2). Neonates of patients with type 2 diabetes (compared with type 1 diabetes) had similar rates of composite neonatal morbidity (83.7% vs. 83.8%). However, neonates born to patients with type 2 diabetes were less likely to be admitted to the NICU or be delivered preterm and were more likely to suffer fetal or neonatal mortality compared with those born to patients with type 1 diabetes (Supplementary Table 2). With regards to the primary analysis evaluating the association between CGM metrics and perinatal outcomes, the direction and magnitude of effects were similar for patients with type 1 and type 2 diabetes (interaction P values = 0.40–0.65 for all) (Supplementary Tables 3 and 4).

CONCLUSIONS

In our single-center cohort, all standard CGM metrics, except TBR, were associated with composite neonatal morbidity and mortality. A 5% increase in TIR was associated with an ∼30% reduction in the odds of the primary outcome, and a 5% increase in TAR was associated with >40% increase in the odds of the primary outcome. Similarly, 5% increases in GV and 5 mg/dL increases in average glucose were associated with an ∼35% increase in the odds of the primary outcome. An increase in the GMI by 0.5 was also associated with a greater than threefold-higher odds of the primary outcome. Among secondary outcomes, higher TIR and lower TAR were associated with reduced risks of large for gestational age neonates, NICU admission, hypoglycemia, and cesarean delivery, while higher average glucose and GMI were associated with earlier gestational age at delivery. Higher GV was uniquely associated with increased risks for preeclampsia and preterm birth at <37 weeks' gestational age. These findings were similar when stratified by diabetes type, meaning that the relationship between CGM metrics and pregnancy outcomes was not different for individuals with type 1 versus type 2 diabetes. Similar to ADA recommendations for pregnant individuals with type 1 diabetes, a TIR of 66–71% was the statistically identified optimal cutoff that was associated with a reduced risk of composite adverse neonatal morbidity and mortality. Among all CGM metrics, TIR predicted the primary outcome well and was only slightly outperformed by average glucose and GMI.

Our findings confirm and extend what has been noted in prior studies. Among a retrospective cohort study of 386 patients with type 1 diabetes from two international multicenter studies, higher TIR (55% [95% CI 54–56] vs. 50% [95% CI 49–51]) and lower average glucose (7.1 mmol/L [95% CI 7.05–7.15] vs. 7.5 mmol/L [95% CI 7.45–7.55]) in the second and third trimester were associated with reduced risks of large for gestational age neonates (23). In an observational cohort of 186 patients with type 1 diabetes, lower TBR and higher TAR in the second and third trimester were associated with increased composite risk of

Table 3—Association of CGM metrics with primary and secondary outcomes for patients with preexisting diabetes in pregnancy

Outcomes	TIR (per 5%)	TAR (per 5%)	TBR (per 5%)	GV (per 5%)	Average glucose (per 5 mg/dL)	GMI (per 0.5%)
Composite neonatal morbidity	0.72 (0.58–0.89)*	1.42 (1.14–1.78)*	0.46 (0.18–1.17)	1.36 (1.03–1.79)*	1.35 (1.11–1.65)*	3.52 (1.52–8.13)*
Fetal or neonatal mortality	1.05 (0.85–1.29)	0.96 (0.78–1.18)	0.46 (0.03–6.14)	0.97 (0.70–1.34)	0.95 (0.80–1.13)	0.81 (0.39–1.68)
Large for gestational age	0.79 (0.69–0.92)*	1.27 (1.10–1.46)*	0.37 (0.11–1.26)	1.15 (0.95–1.37)	1.20 (1.08–1.34)*	2.14 (1.35–3.39)*
Small for gestational age	1.02 (0.88–1.18)	0.98 (0.84–1.13)	1.62 (0.62–4.23)	1.17 (0.95–1.44)	0.99 (0.89–1.11)	0.96 (0.61–1.52)
NICU admission	0.82 (0.71–0.94)*	1.23 (1.07–1.41)*	0.64 (0.27–1.49)	1.26 (1.04–1.54)*	1.19 (1.06–1.34)*	2.06 (1.26–3.38)*
Hypoglycemia	0.82 (0.71–0.95)*	1.22 (1.06–1.41)*	0.70 (0.25–1.94)	1.12 (0.93–1.35)	1.16 (1.04–1.30)*	1.87 (1.18–2.97)*
Birth trauma/shoulder dystocia	0.98 (0.78–1.22)	1.04 (0.84–1.29)	0.37 (0.03–4.29)	1.15 (0.84–1.58)	1.05 (0.88–1.25)	1.24 (0.60–2.56)
Hyperbilirubinemia	0.92 (0.81–1.04)	1.09 (0.97–1.23)	0.88 (0.39–2.01)	1.17 (0.98–1.39)	1.07 (0.98–1.17)	1.33 (0.91–1.95)
Preeclampsia	0.93 (0.83–1.05)	1.06 (0.95–1.19)	1.59 (0.70–3.63)	1.21 (1.02–1.44)*	1.04 (0.95–1.14)	1.18 (0.82–1.71)
Cesarean delivery	0.87 (0.76–0.99)*	1.15 (1.01–1.31)*	0.83 (0.38–1.82)	1.16 (0.97–1.39)	1.13 (1.01–1.25)*	1.64 (1.05–2.56)*
Gestational age at delivery†	0.14 (−0.02 to 0.29)	−0.14 (−0.29 to 0.02)	0.21 (−0.86 to 1.28)	−0.28 (−0.50 to −0.07)*	−0.12 (−0.24 to −0.01)*	−0.52 (−1.01 to −0.03)*
Preterm birth	0.89 (0.78–1.00)	1.12 (1.00–1.27)	0.96 (0.44–2.13)	1.24 (1.04–1.48)*	1.10 (1.00–1.20)	1.46 (0.99–2.16)

