Placental Weight for Gestational Age and Adverse Perinatal Outcomes

Jennifer A. Hutcheon, PhD, Helen McNamara, MD, MSc, Robert W. Platt, PhD, Alice Benjamin, MD, and Michael S. Kramer, MD

OBJECTIVE: The fetoplacental ratio has been used conventionally to study the contribution of the placenta to fetal growth restriction. However, this measure is problematic because a normal fetoplacental ratio can reflect birth weight and placental weight that are both normal, both low, or both high. The objective of this study was to examine the independent association between placental weight for gestational age and perinatal mortality or serious neonatal morbidity.

METHODS: A sex- and gestational age–specific placental weight z score was calculated for a cohort of 87,600 singleton births at the Royal Victoria Hospital in Montreal, Canada, 1978–2007. The relationship between placental weight z score and adverse perinatal outcomes (stillbirth, neonatal death, 5-minute Apgar score lower than 7, seizures, or respiratory morbidity) was examined using logistic regression. Multivariable models examined whether the relationship was independent of birth weight and other pregnancy risk factors.

RESULTS: After controlling for birth weight, fetuses with a low placental weight z score were at significantly increased risk of stillbirth (odds ratio [OR] 2.0, 95% confidence interval [CI] 1.4–2.6, percent population attributable risk 17.8%). In contrast, adverse neonatal outcomes were significantly more likely among those with high placental weight z scores (OR 1.4, 95% CI 1.2–1.7, percent population attributable risk 5% for any serious neonatal morbidity). Similar trends were observed after further adjusting for pregnancy risk factors.

CONCLUSION: Placental weight for gestational age is an independent risk factor for adverse perinatal outcomes, above and beyond the known association with birth weight. The mechanisms behind the opposing effects of placental weight z score on risk of stillbirth compared with adverse neonatal outcomes require further elucidation.
(Obstet Gynecol 2012;119:1251–8)
DOI: 10.1097/AOG.0b013e318253d3df

LEVEL OF EVIDENCE: III

Fetal growth restriction long has been associated with adverse perinatal outcomes.[1] As the placenta is the sole source of fetal oxygen and nutrients, placental insufficiency is believed to play a key role in fetal growth restriction. A number of studies have observed that placental weight and fetal weight are highly correlated,[2,3] and that the size of a newborn's placenta in relation to its birth weight (the so-called fetoplacental ratio) is a significant determinant of adverse outcomes such as perinatal death, intrapartum distress, and low Apgar scores at birth.[3–5] However, although some researchers have reported increased risks with a high fetoplacental ratio (ie, a fetus that is large relative to its placenta),[4] others have reported increased risks with oversized placentas.[5]

Although the interrelationship between fetal and placental growth has conventionally been assessed using the fetoplacental ratio, that measure is problematic because a "normal" ratio can reflect birth weight and placental weight that are both normal, both low, or both high. By combining fetal weight and placental weight into a single measure, the fetoplacental ratio is unable to establish the extent to which placental weight is an independent predictor of adverse perina-

tal outcome, above and beyond the known effects of birth weight. Moreover, the fetoplacental ratio changes with gestational age,[3] making it difficult to separate the effects of poor placental growth from the effects of preterm birth on adverse outcomes. Several placental-weight-for-gestational-age reference charts have been developed to classify placental size based on population percentiles,[6–8] but the extent to which different statistical thresholds of placental weight (such as the 10th or 3rd percentiles) are associated with adverse perinatal outcomes has not been well established, and any such associations are likely to be confounded by factors associated with birth weight. The goal of this study was to examine the relationship between placental weight for gestational age and perinatal mortality or serious neonatal morbidity, independent of the known association with birth weight.

MATERIALS AND METHODS

The study population was drawn from births at the Royal Victoria Hospital, a McGill University tertiary care teaching hospital in Montreal, Canada, between 1978 and 2007. The maternal and neonatal medical records of deliveries at the Royal Victoria Hospital are contained in a quality-controlled clinical database, the McGill Obstetrics and Neonatal Database.[9] All singleton births with no congenital anomalies were included in our study. Pregnancies with missing fetal sex, missing gestational age, gestational age less than 24 weeks or more than 43 weeks, missing placental weight, or implausible placental weight (3 standard deviations above or below the sample population mean) were excluded. Ethics approval was obtained from the McGill University institutional review board (#SDR-06–033).

