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Open Fetal Surgical Outcomes for Myelomeningocele Closure Stratified by Maternal Body Mass Index in a Large Single-Center Cohort

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Fetal therapy · Myelomeningocele · Myeloschisis · Neural tube defect · Obesity · Open maternal-fetal surgery

Abstract
Background: Open maternal-fetal surgery for in utero closure of myelomeningocele (MMC) has become an accepted treatment option for prenatally diagnosed open neural tube defects. Historically, this option has been limited to women with BMI < 35 due to concern for increasing complications in patients with obesity. ***Objective:*** The aim of this study was to evaluate maternal, obstetric, and fetal/neonatal outcomes stratified by maternal BMI classification in women who undergo open maternal-fetal surgery for fetal myelomeningocele (fMMC) closure. ***Methods:*** A single-center fMMC closure registry was queried for maternal demographics, preoperative factors, fetal surgery outcomes, delivery outcomes, and neonatal outcomes. Data were stratified based on maternal BMI: <30, 30–34.99, and ≥35–40, corresponding to normal weight/overweight, obesity class I, and obesity class II. Statistical analysis was performed using statistical software SAS v.9.4 (SAS Institute Inc., Cary, NC, USA). ***Results:*** A total of 264 patients were analyzed, including 196 (74.2%) with BMI <30, 54 (20.5%) with BMI 30–34.99, and 14 (5.3%) with BMI ≥ 35–40. Maternal demographics and preoperative characteristics were similar among the groups. Operative time increased with increasing BMI; otherwise, perioperative outcomes were similar among the groups. Obstetric and neonatal outcomes were similar among the groups. ***Conclusion:*** Increasing maternal BMI did not result in a negative impact on maternal, obstetric, and fetal/neonatal outcomes in a large cohort of patients undergoing open maternal-fetal surgery for fMMC closure. Further study is warranted to determine the generalizability of these results.

Introduction

Overweight and obesity are increasing on a global scale. The rate of obesity worldwide has nearly tripled in the last 4 decades according to the WHO [1]. Patients are categorized based on BMI: normal weight: 18.5–24.9,

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overweight: 25.0–29.9, obesity class I: 30.0–34.9, obesity class II: 35.0–39.9, and obesity class III: ≥40. Increasing BMI is associated with multiple chronic health issues.

Additionally, obesity in pregnancy is also associated with increased maternal and fetal risks such that management strategies have been outlined [2]. Gestational diabetes, gestational hypertension, preeclampsia, operative delivery, wound infections, preterm delivery, fetal and perinatal loss, and large for gestational age neonates occur more commonly in obese women than their normal-weight counterparts [3]. The risk of congenital anomalies is also increased with increasing BMI. In particular, obese women are at increased risk for their pregnancy to be diagnosed with a neural tube defect [3, 4].

Despite an increased risk for neural tube defects in the obese population, a BMI over 35 in the obesity class II range was an exclusion criteria in the original Management of Myelomeningocele Study (MOMS) comparing open maternal-fetal surgery for myelomeningocele (MMC) closure to standard postnatal closure [5]. The trial results showed an improvement in neonatal outcomes for fMMC closure related to MMC morbidity, although fMMC closure was associated with an increase in maternal and obstetric risks. Since the publication of the MOMS trial, fMMC closure has come to be an accepted standard of care option for women whose fetus is diagnosed prenatally with a neural tube defect in appropriate cases. We sought to determine if expansion of BMI criteria to include obesity class II (35.0–39.9) for open fMMC closure would be associated with similar outcomes as compared to women with BMI < 35.

Materials and Methods

A single-center fMMC closure registry was queried for maternal demographics, preoperative factors, fetal surgery outcomes, delivery outcomes, and neonatal outcomes. Dates of inclusion were from January 1, 2011, through October 31, 2019. Study data were collected and managed using Research Electronic Data Capture (REDCap) electronic data capture tools hosted at the Children's Hospital of Philadelphia [6, 7]. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing (1) an intuitive interface for validated data capture; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for data integration and interoperability with external sources. Data were stratified based on maternal BMI: <30, 30–34.99, and ≥35–40, corresponding to normal weight/overweight, obesity class I, and obesity class II.

