ORIGINAL ARTICLE

Outcomes of Pregnancy after Bariatric Surgery

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ABSTRACT

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IN 2008, AN ESTIMATED 300 MILLION WOMen worldwide were obese (body-mass index [BMI; the weight in kilograms divided by the square of the height in meters], ≥30).[1] In 2011–2012 in the United States, 36% of adult women were obese,[2] and the majority of women in early pregnancy were either overweight or obese (BMI, ≥25).[3]

Maternal obesity is a risk factor for gestational diabetes, with attendant increased risks of macrosomia, delivery complications, obesity in the offspring, and later development of type 2 diabetes in the mother.[4-6] Maternal obesity is also associated with an increased risk of stillbirth,[7] preterm birth,[8] and some congenital malformations[9] and a reduced risk of infants born small for gestational age.[7]

Among obese persons with type 2 diabetes, bariatric surgery results in higher rates of short-term[10,11] and long-term[12,13] diabetes remission and prevention of incident diabetes than does conventional therapy for obesity.[14] The effect of prepregnancy bariatric surgery on gestational diabetes has been investigated in small studies with inconclusive results, and the majority of studies have not taken presurgery BMI into account.[15,16] Similarly, although systematic reviews have concluded that the risks of neonatal complications may be lower after bariatric surgery, this conclusion is based on studies with small sample sizes, heterogeneous study designs, and lack of matching for presurgery BMI.[15,16]

We therefore conducted a population-based study using data from nationwide Swedish registries, including information on presurgery BMI among women who had undergone bariatric surgery. We investigated the risks of gestational diabetes and adverse perinatal outcomes among women with a history of bariatric surgery as compared with women without such a history but with similar characteristics.

METHODS

STUDY DESIGN AND DATA SOURCES

In Sweden, prenatal care and delivery care are tax-funded, and the participation rate in the prenatal care program is almost 100%. The first prenatal visit commonly takes place at the end of the first trimester.[17] The Swedish Medical Birth Register includes information on more than 98% of all births in Sweden since 1973. Information is prospectively collected from standardized prenatal, obstetrical, and neonatal records.[18]

With the use of the unique personal identification number assigned to each Swedish resident,[19] we linked data from the Medical Birth Register to the National Patient Register, the Scandinavian Obesity Surgery Registry (SOReg), the Prescribed Drug Register, and the Education Register. The study was approved by the regional ethics committee at Karolinska Institutet, Stockholm.

The National Patient Register includes diagnostic and surgical information on hospital admissions and non–primary care outpatient visits, coded according to the Swedish versions of the *International Classification of Diseases, 10th revision* (ICD-10-SE) (for diagnostic information), and the *Classification of Surgical Procedures* (Nordic Medico-Statistical Committee) (for surgical information). SOReg was established nationwide in 2007; local data from a few hospitals were available beginning in 2004. The registry covers approximately 98.5% of all bariatric procedures in Sweden and includes presurgery and follow-up information. The nationwide Prescribed Drug Register was established in 2005 and includes all dispensed prescription drugs classified according to the World Health Organization Anatomical Therapeutic Chemical (ATC) classification system. The Swedish Education Register includes information about the number of years of formal education.

INTERVENTION COHORT

Between 2006 and 2011, there were 651,561 deliveries recorded in the Swedish Medical Birth Register. We excluded multiple-birth pregnancies (since they are associated with a higher occurrence of complications and differences in fetal growth[20]) and women without a valid personal identification number at the time of delivery, who could therefore not be linked to other registries. After these exclusions, 628,778 singleton pregnancies remained, of which 1755 were in women who had undergone bariatric surgery between 1983 and 2011. Of these pregnancies, 670 occurred in women who had undergone bariatric surgery between 2004 and 2011, whose data were included in SOReg, and whose data on presurgery BMI were available (Fig. 1). From SOReg, we recorded the date of bariatric surgery, so that we could calculate the time between bariatric surgery