Placental weight at delivery was measured by nursing staff after the cord had been cut and blood clots removed. An internal, sex-specific placental-weight-for-gestational-age reference was created based on the placental weights of all singleton live-born neonates in the McGill Obstetrics and Neonatal Database with an ultrasound-confirmed estimate of gestational age (last menstrual period is used to estimate gestational age if it is within 1 week of the early ultrasound-based estimate; otherwise, the ultrasound-based estimate is used). The means and standard deviations in this reference were used to calculate a sex- and gestational age–specific placental weight z score for each neonate in the study cohort. z Scores quantify how far a given neonate's placental weight is from the mean placental weight for neonates of similar sex and gestational age by standardizing

weight measurements to a normal distribution with a mean of 0 and a standard deviation of 1. For example, a z score of −1 indicates a placental weight 1 standard deviation below the sex- and gestational age–specific average. The score is calculated as (neonate's placental weight−mean placental weight for gestational age and sex)/standard deviation of placental weight for gestational age and sex). Birth weight was also standardized for gestational age and sex using the same internal z score approach as for placental-weight-for-gestational-age. Pearson product-moment correlation was used to quantify the association between placental weight and birth weight.

The adverse perinatal outcomes examined were 1) stillbirth, 2) in-hospital neonatal death, 3) neonatal seizures, 4) serious respiratory morbidity (defined as the receipt of assisted ventilation for more than 3 minutes), and 5) 5-minute Apgar score less than 7. We also created a composite neonatal morbidity outcome variable, defined as the occurrence of any of neonatal seizures, serious respiratory morbidity, or 5-minute Apgar score less than 7.

The relationship between placental weight z score and each adverse perinatal outcome was examined using logistic regression. We modeled placental weight z score using a restricted cubic spline[10] (with knots at the 0.05, 0.275, 0.5, 0.725, and 0.95 percentiles of placental weight z score) to allow smooth, flexible, curvilinear relationships with the adverse perinatal outcomes. As nonlinear relationships were observed, placental weight z scores were then classified as <-1, -1 to $+1$, and >1, and the odds of adverse perinatal outcome among births with z scores <-1 or >1 were compared with the odds among births between -1 and $+1$ (reference group). Models were adjusted for birth-weight-for-gestational-age z score, then further adjusted for potential confounders (maternal diabetes in pregnancy, hypertension in pregnancy, anemia, smoking in pregnancy, calendar year, history of stillbirth, circumvallate placenta, marginal cord insertion, and velamentous cord insertion). Although mode of delivery is known to be associated with placental weight (lower mean placental weight after vaginal delivery, believed to result from maternal blood being squeezed out by uterine contractions),[7] we did not adjust for it in our models because we hypothesized that it was likely on the causal pathway between placental size and adverse outcome (eg, fetal compromise resulting from suboptimal placental weight may result in the need for a cesarean delivery). Placental weights of antepartum and intrapartum stillbirths were compared using a Wilcoxon rank-sum test. We calculated percent population at-

tributable risks using the formula %PAR=pd× (RR−1)/RR, where pd is the proportion of cases exposed to high or low placental weight, and RR is the adjusted relative risk.

Birth weight z scores derived from neonatal weight references are known to be biased toward lower weights at preterm ages because preterm newborns are systematically smaller than their in utero peers.[11–13] Placental weight z scores may likewise be biased at preterm ages if the placental development of preterm births differs from that of ongoing pregnancies. We therefore conducted sensitivity analyses in which preterm births (less than 37 weeks) were excluded to assess the robustness of our findings to these potential biases. We also conducted sensitivity analyses in which an interaction term between calendar year and placental weight z score categories was added to the fully adjusted models. All statistical analyses were performed using Stata 11.0.

RESULTS

There were 95,512 singleton births without congenital anomalies at the Royal Victoria Hospital between 1978 and 2007. Neonates with missing gestational age or gestational age less than 24 or more than 43 weeks (n=2,343) or missing sex (n=3) were excluded. A valid placental weight was available in 94% of the remaining 93,166 births, leaving a total of 87,600 births for analysis. Neonates with missing placental weights were smaller (100 g) and younger (2.5 days) than neonates with recorded placental weights and were more likely to be born after cesarean delivery (33% compared with 21%). A higher proportion of placental weights were missing from the earlier years in the study period. No meaningful differences were observed in maternal characteristics between those with missing and recorded placental weight (parity, age, prepregnancy body mass index, diabetes, or hypertension status). Maternal and fetal characteristics of the study population are shown in Table 1. The correlation between birth weight and placental weight was +0.60 (95% confidence interval [CI] 0.59–0.60).