Student's *t* test was used for continuous variables and the Fisher's exact test for categorical variables. A p value <0.05 was considered significant. Statistical analysis was performed using statistical software SAS v.9.4 (SAS Institute Inc., Cary, NC, USA). This study was approved by the Children's Hospital of Philadelphia Institutional Review Board (11-008262) and written consent was obtained from all study subjects.

Our center has been offering fMMC closure to women with a BMI of 35–40 since 2013 under the guidance of the Fetal Therapy Oversight Committee. A description of our surgical approach has been previously described [8]. Perioperative care is similar among the groups. All patients receive an epidural preoperatively (to be used for postoperative pain management) and general anesthesia intraoperatively. Before surgery, women are advised to vigorously oral hydrate such that intraoperative and postoperative fluids are minimized to avoid pulmonary edema and fluid shifts. Compression boots remain in use until patients are fully ambulatory. All patients receive a physical therapy consultation and are taught bed exercises and additional movement techniques. Tocolytics and perioperative medication regimens are consistent across all patients.

Results

A total of 264 patients were analyzed. This included 196 (74.2%) with BMI <30, 54 (20.5%) with BMI 30–34.99, and 14 (5.3%) with BMI ≥ 35–40. Maternal demographics and preoperative characteristics were similar among the groups, outside of increasing BMI. These data are presented in Table 1.

Outcomes of maternal-fetal surgery are presented in Table 2. Operative time for the maternal-fetal surgery increased with increasing BMI. In the normal/overweight BMI group, the mean operative time was 74.6 min, 78.8 min in the obesity class I group, and 88.1 min for the obesity class II group. Maternal length of stay (LOS) post-maternal-fetal surgery was increased in the obesity class II group compared to the lower BMI groups. One patient was managed in hospital from maternal-fetal surgery until delivery due to provider preference due to a larger hysterotomy. If this patient is excluded from analysis, the maternal LOS is similar among the groups. The remaining perioperative outcomes were similar among the groups. There were 6 patients treated for pulmonary edema in the overall study group – all of which had a BMI in the normal weight range. There were no differences in the rate of wound complications among the groups after the open maternal-fetal surgery.

Obstetric outcomes are detailed in Table 3. Overall outcomes were similar among the groups. The rate of preterm delivery <37 weeks was lowest in the highest BMI group. One deep vein thrombosis occurred in the entire study population. This was in a patient of normal body weight BMI. The rate of gestational diabetes was highest

Table 1. Maternal demographics and preoperative characteristics

	BMI < 30 *N* = 196	BMI 30–34.9 *N* = 54	BMI ≥ 35–40 *N* = 14	*p* value
Age, yrs, mean ± SD	30.1±4.7	30.4±4.8	30.9±6.1	0.8
Race-White, *N* (%)	174 (88.8)	47 (87.0)	13 (92.9)	0.8
BMI, kg/m^2, mean ± SD	**25.2±2.7**	**32.0±1.4**	**37.3±1.4**	**<0.0001**
Multiparity, *N* (%)	119 (60.7)	35 (64.8)	9 (64.3)	0.8
Placental location, *N* (%)				
Anterior placenta	90 (45.9)	23 (42.6)	10 (71.4)	0.2
Posterior placenta	95 (48.5)	28 (51.9)	4 (28.6)	0.3
Level of lesion, *N* (%)				
T11–12	3 (1.5)	2 (3.7)	0	0.5
L1–3	111 (56.6)	25 (46.3)	10 (71.4)	0.2
L4–5	82 (41.8)	26 (48.1)	4 (28.6)	0.4
Type of lesion, *N* (%)				
MMC	145 (74.0)	35 (64.8)	11 (78.6)	0.4
Myeloschisis	51 (26.0)	19 (35.2)	3 (21.4)	
Size of ventricles				
Right ventricle, mm, mean ± SD	10.0±3.1	9.7±3.6	11.0±2.7	0.4
Left ventricle, mm, mean ± SD	10.8±3.1	10.5±3.5	11.1±3.2	0.8
Presence of talipes, *N* (%)	38 (19.4)	12 (22.2)	3 (21.4)	0.9
Gestational age at fetal surgery, weeks, mean ± SD	24.0±1.1	23.8±1.2	24.3±0.9	0.3

MMC, myelomeningocele; SD, standard deviation.