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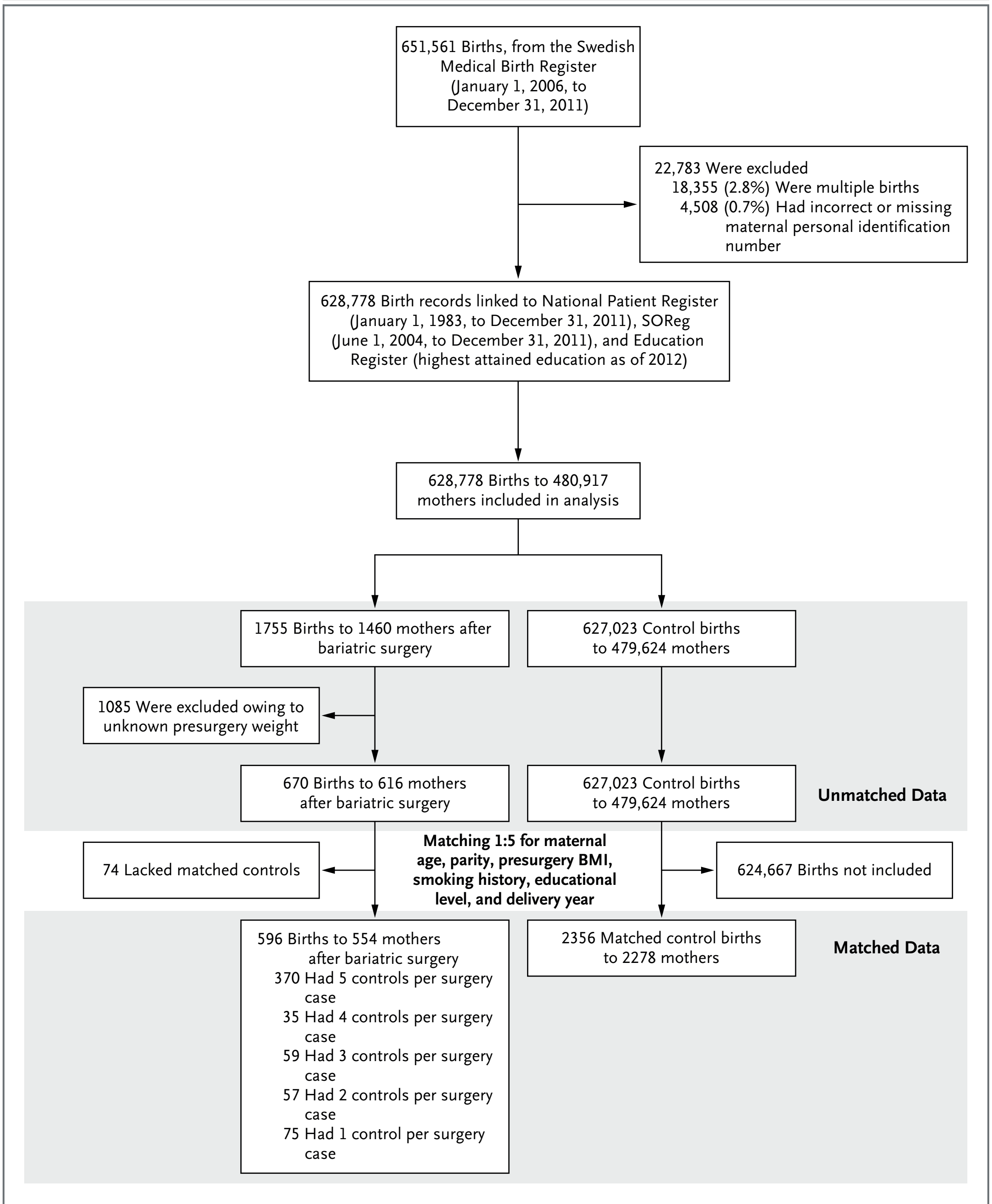

Figure 1. Identification of the Study Population and the Matched Control Population.

The exclusions for multiple births and incorrect or missing maternal personal identification numbers do not sum to 22,783 because there were 80 exclusions for both a multiple birth and an incorrect or missing maternal personal identification number. BMI denotes body-mass index, and SOReg Scandinavian Obesity Surgery Registry.

and delivery, and the type of the most recent procedure (6% of women underwent reoperation). (Surgery codes are provided in Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org.)

CONTROL COHORT

We created a matched control cohort composed of pregnancies in women without a history of bariatric surgery. Up to five control pregnancies were matched without replacement to each postsur-

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gery pregnancy; once a pregnancy in a woman without a history of bariatric surgery was selected as a control, the same pregnancy could not be used as a control again. The matching factors were age (within 1 year older or younger), parity (nulliparous or parous), presurgery BMI (defined as presurgery BMI in the bariatric-surgery cohort and BMI during early pregnancy [i.e., at the first prenatal visit] in the control cohort; 30 to 34.9, 35 to 39.9, 40 to 44.9, 45 to 49.9, or ≥50), early-pregnancy smoking status (nonsmoker, smoker of 1 to 9 cigarettes per day, or smoker of ≥10 cigarettes per day, or missing data), educational level (≤9 years, 10 to 12 years, >12 years, or missing data), and delivery year (2006 to 2011).

COVARIATES

Weight and height measurements at the time of surgery were used to calculate presurgery BMI. Measured weight and self-reported height at the first prenatal visit were used to calculate early-pregnancy BMI; at that time, self-reported smoking status was also recorded. Data on maternal educational level and the mother's region of birth (Nordic [Sweden, Denmark, Norway, Finland, and Iceland] or non-Nordic) were retrieved and linked to data from other registries. A history of hospitalization for coexisting psychiatric, cardiovascular, or respiratory conditions (ICD-10 chapters V, IX, and X, respectively) and of substance abuse (ICD-10 codes F10 through F19) was identified with the use of the National Patient Register. In a subgroup of women, we had information on weight at delivery and could calculate weight gain during pregnancy (from the first prenatal visit).

OUTCOMES

Gestational diabetes was identified by the ICD-10 code (O244) in the Medical Birth Register or the National Patient Register or by ATC code A10A (prescription of insulin during pregnancy) in the Prescribed Drug Register (ICD-10 and ATC codes are provided in Table S2 in the Supplementary Appendix). For analyses of gestational diabetes, we excluded women with a diagnosis of diabetes before pregnancy.