Data are presented as aORs (95% CI), unless indicated otherwise. All models were adjusted for diabetes type and prepregnancy HbA_{1c}. †Data are presented as β coefficients (95% CI); *$P < 0.05$.

macrosomia, shoulder dystocia, neonatal hypoglycemia, and NICU admission >24 h, while GV was not associated with large for gestational age (12). While prior studies consistently report increased risks of large for gestational age with higher average glucose, the association between other CGM metrics and large for gestational age have varied (23,24). In contrast, among our study population, all CGM metrics, except TBR and GV, were associated with increased risks of large for gestational age. These disparate findings may be due to differences in demographics and comorbidity distributions of source populations and our assessment of multiple other outcomes apart from LGA. Additionally, our results demonstrate an association with other clinically important maternal and neonatal outcomes not previously studied.

Our study is novel as it uses statistical methods to identify an evidence-based cutoff for a TIR threshold that is associated with improved clinically relevant neonatal outcomes. Pending validation, a TIR of 66–71%, similar to the ADA-recommended goal of 70% in pregnancy, may be the optimal cut point that reduces adverse neonatal outcomes. In addition to TIR, average glucose and GMI were also noted to be good predictors of neonatal morbidity. Further studies are needed to evaluate the combined utility of average glucose, GMI, and TIR to determine whether recommendations should include not only a target for TIR but also concurrent targets for both TIR and average glucose.

Our study has numerous strengths. It is novel in providing data on multiple CGM metrics that can help guide management of patients with preexisting diabetes in pregnancy to reduce adverse pregnancy outcomes.

Second, we examined multiple clinically relevant maternal and neonatal outcomes, in contrast to prior studies that have been largely focused on large for gestational age neonates.

Third, while a majority of previous studies have been in patients with type 1 diabetes, >40% of our study population had type 2 diabetes, a population with very limited data on CGM metrics in pregnancy.

Fourth, our study data were rigorously collected through individual medical record review, reducing misclassification errors.