The curvilinear relationships between placental weight z score as a continuous variable and risk of each adverse outcome (predicted by the spline-based model) are denoted in Figure 1 (crude relationship) and Figure 2 (after adjustment for birth weight). The risks of adverse perinatal outcome according to placental weight z score categories are presented in Table 2, and odds ratios (ORs) among neonates with high (>1) or low (<−1) placental weight z scores are shown in Table 3. Low placental weight z score was associated with an increased risk of stillbirth (the OR among births with a placental weight z score <−1 was 3.4, 95% CI 2.6–4.3), with a steep linear increase in risk below −1 (Fig. 1A). Adjustment for birth weight attenuated the relationship, but low placental weight for gestational age remained an independent predictor of stillbirth (2.0-fold increased risk among neonates with placental weight z scores <−1, 95% CI 1.4–2.6). This corresponds to a percent population attributable risk of 17.8% (or in other words, 17.8% of the stillbirths in this population were potentially attributable to low placental weight z scores). High

Table 1. Maternal and Neonatal Descriptive Characteristics of 87,600 Singleton Births With No Congenital Anomalies in the Royal Victoria Hospital in Montreal, Canada, 1978–2007

Characteristic	Placental Weight z Score		
	<−1 SD	−1 to+1 SD	>+1 SD
Maternal age (y)	29.8±5.1	30.2±5.1	30.6±5.2
Maternal prepregnancy BMI (kg/m²)*	21.9±3.9	22.8±4.3	24.2±5.0
Parity			
0	7,362 (55.15)	28,259 (46.53)	5,432 (40.18)
1	4,105 (30.75)	21,847 (35.97)	5,243 (38.78)
2 or more	1,881 (14.09)	10,627 (17.50)	2,844 (21.04)
Hypertension in pregnancy	1,256 (9.41)	4,390 (7.23)	1,084 (8.02)
Gestational diabetes	337 (2.52)	2,149 (3.54)	800 (5.92)
Smoking in pregnancy	2,307 (17.28)	9,311 (15.33)	2,063 (15.26)
Birth weight (g)	2,994±502	3,371±502	3,777±527
Placental weight (g)	475±60	649±83	884±86
Gestational age (wk)	3 8.9±1.9	38.8±2.0	38.9±1.9
Sex (male)	6,543 (49.02)	30,131 (49.61)	6,664 (49.29)

SD, standard deviation; BMI, body mass index.
Data are mean±SD or n (%).
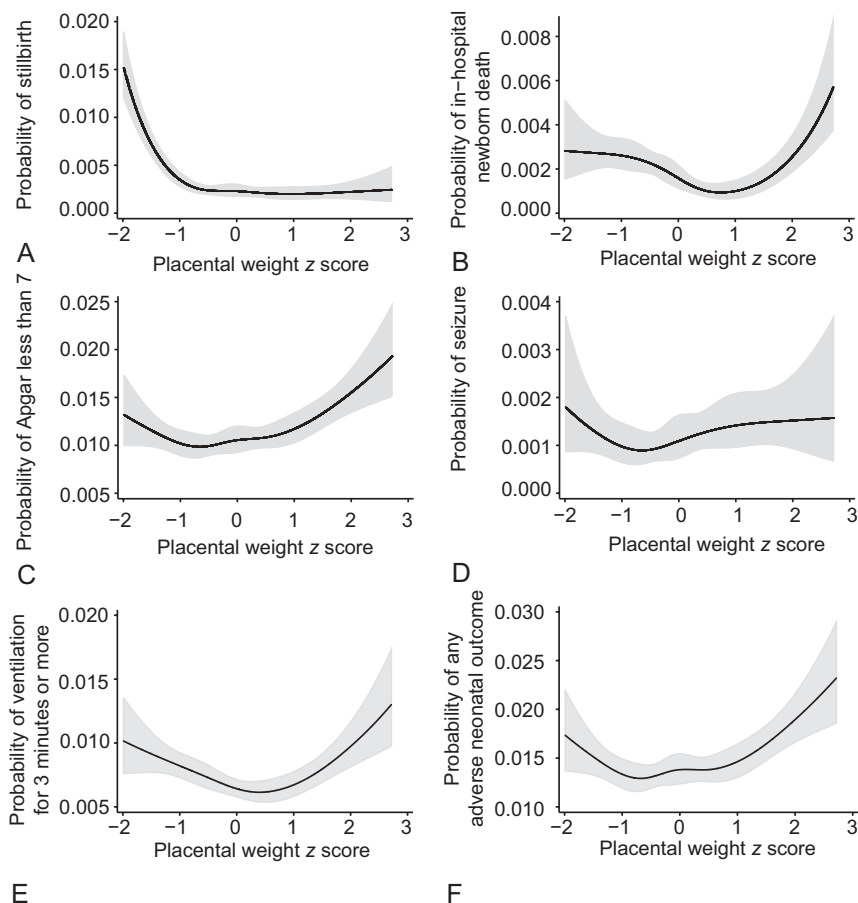* Available in 44,381 births.