In Sweden, women generally undergo random testing of capillary blood glucose levels four to six times during pregnancy. Women with a plasma blood glucose level of 8.0 mmol per liter (144 mg per deciliter) or higher or women who belong to a risk group (e.g., women with obesity, previous gestational diabetes or macrosomia, or a family history of diabetes) undergo an oral glucose-tolerance test conducted with a loading dose of 75 g. The diagnosis of gestational diabetes is generally made (and was made in this study) on the basis of a 2-hour plasma glucose level of 10.0 mmol per liter (180 mg per deciliter) or higher during such a glucose-tolerance test (range among Swedish counties, 8.9 to 12.2 mmol per liter [160 to 220 mg per deciliter]) or a fasting plasma glucose level of 7.0 mmol per liter (126 mg per deciliter) or higher. If oral glucose-tolerance testing is deemed unsafe (e.g., owing to the risk of the dumping syndrome [i.e., rapid gastric emptying]), fasting glucose levels and preprandial and postprandial glucose values are assessed instead.

Large-for-gestational-age infants were defined as those with a birth weight greater than the 90th percentile for sex and gestational age, and small-for-gestational-age infants as those with a birth weight less than the 10th percentile.[21] Other outcomes included low birth weight (<2500 g), macrosomia (>4500 g), preterm birth (<37 completed weeks of gestation), stillbirth (fetal death at ≥22 completed weeks of gestation on or after July 1, 2008 [97% of pregnancies ending in fetal death] and at ≥28 weeks before July 1, 2008 [<3% of pregnancies ending in fetal death]), neonatal death (death before 28 days of life), and major congenital malformations detected during the first year of life (divided into two categories: all malformations and malformations excluding chromosomal abnormalities) (ICD-10 codes are provided in Table S3 in the Supplementary Appendix).

The number of weeks of gestation was determined by ultrasound examination or, if ultrasonography was unavailable, by the recorded date of the first day of the last menstrual period. Since 1990, Swedish women have been routinely offered an ultrasound examination, generally early in the second trimester, for the purpose of estimating the weeks of gestation; approximately 95% accept this offer.[22]

Information on large-for-gestational-age infants, small-for-gestational-age infants, preterm births, stillbirths, and neonatal deaths was derived from the Medical Birth Register. Major congenital malformations were identified from the Medical Birth Register and the National Patient Register (through the first year of life).

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Table 1. Maternal Characteristics in Singleton Pregnancies in Sweden between 2006 and 2011.*

Characteristic	Before Matching			After Matching		
	Pregnancies after Bariatric Surgery (N=670)†	General-Population Pregnancies (N=627,023)‡	P Value	Pregnancies after Bariatric Surgery (N=596)†	Matched Control Pregnancies (N=2356)	P Value§
Surgery-to-delivery interval						
Mean — yr	2±1			2±1		
<1 Yr — no. (%)	47 (7.0)			42 (7.0)		
1 to <2 Yr — no. (%)	342 (51.0)			305 (51.2)		
2 to <5 Yr — no. (%)	279 (41.6)			247 (41.4)		
≥5 Yr — no. (%)	2 (0.3)			2 (0.3)		
Maternal age						
Mean — yr	31±5	30±5	<0.001	31±5	31±5	0.19
13–24 Yr — no. (%)	64 (9.6)	91,695 (14.6)	<0.001	57 (9.6)	221 (9.4)	0.64
25–29 Yr — no. (%)	197 (29.4)	180,274 (28.8)	<0.001	182 (30.5)	744 (31.6)	0.64
30–34 Yr — no. (%)	222 (33.1)	218,441 (34.8)	<0.001	195 (32.7)	779 (33.1)	0.64
≥35 Yr — no. (%)	187 (27.9)	136,610 (21.8)	<0.001	162 (27.2)	612 (26.0)	0.64
BMI						
Before surgery						
Mean	44.5±5.8			43.7±5.4	41.8±4.8	<0.001¶
30.0–34.9 — no. (%)	15 (2.2)			15 (2.5)	75 (3.2)	NA
35.0–39.9 — no. (%)	126 (18.8)			126 (21.1)	611 (25.9)	NA
40.0–44.9 — no. (%)	262 (39.1)			250 (41.9)	1162 (49.3)	NA
45.0–49.9 — no. (%)	149 (22.2)			127 (21.3)	394 (16.7)	NA
≥50 — no. (%)	118 (17.6)			78 (13.1)	114 (4.8)	NA
In early pregnancy‖						
Mean	30.6±5.2	24.6±4.6	<0.001	30.3±4.9	41.8±4.8	<0.001
<18.5 — no. (%)	1 (0.1)	14,044 (2.2)	<0.001	1 (0.2)	0	<0.001
18.5–24.9 — no. (%)	77 (11.5)	350,573 (55.9)	<0.001	75 (12.6)	0	<0.001
25.0–29.9 — no. (%)	249 (37.2)	142,015 (22.6)	<0.001	230 (38.6)	0	<0.001
30.0–34.9 — no. (%)	194 (29.0)	48,195 (7.7)	<0.001	176 (29.5)	75 (3.2)	<0.001
35.0–39.9 — no. (%)	79 (11.8)	14,834 (2.4)	<0.001	65 (10.9)	611 (25.9)	<0.001
≥40 — no. (%)	42 (6.3)	5476 (0.9)	<0.001	30 (5.0)	1670 (70.9)	<0.001
Mean change in weight and BMI from surgery to early pregnancy**						
Weight loss — kg	38±13			37±12		
Decrease in BMI — units	13.8±4.5			13.4±4.3		
Smoking status — no. (%)††						
Nonsmoker	543 (81.0)	560,059 (89.3)	<0.001	513 (86.1)	2064 (87.6)	NA
1–9 Cigarettes per day	75 (11.2)	31,525 (5.0)	<0.001	59 (9.9)	214 (9.1)	NA
≥10 Cigarettes per day	40 (6.0)	9401 (1.5)	<0.001	22 (3.7)	75 (3.2)	NA
Educational level — no. (%)‡‡						
≤9 Yr	126 (18.8)	66,246 (10.6)	<0.001	103 (17.3)	378 (16.0)	NA
10–12 Yr	408 (60.9)	237,712 (37.9)	<0.001	368 (61.7)	1432 (60.8)	NA
>12 Yr	133 (19.9)	306,314 (48.9)	<0.001	122 (20.5)	533 (22.6)	NA

[redacted]

Table 1. (Continued.)