Finally, CGM metrics were assessed longitudinally through pregnancy, and all

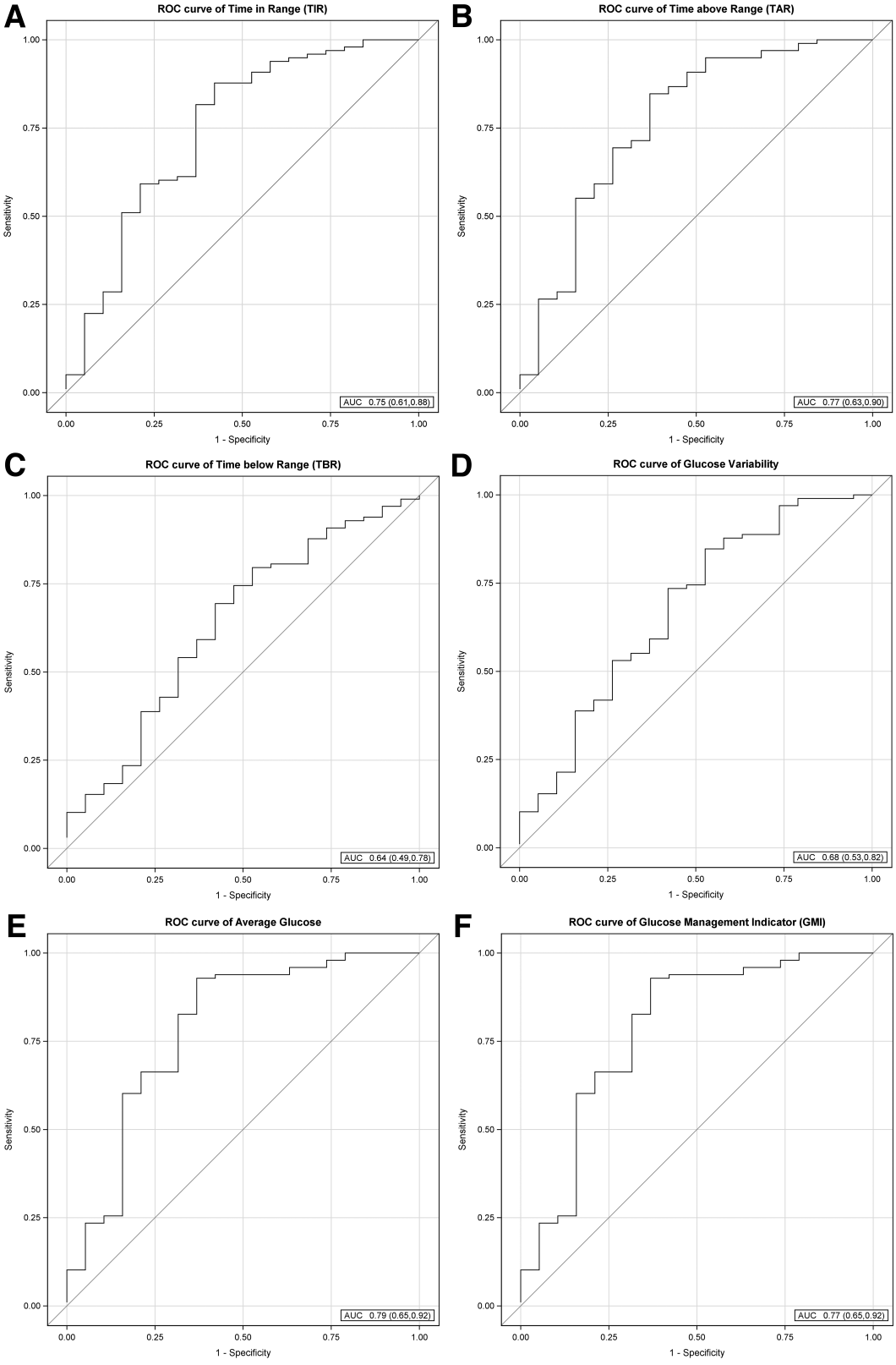

Figure 1—Receiver operating characteristic (ROC) curves for associations of glycemic control metrics with primary composite outcome. Compared with the AUC for TIR (*A*), the AUCs for TAR (*B*), TBR (*C*), and GV (*D*) were not significantly different in predicting the primary outcome ($P > 0.05$), while AUCs for average glucose (*E*) and GMI (*F*) were marginally better predictors of the primary outcome compared with TIR ($P < 0.05$ for both).

outcomes were ascertained from a well-characterized cohort that was consistently managed through two dedicated prenatal care clinics that follow a standardized clinical protocol for treatment of diabetes in pregnancies.

Our study's limitations include the relatively small number of patients in our cohort, which limits rigorous statistical analysis after stratification by diabetes type or other clinical characteristics. However, the effect of fetal exposure to hyperglycemia on adverse neonatal outcomes is likely to be similar regardless of diabetes type, as demonstrated by lack of effect modification by diabetes type. Additionally, we adjusted for diabetes type in the multivariable regression models to account for any confounding.

Second, only a limited number of patients in our cohort used a CGM prior to pregnancy, and most were unable to obtain a CGM until the second trimester.

Third, the limited variability of CGM metrics across trimesters impaired our ability to assess the effect of longitudinal changes in these metrics on maternal and neonatal outcomes. We also acknowledge the limited power to detect associations with rare outcomes as well as for associations between TBR and outcomes. Although, we did not adjust for multiple comparisons, our findings are consistent with prior literature and biologically plausible. Further, the direction of effects is as expected and also consistent across different CGM metrics.

Fourth, the mean gestational age at the initiation of CGM at 20 weeks may limit the generalizability of our findings to cohorts initiating CGM use earlier; however, patients in our cohort had >4 months of CGM data with >80% time CGM in use.

Finally, this analysis cannot determine what TIR can safely be attained by all patients, and many patients in this cohort did not achieve a mean TIR in the third trimester of >70%.

Several areas of CGM use in pregnancy are still understudied. All metrics except TBR were associated with pregnancy outcomes. However, while the role of TBR requires further analysis in larger studies, its clinical utility may lie in its use as a safety metric for patients with diabetes in pregnancy. Our statistical approach to identifying the optimal TIR focused on maximizing the Youden and Liu indices. As recommended by the ADA, a TIR ≥70% should continue to be used by clinical providers and patients in pregnancy. Additional studies are still needed to evaluate whether higher TIR goals can be safely achieved without increasing TBR, whether this differs by diabetes type, and whether tighter glycemic control further reduces pregnancy risks. Understanding barriers to achieving higher TIR, the combined predictive ability of multiple CGM measures, and how longitudinal changes in CGM metrics in pregnancy are associated with pregnancy outcomes, may help improve the utility of CGM in pregnant patients.

In summary, this study provides salient information that can be used to counsel and manage pregnant patients with diabetes to reduce adverse pregnancy outcomes. It also reaffirms that the current TIR goals of ≥70% should be used to improve neonatal outcomes in patients with preexisting diabetes in pregnancy.

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