Fig. 1. Predicted probability of **A.** stillbirth, **B.** neonatal death, **C.** 5-minute Apgar score less than 7, **D.** neonatal seizure, **E.** serious respiratory morbidity, and **F.** composite neonatal morbidity (any of Apgar score less than 7, neonatal seizure, or serious respiratory morbidity) according to placental-weight-for-gestational-age z score among births at the Royal Victoria Hospital, Montreal, Canada (1978–2007), with 95% confidence intervals.

Hutcheon. Placental Weight and Adverse Perinatal Outcomes. Obstet Gynecol 2012.

placental weight z score was not associated with risk of stillbirth. The placental weight z score of intrapartum stillbirths (n=19) was not significantly different than that of antepartum stillbirths (n=252; z scores of −0.55 compared with −0.51, respectively, P=.96), and restricting our models to antepartum stillbirths did not change the associations with placental weight z score (data available on request).

In contrast to the pattern observed with stillbirth, the unadjusted relationship between placental weight z score and adverse neonatal outcomes was U-shaped (Fig. 1B–F), with increased risks associated with both low and high placental weight z scores. After adjusting for birth weight z score, however, the risks associated with lower placental weight z scores disappeared, and increased neonatal risks remained only among neonates with high placental weight z scores (Fig. 2B–F). Neonates with placental weight z scores >+1 had significantly increased risks of having a 5-minute Apgar score lower than 7 (OR 1.4, 95% CI 1.2–1.7), neonatal seizures (OR 1.9, 95% CI 1.1–3.4), ventilation for more than 3 minutes (OR 1.3, 95% CI 1.1–1.7), or of the composite neonatal morbidity

outcome (OR 1.4, 95% CI 1.2–1.7) (Table 3). The percent population attributable risk was 5% (or, 5% of the adverse neonatal outcomes were potentially attributable to high placental weight z score). The OR for neonatal death was comparable, but did not reach statistical significance (OR 1.4, 95% CI 0.9–2.3). Among neonates of similar birth weight, small placental size was not associated with increased risk of adverse neonatal outcome, and was protective for at least one adverse neonatal outcome.

Adjusting for maternal diabetes, hypertension, anemia, smoking during pregnancy, calendar year, history of stillbirth, circumvallate placenta, marginal cord insertion, and velamentous cord insertion had minimal effect on our findings. Sensitivity analyses excluding preterm births likewise did not have a major effect. If anything, point estimates of the ORs for stillbirth, low Apgar score, receipt of ventilation, and the composite neonatal morbidity outcome appeared to be higher. We found no significant interaction between calendar time and placental weight z scores.