Characteristic	Before Matching			After Matching		
	Pregnancies after Bariatric Surgery (N=670)†	General-Population Pregnancies (N=627,023)‡	P Value	Pregnancies after Bariatric Surgery (N=596)†	Matched Control Pregnancies (N=2356)	P Value§
Nulliparous — no. (%)	280 (41.8)	281,705 (44.9)	<0.001	238 (39.9)	900 (38.2)	NA
Coexisting conditions before pregnancy — no. (%)						
Diabetes	20 (3.0)	4802 (0.8)	<0.001	18 (3.0)§§	62 (2.6)§§	0.62
Cardiovascular disease	21 (3.1)	6216 (1.0)	<0.001	17 (2.9)	38 (1.6)	0.12
Respiratory disease	79 (11.8)	23,359 (3.7)	<0.001	71 (11.9)	172 (7.3)	<0.001
Psychiatric disease	72 (10.7)	21,747 (3.5)	<0.001	62 (10.4)	130 (5.5)	<0.001
Substance abuse	9 (1.3)	2571 (0.4)	<0.001	9 (1.5)	10 (0.4)	<0.001

* Plus–minus values are means ±SD. The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters. NA denotes not applicable (P=1.0 for all comparisons of categorical matching factors).
† Data on presurgery weight were obtained from the Scandinavian Obesity Surgery Registry (SOReg).
‡ General-population pregnancies were those in women with no history of bariatric surgery.
§ Comparisons of continuous variables were performed with the use of two-way analysis of variance, and comparisons of categorical variables were performed with the use of conditional logistic regression (both conditioned on the matching set).
¶ The mean between-group difference in BMI (mean difference, 0.47; 95% confidence interval, 0.34 to 0.63) was conditioned on the matching set. The matching was performed according to BMI categories; hence, mean BMI in each BMI category was slightly higher in the bariatric-surgery group.
‖ BMI data were missing for 28 women in the bariatric-surgery cohort before matching and 51,886 women in the general population, as well as 19 women in the bariatric-surgery cohort and no women in the control cohort after matching.
** Data on early-pregnancy weight and BMI were missing for 28 women in the bariatric-surgery cohort before matching and 19 women in the bariatric-surgery cohort after matching.
†† Data on early-pregnancy smoking status were missing for 12 women in the bariatric-surgery cohort before matching and 26,038 women in the general population, as well as 2 women in the bariatric-surgery cohort and 3 women in the control cohort after matching.
‡‡ Data on education were missing for 3 women in the bariatric-surgery cohort before matching and 16,751 women in the general population, as well as 3 women in the bariatric-surgery cohort and 13 women in the control cohort after matching.
§§ Women with prepregnancy diabetes were excluded from analyses of gestational diabetes.

STATISTICAL ANALYSIS

Singleton pregnancies in women with a history of bariatric surgery were compared with matched controls (singleton pregnancies in women without a history of bariatric surgery). We estimated odds ratios for postsurgery pregnancies versus control pregnancies with the use of logistic regression conditioned on the matching set, with each set consisting of one pregnancy after bariatric surgery and up to five matched control pregnancies. Adjustments were made for a history of hospitalization of the mother for coexisting psychiatric, cardiovascular, or respiratory conditions, as well as for a history of substance abuse and for the mother's country of birth.

These analyses were performed on individual pregnancies, which made it possible for a woman to contribute more than one pregnancy; therefore, risk estimation was also performed by the generalized-estimating-equation method (with the mother's identification as a cluster and assuming an exchangeable correlation structure), with adjustment for the possible dependence in outcome that could be introduced by having repeated pregnancies in the same mother. In another sensitivity analysis, we restricted inclusion to one pregnancy per woman (and therefore excluded 42 postsurgery pregnancies and 238 control pregnancies).

To assess the homogeneity of effects, we tested for interactions between bariatric-surgery status (surgery or no surgery) and parity (nulliparous or multiparous), as well as presurgery BMI, the interval from surgery to delivery, and the decrease in BMI from presurgery to early pregnancy (at or above vs. below the median levels for all three subgroups). The effect of weight gain during pregnancy was assessed in the subgroup of women for whom data on weight gain were available.

Data were analyzed with the use of SAS software, version 9.4 (SAS Institute). Two-sided P values of less than 0.05 were considered to indicate statistical significance. No adjustment was made for multiple comparisons.

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RESULTS

PARTICIPANT CHARACTERISTICS

As compared with pregnant women in the general population, women in the bariatric-surgery cohort were older, had lower educational levels, and were more likely to be obese, to smoke, and to be multiparous (P<0.001 for all comparisons) (Table 1). These differences were eliminated by the matching procedure, in which controls were identified for all but 74 (11%) of the 670 postsurgery pregnancies. In analyses of the matched cohorts, women with a history of bariatric surgery, as compared with women in the control cohort, had a slightly but significantly higher mean presurgery BMI (mean between-group difference in BMI, 0.5) and a history of more hospitalizations for cardiovascular, respiratory, or psychiatric disease and of more substance abuse (Table 1).