Table 2. Maternal-fetal surgery outcomes

	BMI < 30 *N* = 196	BMI 30–34.9 *N* = 54	BMI ≥ 35–40 *N* = 14	*p* value
Operative time, *N*, min, mean ± SD	**74.6±9.5**	**78.8±11.2**	**88.1±12.2**	**<0.0001**
Need for Alloderm skin patch, *N* (%)	19 (9.7)	7 (13.0)	1 (7.1)	0.7
Intraoperative complications				
Uterine bleeding intraoperatively, *N* (%)	1 (0.5)	1 (1.9)	0	0.6
Fetal bradycardia intraoperatively, *N* (%)	4 (2.0)	3 (5.6)	1 (7.1)	0.3
Need for fetal resuscitation, *N* (%)	3 (1.5)	3 (5.6)	1 (7.1)	0.1
Maternal estimated blood loss, mL, mean ± SD	130.7±57.7	136.3±47.6	153.6±82.0	0.3
Pulmonary edema, *N* (%)	6 (3.1)	0	0	0.3
Maternal LOS post-fetal surgery, days, mean ± SD	4.1±0.4	4.1±0.7	7.6±13.1	**0.0001**
Maternal LOS post-fetal surgery, days, mean ± SD (adjusted)*	4.1±0.4	4.1±0.7	4.1±0.3	0.7
Wound complications, *N* (%)	3 (1.5)	2 (3.7)	0	0.5

LOS, length of stay; SD, standard deviation. Wound complications = infection, hematoma, separation. * Data adjusted for patient who was kept in hospital from fetal surgery until delivery based on provider preference.

in highest maternal BMI group. There were no differences in the rate of wound complications after delivery among the groups. Neonatal outcomes were comparable among the groups (Table 4).

Discussion

We previously reported our surgical, obstetric, and neonatal outcomes for fMMC closure in a cohort of 100 patients that were comparable to those reported in the MOMS trial [8]. Since that time, we have performed an

Table 3. Obstetric outcomes

	BMI < 30 *N* = 192	BMI 30–34.9 *N* = 53	BMI ≥ 35–40 *N* = 14	*p* value
Gestational diabetes, *N* (%)	3 (1.6)	0	2 (14.3)	0.002
Membrane separation, *N* (%)	35 (18.2)	14 (26.4)	2 (14.3)	0.4
Global membrane separation, *N* (%)	22 (11.5)	10 (18.9)	2 (14.3)	0.4
Rate of PPROM, *N* (%)	38 (19.8)	15 (28.3)	4 (21.4)	0.3
Rate of spontaneous preterm labor, *N* (%)	63 (32.8)	21 (39.6)	5 (35.7)	0.7
Rate of preterm delivery <37, weeks, *N* (%)	126 (65.6)	44 (83.0)	9 (64.3)	0.049
Gestational age at delivery, wks, mean ± SD	34.9±2.9	34.4±2.7	34.7±2.4	0.5
Status of hysterotomy at delivery with area of dehiscence, *N* (%)	12 (6.3)	5 (9.4)	0	0.4
Maternal estimated blood loss at delivery, mL, mean ± SD	745.7±179.9	796.2±232.8	753.6±139.3	0.2
Wound complications after delivery, *N* (%)	3 (1.6)	2 (3.8)	1 (7.1)	0.3
Stillbirth, *N* (%)	3 (1.6)	0	0	0.6

PPROM, preterm premature rupture of membranes.