In exploratory analyses, we examined the occurrence of placental pathologies according to placental
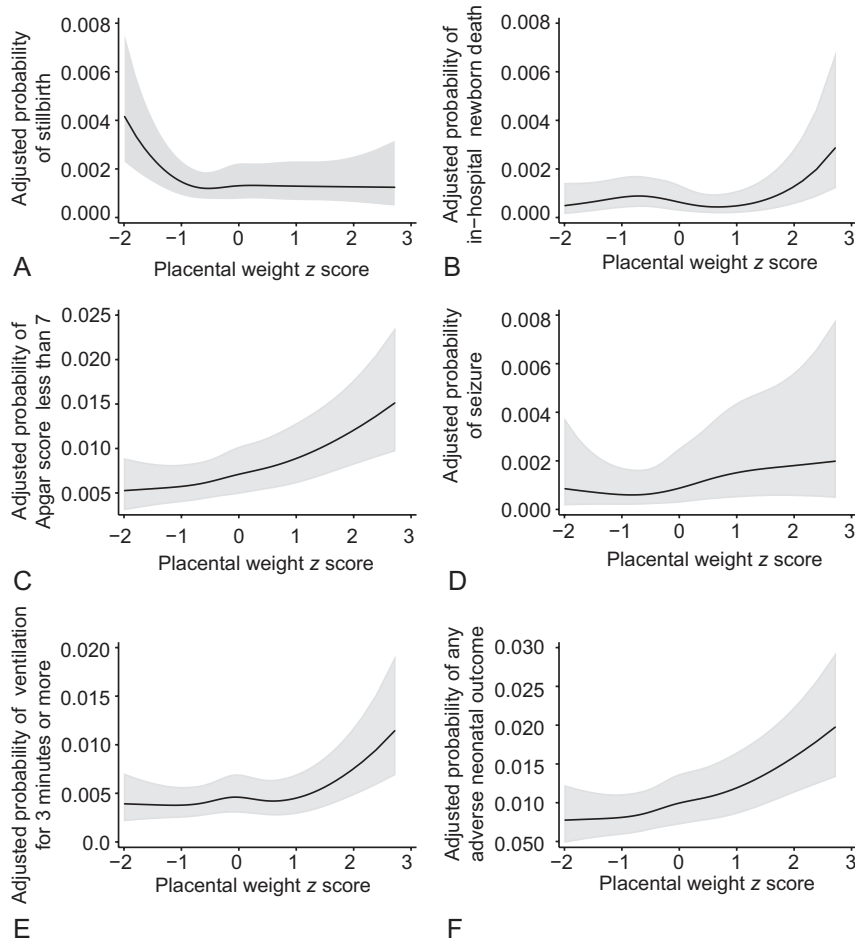
Fig. 2. Predicted probability after adjustment for birth weight z score of **A.** stillbirth, **B.** neonatal death, **C.** 5-minute Apgar score less than 7, **D.** neonatal seizure, **E.** serious respiratory morbidity, and **F.** composite neonatal morbidity (any of Apgar score less than 7, neonatal seizure, or serious respiratory morbidity) according to placental-weight-for-gestational-age z score among births at the Royal Victoria Hospital, Montreal, Canada (1978–2007), with 95% confidence intervals.

Hutcheon. Placental Weight and Adverse Perinatal Outcomes. Obstet Gynecol 2012.

weight z score groups (Table 2). Neonates with a placental weight z score above +1 were more likely to have chorioamnionitis defined as severe or definite on microscopic examination (4% compared with 2.9% and 3.3% among neonates with z scores <-1 or -1 to $+1$, respectively, $P<.001$), whereas neonates with a placental weight less than -1 were more likely to have placental infarctions noted (2.3% compared with 0.9% and 0.7% among neonates with placental weight z score -1 to $+1$ and $>+1$, respectively, $P<.001$).

DISCUSSION

In this study, we demonstrated that placental weight for gestational age z score is an independent predictor of perinatal mortality and serious neonatal morbidity. A novel finding of this study was that the relationship between placental weight and stillbirth was opposite to that between placental weight and adverse neonatal outcomes. Past studies have reported both increased risks associated with low placental weight and increased risks associated with high placental weight,

but not opposing effects according to outcome.[3–6,14] However, these earlier studies did not examine the independent role of placental weight after controlling for both birth weight and gestational age, which may explain the differences between studies.