Nearly 98% (582) of the bariatric-surgery procedures were gastric bypass, 2% (11) were gastric banding, and less than 1% (3) were another procedure. Of the women who underwent bariatric surgery, 14% had a history of diabetes before surgery. The median interval from surgery to delivery was 1.8 years (interquartile range, 1.4 to 2.5). The mean presurgery BMI was 43.7, and the mean weight loss between surgery and early pregnancy was 37 kg (mean decrease in BMI, 13.4) (Table 1, and Fig. S1 in the Supplementary Appendix).

OUTCOMES

Gestational Diabetes

Gestational diabetes was diagnosed in 1.9% of the postsurgery pregnancies and in 6.8% of the control pregnancies (odds ratio 0.25; 95% confidence interval [CI], 0.13 to 0.47; P<0.001; Table 2). Among women for whom information on the date of diagnosis of gestational diabetes was available (9 of 11 [82%] in the bariatric-surgery group and 134 of 157 [85%] in the control group), the median time of gestation at which the diagnosis was made was 32 weeks in both groups.

Birth Weight and Related Measures

Postsurgery pregnancies, as compared with control pregnancies, were associated with a lower risk of large-for-gestational-age infants (8.6% vs. 22.4%; odds ratio, 0.33; 95% CI, 0.24 to 0.44; P<0.001) and of macrosomia (1.2% vs. 9.5%; odds ratio, 0.11; 95% CI, 0.05 to 0.24; P<0.001) (Table 2). However, postsurgery pregnancies were associated with an increased risk of small-for-gestational-age infants (15.6% vs. 7.6%; odds ratio, 2.20; 95% CI, 1.64 to 2.95; P<0.001) and a nonsignificantly increased risk of low-birth-weight infants (6.8% vs. 4.5%; odds ratio, 1.34; 95% CI, 0.88 to 2.04; P=0.17) (Table 2).

Preterm Birth, Congenital Malformations, and Mortality

Although postsurgery pregnancies, on average, had a shorter gestation than did control pregnancies (273.0 days vs. 277.5 days; mean difference, −4.5 days; 95% CI, −2.9 to −6.0; P<0.001), the risk of preterm birth did not differ significantly between the groups (10.0% vs. 7.5%; odds ratio, 1.28; 95% CI, 0.92 to 1.78; P=0.15). The risk of the combined outcome of stillbirth or neonatal death was 1.7% in the postsurgery group and 0.7% in the control group (odds ratio, 2.39; 95% CI, 0.98 to 5.85; P=0.06). There was no significant between-group difference in the frequency of congenital malformations (Table 2).

SUBGROUP ANALYSES

In the four interaction tests, we found no significant effect modification of bariatric surgery on gestational diabetes according to presurgery BMI, the interval from surgery to delivery, or the magnitude of reduction in BMI from presurgery to early pregnancy (at or above vs. below the median levels for all three subgroups) or according to parity (nulliparous or multiparous) (Fig. 2). There was also no significant effect modification of bariatric surgery on perinatal outcomes, except in 3 of the 16 interaction tests, which yielded the following significant interactions: a greater decrease in BMI was associated with a lower risk of large-for-gestational-age infants and a higher risk of preterm birth, and a longer surgery-to-delivery interval was associated with a higher risk of small-for-gestational-age infants (Fig. 2).

SENSITIVITY ANALYSES

Data about weight gain during pregnancy were available for 33% of postsurgery pregnancies (219 of 670) and 33% of control pregnancies (209,265 of 627,023). Weight gain was similar in the two groups of women (8.8 kg in the postsurgery-pregnancy group and 9.0 kg in the control-pregnancy group; mean difference, −0.2 kg; 95% CI, −1.1 to 1.4; P=0.77). Adjustment for weight gain during pregnancy did not materially affect

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Table 2. Gestational Diabetes and Perinatal Outcomes among Women with and Those without a History of Bariatric Surgery.

Variable	Bariatric-Surgery Group (N=596)	Matched Control Group (N=2356)	Risk Difference	Odds Ratio (95% CI)*	P Value
	no./total no. (%)		*percentage points (95% CI)*		
Gestational diabetes†					
Total	11/578 (1.9)	157/2294 (6.8)	−4.9 (−6.5 to −3.4)	0.25 (0.13 to 0.47)	<0.001
Insulin-treated	4/578 (0.7)	83/2294 (3.6)	−2.9 (−3.9 to −1.9)	0.17 (0.06 to 0.49)	<0.001
Large-for-gestational-age infant‡	51/590 (8.6)	523/2336 (22.4)	−13.8 (−16.6 to −11.0)	0.33 (0.24 to 0.44)	<0.001
Macrosomia‡	7/590 (1.2)	221/2336 (9.5)	−8.3 (−9.7 to −6.8)	0.11 (0.05 to 0.24)	<0.001
Small-for-gestational-age infant‡	92/590 (15.6)	178/2336 (7.6)	8.0 (4.8 to 11.1)	2.20 (1.64 to 2.95)	<0.001
Low-birth-weight infant‡	40/590 (6.8)	105/2336 (4.5)	2.3 (0.1 to 4.5)	1.34 (0.88 to 2.04)	0.17
Preterm birth§	59/590 (10.0)	176/2344 (7.5)	2.5 (−0.2 to 5.1)	1.28 (0.92 to 1.78)	0.15
Stillbirth¶	6/596 (1.0)	12/2356 (0.5)	0.5 (−0.4 to 1.3)	1.89 (0.59 to 6.05)	0.28
Neonatal death <28 days after live birth§	4/590 (0.7)	5/2344 (0.2)	0.5 (−0.2 to 1.2)	2.93 (0.57 to 15.14)	0.20
Stillbirth or neonatal death	10/596 (1.7)	17/2356 (0.7)	1.0 (−0.1 to 2.0)	2.39 (0.98 to 5.85)	0.06
Major congenital malformations§					
Total	14/590 (2.4)	83/2344 (3.5)	−1.2 (−2.6 to 0.3)	0.72 (0.40 to 1.29)	0.27
Excluding chromosomal abnormalities§	12/590 (2.0)	79/2344 (3.4)	−1.3 (−2.7 to 0.0)	0.63 (0.34 to 1.18)	0.16