Table 4. Neonatal outcomes

	BMI < 30 *N* = 192	BMI 30–34.9 *N* = 53	BMI ≥ 35–40 *N* = 14	*p* value
Birth weight, grams, mean ± SD	2,528.5±605.0	2,407.8±622.9	2,523±633.0	0.4
Perinatal death, *N* (%)	5 (2.6)	2 (3.8)	0	0.7
NICU LOS, days, mean ± SD	19.2±23.0	24.5±24.4	26.1±18.9	0.2
Shunt placement at 12 months, *N* (%)	54 (28.1)	17 (32.1)	5 (35.7)	0.7

NICU, neonatal intensive care unit; LOS, length of stay; SD, standard deviation.

additional 164 cases including a portion with BMI 35–40. We began to offer fMMC closure in this expanded BMI group in 2013, about the time that other groups were beginning to offer open maternal-fetal surgery in this higher BMI cohort among other changes to the original MOMS trial protocol [9]. The data from our cohort do not suggest an increased maternal or fetal risk associated with open maternal-fetal surgery for fMMC closure for women with BMI up to 40 (class II obesity).

One trend we identified among the increasing BMI groups was an increase in operative time. This is defined as skin-to-skin time to complete the surgery. Overall, the increase in time was nearly 15 min from the normal/overweight BMI group to the obesity class II BMI group. This is to be expected given the increase in abdominal wall thickness that is encountered in these cases, adding to operative time both upon entry into the abdomen and during closure. Despite this increase in time, we did not encounter an increase in intraoperative complications such as bleeding, fetal bradycardia, or need for fetal resuscitation in the higher BMI groups compared to the BMI < 30 group.

When all BMI ≥ 35–40 patients were included in the post-open maternal-fetal surgery LOS analysis, that group had a statistically significantly longer hospitalization of mean 7.6 days, compared to 4.1 days in the other groups. That group is the smallest among the 3 cohorts, made up of only 14 patients. One patient from the BMI ≥ 35–40 group was kept in the hospital after open maternal-fetal surgery until delivery because of provider preference. This patient had a particularly large hysterotomy due to fetal position, and there was concern for an increased risk for postoperative complications, although she delivered after 32 weeks. If this patient is excluded from the analysis, the mean LOS is similar among the groups at 4.1 days.

The rate of gestational diabetes was significantly higher in the highest BMI group, 14.3% compared to 1.6% in the normal/overweight BMI group. This may be a function of the small number of patients in the highest BMI

group. Regardless, because of the known risk for gestational diabetes in obese women, standard screening protocols and prenatal care should always be emphasized in these patients to avoid any additional complications. There was no increased risk for wound complications or thromboembolism in the higher BMI groups.

Similar results have been published by another fetal surgery group who reported no adverse maternal outcomes associated with maternal obesity [10]. However, the gestational age at delivery in that cohort was ~32 weeks. In our study, the rate of preterm delivery <37 weeks was lowest in the highest BMI group, and the average gestational age at delivery was comparable among all 3 BMI groups at over 34 weeks. We also report a lower shunt rate at 12 months in the BMI 35–40 cohort of 35.7%, compared to the 45% rate in the previously reported expanded BMI series. However, these data may be limited by the small sample size in the BMI 35–40 group. Further investigation into outcomes differences among the various BMI groups is warranted.

Although the overall surgical outcomes are favorable, a limitation of this study is the small proportion of women in the BMI 35–40 group. Outcomes within our cohort are not associated with increased maternal or fetal risk, but the generalizability of these data is yet unknown. Further studies, among many centers are still needed to best gauge the applicability and safety of expanded maternal BMI in women undergoing open maternal-fetal surgery for fMMC closure.

Statement of Ethics

Our research complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The Children's Hospital of Philadelphia Institutional Review Board approved this study (11-008262), and written consent was obtained from all study subjects.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

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Author Contributions

Study concept and design: J.S.M. and J.J. Data collection: J.J. and J.S.M. Data analysis: S.S. Manuscript development: J.S.M. Critical review of manuscript: J.J., S.S., J.G., N.K., C.P.T., M.P.J., A.W.F., H.L.H., W.H.P., G.H., and N.S.A.

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