Our study population included more than twice as many births as the largest study previously published[5] on placental weight and perinatal outcomes. Placental weight was available in 94% of eligible births through routine collection at our institution, minimizing the potential for selection bias. Our large sample size and advanced analytic methods may have allowed the opposing effects of placental weight on stillbirth and adverse neonatal outcomes to be detected. It is notable that each of the adverse neonatal outcomes followed a similar pattern, decreasing the likelihood that our results are a chance finding. Further, results were not meaningfully different when preterm births were excluded. Bias introduced by calculating birth weight and placental weight z scores from the mean and standard deviation of preterm

Hutcheon et al *Placental Weight and Adverse Perinatal Outcomes*

Table 2. Serious Adverse Perinatal Outcomes According to Placental Weight for Gestational Age z Score Among 87,600 Singleton Births at the Royal Victoria Hospital in Montreal, Canada, 1978–2007

Perinatal Outcome	Placental Weight for Gestational Age z Score		
	< −1 SD	−1 to+1 SD	> +1 SD
n	13,348	60,733	13,519
Mean placental weight z score	−1.4	−0.08	1.7
Stillbirth	102 (7.6)	139 (2.3)	30 (2.2)
Newborn in-hospital death	32 (2.4)	111 (1.8)	29 (2.1)
5-min Apgar score less than 7	151 (11.6)	630 (10.5)	182 (13.7)
Neonatal seizures	20 (1.5)	63 (1.0)	20 (1.5)
Ventilation longer than 3 min	108 (8.1)	438 (7.2)	108 (8.0)
Any adverse neonatal outcome	196 (14.7)	828 (13.6)	235 (17.4)
Severe or definite chorioamnionitis*	381 (29)	2,027 (33)	538 (40)
Placental infarction*	313 (23)	539 (9)	98 (7)

Data are n (risk per 1,000).
SD, standard deviation.
* Noted on microscopic examination.

births at preterm ages[13] is therefore unlikely to be responsible for our findings.

The explanation for these opposing patterns is unclear. The increased risk of stillbirth associated with low placental weight supports the hypothesis that a decreased placental surface area for gas and nutrient exchange may lead to fetal compromise.[3,4,14] The increased placental weight associated with adverse neonatal outcome may reflect a compensatory adaptation to increase gas and nutrient exchange that allowed the fetus to survive until birth. Compensatory placental hypertrophy is believed to explain the relatively larger placental weights of births at high altitudes, or pregnancies in affected by maternal anemia, or smoking.[15–18] Alternatively, it has been hypothesized that the increased risk observed with high placental weight is due to placental villous edema, which may create a barrier to gas exchange between mother and fetus by compressing blood vessels.[5,19] The high placental weight z scores among pregnancies with chorioamnionitis noted in our study may be the result of placental villous edema.[20] Unfortunately, we were unable to establish whether the origin of the infection was antepartum or intrapartum (which would be less likely to affect placental weight).

Further work to explore this hypothesis is needed. The hypothesis would not, however, explain the link between low placental weight and risk of stillbirth. It is also possible that factors such as race, socioeconomic status, thrombophilias, or undiagnosed diabetes may explain the risk associated with abnormally low or high placental weights. Further research to better understand determinants of abnormal placental weight and mechanisms for increased risks would be valuable. Finally, loss of fetal weight is believed to occur between the time of death and the time of delivery,[21] and a similar process is possible for the placenta. The lower placental weight could therefore be the result of, not the cause of, the stillbirth. Although the number of intrapartum stillbirths in our study was small, the similarity between the placental weight z scores of antepartum and intrapartum stillbirths makes this explanation less likely, however. Further, stillbirths are typically delivered within 48–72 hours at our institution.

Several limitations to our study should be mentioned. First, placental weights in this study were obtained through routine clinical practice, and an assessment of the degree of potential interindividual variation in delivery room measurement is unavailable. As with all studies, the precision of placental weight measurements should not be interpreted in the same way as birth weight measurements. Inconsistencies in the degree of placental trimming before weighing in the delivery room may change placental weight by up to 16%.[22] However, the correlation between untrimmed placentas and placentas with the umbilical cord cut and membranes removed has been found to remain high (98%),[22] and the correlation between placental weight and birth weight observed in our study is similar to that reported in the literature. Further, measurement error in placental weight would likely have attenuated any observed associations, so could not explain the significant associations reported in this study. Second, placental weight is only a crude marker for placental function, and characteristics such as the placenta's lateral growth across the uterine lining (reflecting the number of maternal spiral arteries supplying the placenta) may be more important determinants of adverse perinatal outcome.[23] Finally, as our study population was drawn from women delivering at a tertiary care hospital, confirmation of our findings using a large population-based sample would be valuable.