* Odds ratios were conditioned on the matching set, including one pregnancy after bariatric surgery and up to five controls, with matching for maternal age, parity, presurgery BMI (with the use of early-pregnancy BMI in the controls), smoking, educational level, and delivery year; adjustments were made for history of coexisting conditions, history of substance abuse, and mother's country of birth.

† Analyses of gestational diabetes excluded women with prepregnancy diabetes (18 women [3%] in the bariatric-surgery cohort and 62 women [3%] in the matched control cohort).

‡ Analyses of large-for-gestational-age infants (>90th percentile), small-for-gestational-age infants (<10th percentile), macrosomia (birth weight >4500 g), and low birth weight (<2500 g) excluded stillbirths and births without data on birth weight. Analyses of large-for-gestational-age infants and small-for-gestational-age infants also excluded births without data on gestational age. There were 6 exclusions in the bariatric-surgery group (1.0%) and 20 in the matched-control group (0.9%).

§ Analyses of preterm birth, neonatal death, and congenital malformations excluded stillbirths and births without data on gestational age. There were 6 exclusions in the bariatric-surgery group (1.0%) and 12 in the matched-control group (0.5%).

¶ Stillbirth was defined as fetal death at 22 or more completed weeks of gestation on or after July 1, 2008 (97% of pregnancies), and at 28 or more weeks before July 1, 2008 (<3% of pregnancies).

the association between bariatric surgery and any of the outcomes (Table S4 in the Supplementary Appendix). Results were similar in analyses that included only one pregnancy per woman after bariatric surgery (Table S5 in the Supplementary Appendix) and in analyses with the use of a generalized-estimation-equation framework (adjusted for, instead of conditioned on, the matching factors) (Table S6 in the Supplementary Appendix).

DISCUSSION

In this nationwide prospective cohort study, women with a history of bariatric surgery had a lower risk of gestational diabetes and large-for-gestational-age infants and an increased risk of small-for-gestational-age infants and a shorter gestation than did women in a control group matched for presurgery BMI (with the use of early-pregnancy BMI in the control cohort). Previous studies have reported conflicting results regarding the effect of bariatric surgery on the development of gestational diabetes; these inconsistencies are most likely explained by small sample sizes and heterogeneous study designs.[15,16] In one previous study[23] in which, as in the present study, cases were matched to controls according to presurgery BMI, there were no cases of gestational diabetes among 70 women who had a history of bariatric surgery and 21 cases among 140 matched controls; in our cohort, gestational diabetes was diagnosed in 1.9% of the women who had undergone bariatric surgery and in 6.8% of matched controls. The previous study also reported perinatal mortality of

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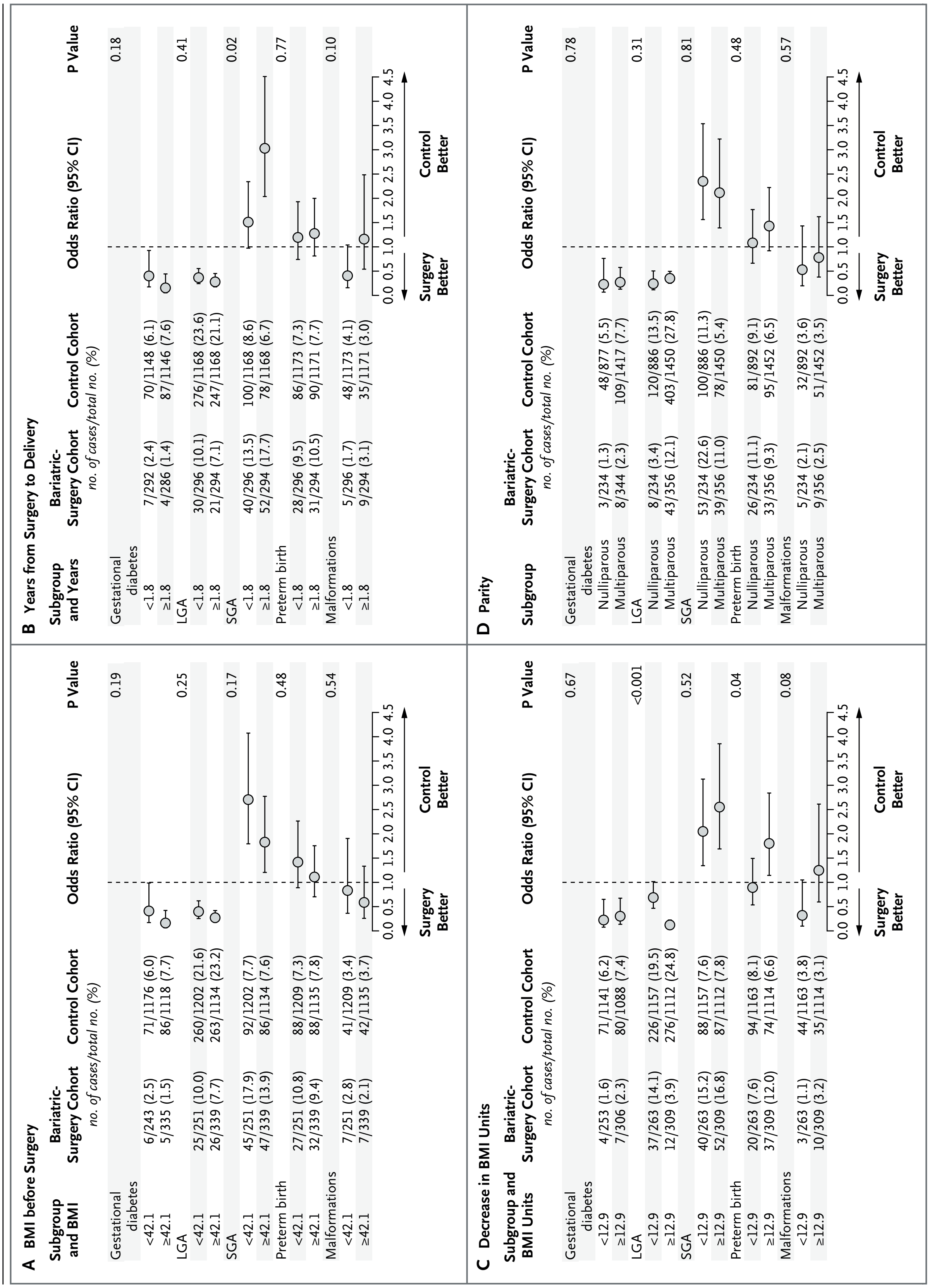
A BMI before Surgery
Subgroup and BMI
Bariatric-Surgery Cohort
Control Cohort
no. of cases/total no. (%)
Odds Ratio (95% CI)
P Value
Gestational diabetes 0.19
<42.1 6/243 (2.5) 71/1176 (6.0)
≥42.1 5/335 (1.5) 86/1118 (7.7)
LGA 0.25
<42.1 25/251 (10.0) 260/1202 (21.6)
≥42.1 26/339 (7.7) 263/1134 (23.2)
SGA 0.17
<42.1 45/251 (17.9) 92/1202 (7.7)
≥42.1 47/339 (13.9) 86/1134 (7.6)
Preterm birth 0.48
<42.1 27/251 (10.8) 88/1209 (7.3)
≥42.1 32/339 (9.4) 88/1135 (7.8)
Malformations 0.54
<42.1 7/251 (2.8) 41/1209 (3.4)
≥42.1 7/339 (2.1) 42/1135 (3.7)
0.0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5
Surgery Better
Control Better
B Years from Surgery to Delivery
Subgroup and Years
Bariatric-Surgery Cohort
Control Cohort
no. of cases/total no. (%)
Odds Ratio (95% CI)
P Value
Gestational diabetes 0.18
<1.8 7/292 (2.4) 70/1148 (6.1)
≥1.8 4/286 (1.4) 87/1146 (7.6)
LGA 0.41
<1.8 30/296 (10.1) 276/1168 (23.6)
≥1.8 21/294 (7.1) 247/1168 (21.1)
SGA 0.02
<1.8 40/296 (13.5) 100/1168 (8.6)
≥1.8 52/294 (17.7) 78/1168 (6.7)
Preterm birth 0.77
<1.8 28/296 (9.5) 86/1173 (7.3)
≥1.8 31/294 (10.5) 90/1171 (7.7)
Malformations 0.10
<1.8 5/296 (1.7) 48/1173 (4.1)
≥1.8 9/294 (3.1) 35/1171 (3.0)
0.0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5
Surgery Better
Control Better
C Decrease in BMI Units
Subgroup and BMI Units
Bariatric-Surgery Cohort
Control Cohort
no. of cases/total no. (%)
Odds Ratio (95% CI)
P Value
Gestational diabetes 0.67
<12.9 4/253 (1.6) 71/1141 (6.2)
≥12.9 7/306 (2.3) 80/1088 (7.4)
LGA <0.001
<12.9 37/263 (14.1) 226/1157 (19.5)
≥12.9 12/309 (3.9) 276/1112 (24.8)
SGA 0.52
<12.9 40/263 (15.2) 88/1157 (7.6)
≥12.9 52/309 (16.8) 87/1112 (7.8)
Preterm birth 0.04
<12.9 20/263 (7.6) 94/1163 (8.1)
≥12.9 37/309 (12.0) 74/1114 (6.6)
Malformations 0.08
<12.9 3/263 (1.1) 44/1163 (3.8)
≥12.9 10/309 (3.2) 35/1114 (3.1)
0.0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5
Surgery Better
Control Better
D Parity
Subgroup
Bariatric-Surgery Cohort
Control Cohort
no. of cases/total no. (%)
Odds Ratio (95% CI)
P Value
Gestational diabetes 0.78
Nulliparous 3/234 (1.3) 48/877 (5.5)
Multiparous 8/344 (2.3) 109/1417 (7.7)
LGA 0.31
Nulliparous 8/234 (3.4) 120/886 (13.5)
Multiparous 43/356 (12.1) 403/1450 (27.8)
SGA 0.81
Nulliparous 53/234 (22.6) 100/886 (11.3)
Multiparous 39/356 (11.0) 78/1450 (5.4)
Preterm birth 0.48
Nulliparous 26/234 (11.1) 81/892 (9.1)
Multiparous 33/356 (9.3) 95/1452 (6.5)
Malformations 0.57
Nulliparous 5/234 (2.1) 32/892 (3.6)
Multiparous 9/356 (2.5) 51/1452 (3.5)
0.0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5
Surgery Better
Control Better