After adjusting for birth weight, placental weight remained an independent predictor of perinatal mortality and serious neonatal morbidity in our study. We

Table 3. Odds Ratio for Adverse Perinatal Outcomes According to Placental Weight for Gestational Age z Score Among 87,600 Singleton Births at the Royal Victoria Hospital in Montreal, Canada, 1978–2007

Perinatal Outcome	Placental Weight for Gestational Age z Score		
	<−1 SD	−1 to+1 SD	>+1 SD
Stillbirth			
Crude	3.4 (2.6–4.3)	Reference	1.0 (0.7–1.4)
Adjusted for birth weight z score	2.0 (1.4–2.6)	Reference	1.1 (0.7–1.7)
Adjusted for birth weight z score and covariates*	1.9 (1.4–2.6)	Reference	1.1 (0.7–1.7)
Excluding preterm births	2.5 (1.6–4.0)	Reference	0.8 (0.4–1.7)
Newborn in-hospital death			
Crude	1.3 (0.9–2.0)	Reference	1.2 (0.8–1.8)
Adjusted for birth weight z score	0.8 (0.5–1.2)	Reference	1.4 (0.9–2.3)
Adjusted for birth weight z score and covariates*	0.8 (0.5–1.2)	Reference	1.3 (0.8–2.1)
Excluding preterm births	0.9 (0.3–2.9)	Reference	0.9 (0.2–4.0)
5-min Apgar score less than 7			
Crude	1.1 (0.9–1.3)	Reference	1.3 (1.1–1.5)
Adjusted for birth weight z score	0.9 (0.7–1.1)	Reference	1.4 (1.2–1.7)
Adjusted for birth weight z score and covariates*	0.9 (0.7–1.1)	Reference	1.3 (1.1–1.6)
Excluding preterm births	0.9 (0.7–1.2)	Reference	1.6 (1.3–2.0)
Neonatal seizures			
Crude	1.4 (0.9–2.4)	Reference	1.4 (0.9–2.4)
Adjusted for birth weight z score	1.1 (0.6–2.0)	Reference	1.9 (1.1–3.4)
Adjusted for birth weight z score and covariates*	1.1 (0.6–1.9)	Reference	1.9 (1.1–3.3)
Excluding preterm births	1.0 (0.5–2.0)	Reference	1.8 (0.9–3.6)
Ventilation longer than 3 min			
Crude	1.1 (0.9–1.4)	Reference	1.1 (0.9–1.4)
Adjusted for birth weight z score	0.8 (0.6–1.0)	Reference	1.3 (1.1–1.7)
Adjusted for birth weight z score and covariates*	0.8 (0.6–1.0)	Reference	1.3 (1.0–1.6)
Excluding preterm births	0.8 (0.6–1.2)	Reference	1.6 (1.1–2.2)
Any adverse neonatal outcome			
Crude	1.1 (0.9–1.3)	Reference	1.3 (1.1–1.5)
Adjusted for birth weight z score	0.8 (0.7–1.0)	Reference	1.4 (1.2–1.7)
Adjusted for birth weight z score and covariates*	0.9 (0.7–1.0)	Reference	1.4 (1.2–1.6)
Excluding preterm births	0.9 (0.7–1.1)	Reference	1.6 (1.3–1.9)

SD, standard deviation.
Data are odds ratio (95% confidence interval) unless otherwise specified.
* Maternal anemia, diabetes, hypertension in pregnancy, smoking, fetal sex, calendar year, history of stillbirth, circumvallate placenta, marginal cord insertion, and velamentous cord insertion.

conclude that placental weight is not merely a reflection of fetal growth, but has independent effects on fetal and neonatal outcomes. Further work is needed to better understand the reasons for the opposing effects of placental weight on stillbirth and adverse neonatal outcomes, and to establish determinants of extremes of placental weight for gestational age (small or large). Work is ongoing to develop a mathematical formula for estimating placental weight in routine care using two-dimensional ultrasonography.[24] If the accuracy and reliability of this formula are confirmed in large-scale studies, it may provide a valuable tool for obstetricians to improve the prenatal identification of fetuses at increased risk of developing adverse perinatal outcomes. In the meantime, obstetricians may wish to include subjective assessments of placental size on ultrasound scans when forming an overall clinical impression, with the recognition that both small and large placentas are associated with increased risks.