[redacted]

Figure 2 (facing page). Odds Ratios for Gestational Diabetes and Adverse Perinatal Outcomes According to Presurgery BMI, Surgery-to-Delivery Interval, Change in BMI, and Parity in the Bariatric-Surgery Cohort versus the Control Cohort.

Odds ratios were estimated with the use of logistic regression conditioned on the matching set (one pregnancy after bariatric surgery and up to five controls matched for maternal age, parity, presurgery body-mass index [BMI], early-pregnancy smoking status, educational level, and year of delivery) and adjusted for history of coexisting conditions, history of substance abuse, and mother's country of birth. LGA denotes large for gestational age, and SGA small for gestational age.

5.7% among pregnancies in women with a history of bariatric surgery and a rate of 0.7% among the control pregnancies. Similarly, in our study, we noted a higher risk of the combined outcome of stillbirth or neonatal death among women with a history of bariatric surgery than in the controls (1.7% vs. 0.7%), although such events were uncommon and the difference was of borderline significance (P=0.06).

We also found that women who had undergone bariatric surgery had a lower risk of delivering large-for-gestational-age infants but a higher risk of delivering small-for-gestational-age infants. Overall, they did not have a significantly higher risk of preterm birth, but subgroup analyses suggested that this risk may be increased among women with a greater decrease in BMI between surgery and early pregnancy. Similar associations were reported from two cohort studies in which cases and controls were matched for early-pregnancy BMI, although such a design addresses a different research question than does the current study.[24,25] The between-group difference in fetal growth was expected, given that the women with a history of bariatric surgery had, on average, a decrease in weight of 37 kg (decrease in BMI, 13) after surgery. However, given the direct association between BMI and the risk of preterm birth,[8] we expected that the risk of preterm birth would be lower, rather than higher, after bariatric surgery. Our study showed a median surgery-to-conception interval of 1.1 years, which suggested that many women may have been continuing to lose weight when they became pregnant. Continued weight loss may affect fetal nutrition and could influence the risk of preterm birth.

Despite known adverse effects of gastric bypass surgery on the metabolism of iron, vitamin B_{12}, and folate,[26] we found no significant effect of bariatric surgery on the overall risk of congenital malformations. Still, we cannot exclude the possibility that risks of specific malformations differed between the groups.

Although this nationwide study is, to our knowledge, the largest study to date comparing pregnancy outcomes between women with and those without a history of bariatric surgery, with matching for presurgery BMI, limitations of the study must be considered. The matching for presurgery BMI and adjustment for other factors was intended to identify independent effects of bariatric surgery on pregnancy outcomes, but the observational design of the study makes it impossible to determine cause and effect. There may be residual confounding, because women who undergo surgery may have differed from women in the control cohort with respect to other factors not accounted for in the analyses. Also, there is a possibility of chance findings, since we investigated multiple outcomes.

Another potential limitation is selection bias. For example, with regard to prepregnancy diabetes status, women with a history of bariatric surgery may be followed more closely than women in the control cohort with similar characteristics. If women with unrecognized preexisting diabetes were overrepresented in the control group, this could lead to bias toward a lower risk of gestational diabetes in the bariatric-surgery group as compared with the control group. However, all pregnant women undergo glucose screenings starting at their first maternity care visit, and obese women commonly undergo oral glucose-tolerance testing, since they are regarded as a high-risk group. Also, the majority of the diagnoses of gestational diabetes were ascertained at approximately week 30, and it is unlikely that prevalent type 2 diabetes would go undetected for so long.

In addition, it is likely that some women with a history of bariatric surgery were infertile before surgery, whereas the control cohort consisted of a selected group of obese women who were able to conceive. The slightly lower BMI and rates of previous hospitalizations for respiratory and psychiatric coexisting conditions and of substance abuse in the control group suggest that this group may have been a healthier group overall.

Because the Swedish population is mostly

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white, our findings cannot necessarily be generalized to other races. In addition, our sample had a median surgery-to-conception interval of 1.1 years and a maximum of 4.3 years and may not be generalizable to pregnancies with longer surgery-to-conception intervals. Also, 98% of all procedures were gastric bypass surgery, and it is not known whether our results apply to other bariatric procedures.

In conclusion, this nationwide cohort study showed that a history of bariatric surgery was associated with reduced risks of gestational diabetes and large-for-gestational-age infants. However, increased surveillance during pregnancy and the neonatal period is warranted, since a history of bariatric surgery was also associated with small-for-gestational-age infants, a shorter length of gestation, and potentially an increased risk of stillbirth or neonatal death.

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