REFERENCES

1. World Health Organization Expert Group on Prematurity. Technical report, series 27. Geneva: World Health Organization; 1950.
2. Williams LA, Evans SF, Newnham JP. Prospective cohort study of factors influencing the relative weights of the placenta and the newborn infant. BMJ 1997;314:1864–8.
3. Molteni RA. Placental growth and fetal/placental weight (F/P) ratios throughout gestation–their relationship to patterns of fetal growth. Semin Perinatol 1984;8:94–100.
4. Bonds DR, Gabbe SG, Kumar S, Taylor T. Fetal weight/placental weight ratio and perinatal outcome. Am J Obstet Gynecol 1984;149:195–200.
5. Naeye RL. Do placental weights have clinical significance? Hum Pathol 1987;18:387–91.

6. Thomson AM, Billewicz WZ, Hytten FE. The weight of the placenta in relation to birthweight. J Obstet Gynaecol Br Commonw 1969;76:865–72.

7. Burkhardt T, Schaffer L, Schneider C, Zimmermann R, Kurmanavicius J. Reference values for the weight of freshly delivered term placentas and for placental weight-birth weight ratios. Eur J Obstet Gynecol Reprod Biol 2006;128:248–52.

8. Almog B, Shehata F, Aljabri S, Levin I, Shalom-Paz E, Shrim A. Placenta weight percentile curves for singleton and twins deliveries. Placenta 2011;32:58–62.

9. Smith LP, DeLeon A, Funnell WR, Lalonde AB, McLean FH, Usher R. A research-oriented system for McGill Obstetrical and Neonatal Data (MOND). Acta Obstet Gynecol Scand 1982;16(suppl 109):49–50.

10. Harrell FE. Regression modeling strategies with application to linear models, logistic regression, and survival analysis. New York (NY): Springer-Verlag; 2001.

11. Burkhardt T, Schaffer L, Zimmermann R, Kurmanavicius J. Newborn weight charts underestimate the incidence of low birthweight in preterm infants. Am J Obstet Gynecol 2008; 199:139.

12. Morken NH, Kallen K, Jacobsson B. Fetal growth and onset of delivery: a nationwide population-based study of preterm infants. Am J Obstet Gynecol 2006;195:154–61.

13. Hutcheon JA, Platt RW. The missing data problem in birth weight percentiles and thresholds for "small-for-gestational-age." Am J Epidemiol 2008;167:786–92.

14. Kloosterman GJ. On intrauterine growth: the significance of prenatal care. Int J Gynaecol Obstet 1970;8:895–912.

15. Beischer NA, Sivasamboo R, Vohra S, Silpisornkosal S, Reid S. Placental hypertrophy in severe pregnancy anaemia. J Obstet Gynaecol Br Commonw 1970;77:398–409.

16. Kruger H, Arias-Stella J. The placenta and the newborn infant at high altitudes. Am J Obstet Gynecol 1970;106:586–91.

17. Mulcahy R, Murphy J, Martin F. Placental changes and maternal weight in smoking and nonsmoking mothers. Am J Obstet Gynecol 1970;106:703–4.

18. Wingerd J, Christianson R, Lovitt WV, Schoen EJ. Placental ratio in white and black women: relation to smoking and anemia. Am J Obstet Gynecol 1976;124:671–5.

19. Naeye RL, Maisels MJ, Lorenz RP, Botti JJ. The clinical significance of placental villous edema. Pediatrics 1983;71: 588–94.

20. Hargitai B, Marton T, Cox PM. Best practice no 178. Examination of the human placenta. J Clin Pathol 2004;57:785–92.

21. Chard T. Does the fetus lose weight in utero following fetal death: a study in preterm infants. BJOG 2001;108:1113–5.

22. Leary SD, Godfrey KM, Greenaway LJ, Davill VA, Fall CH. Contribution of the umbilical cord and membranes to untrimmed placental weight. Placenta 2003;24:276–8.

23. Salafia CM, Zhang J, Miller RK, Charles AK, Shrout P, Sun W. Placental growth patterns affect birth weight for given placental weight. Birth Defects Res A Clin Mol Teratol 2007;79:281–8.

24. Azpurua H, Funai EF, Coraluzzi LM, Doherty LF, Sasson IE, Kliman M, et al. Determination of placental weight using two-dimensional sonography and volumetric mathematic modeling. Am J Perinatol 2010;27:151–5.