Maternal morbidity at first repeat cesarean: a sub-analysis of Interceed™ barrier placed at primary cesarean section

Hector O Chapa
Gonzalo Venegas
Women’s Specialty Center Dallas, Chapa Medical Consulting, Dallas, TX, USA

Objective: The aim of this study was to compare maternal morbidity at repeat cesarean section (CS) between use of a Gynecare Interceed™ Absorbable Adhesion Barrier (Gynecare, Somerville, NJ, USA) and non-use at primary cesarean delivery.

Design: This was a retrospective study of patients in whom an absorbable adhesion barrier was/was not used at their primary CS.

Methods: Mean and excessive blood loss, the need for adhesiolysis, and postoperative fever were compared between those in whom a barrier was used at first CS and those in whom a barrier was not used. Visceral injury at repeat cesarean was also compared between the two groups.

Results: No statistically significant difference in mean blood loss was noted between the two groups. However, significantly more patients in whom a barrier was not used had excessive intraoperative blood loss (barrier group, 1/53 [1.9%]; no-barrier group, 6/59 [10.1%; \( P = 0.04 \)).

All seven cases of excessive blood loss had adhesiolysis. Significantly more patients in the no-barrier group underwent adhesiolysis (no-barrier group, 35/59 [59.3%]; barrier group, 7/53 [13.2%]; \( P = 0.03 \)). No statistical difference in postoperative metritis was noted (1/59 [1.8%] in the barrier group and 1/59 [1.7%] in the no-barrier group; \( P = 0.99 \)). Only one deserosalization of the bladder dome occurred in a patient in the no-barrier group.

Conclusion: Those in whom a barrier was not used at primary CS were more likely to have adhesiolysis and excessive blood loss (>1250 mL) at repeat CS. No significant difference in postoperative metritis/fever was noted between groups. Adhesion barrier at primary CS may reduce some aspects of maternal morbidity at repeat CS.

Keywords: excessive blood loss, adhesiolysis, postoperative metritis, postoperative fever, visceral injury

Background
In March 2010, the Centers for Disease Control and Prevention (CDC) reported that the national cesarean rate has increased over the last decade among all maternal age groups, all ethnic groups, and all gestational ages, reaching an all-time high rate of 32%. Recent extrapolation of this rise in cesarean deliveries (CDs) has estimated that the national CD rate will reach 50% by 2020, which corresponds to nearly 2 million cesarean births. Thus, the obstetric community must re-evaluate the current state of this intervention. It is well established that the more CDs an individual has, the more frequent the occurrence of adhesive sequelae. In a retrospective study published in 2007, adhesions of all grades were found in 46% of women at their second cesarean birth, 76% at the third, and 83% at the fourth. Similarly, Tulandi et al documented adhesion frequencies of 24% at second CD, 43% at third, and 48% at fourth.
Percent differences between the two studies can be explained by the subjective grading scales employed in each cohort as well as the inclusion/exclusion criteria used in each study. The percentage of moderate–severe adhesions in each cohort varied less due to the more reproducible classification of cohesive disease.

Additionally, Nisenblat et al compared 277 women who were undergoing their third or later more CD to 491 women undergoing their second CD. The authors concluded that excessive blood loss (7.9% vs 3.3%; \( P < 0.005 \)), difficult delivery of the neonate (5.1% vs 0.2%; \( P < 0.001 \)), and dense adhesions (46.1% vs 25.6%; \( P < 0.001 \)) were significantly more common in the three or more previous cesarean group, thus validating what practicing obstetricians have known for years.5

Morbidity from cesarean section (CS)-induced peritoneal adhesions is also found within the gynecologic literature. Wang et al reviewed 141 laparoscopic hysterectomies among prior CS patients.6 The rate of bladder complications increased with the number of previous CSs: 2.5% of patients having had one or two previous CSs and 21.1% of patients having had three or more previous CSs had bladder complications. The rate of inadvertent cystotomy in patients having had three or more CSs was 18 times that of patients who had not had a CS (95% confidence interval [CI] 5.1–66.0). Fifteen (10.6%) patients who had had a previous CS required conversion to laparotomy because of dense bladder or bowel adhesions. Similarly, Sandberg et al demonstrated an increased risk for bladder injury at hysterectomy due to bladder flap adhesions.7 Additionally, infertility and chronic pelvic pain have both been associated with peritoneal adhesions.8,9

Small bowel obstruction due to cesarean adhesions has also been noted. Andolf et al estimated the risk for postoperative adhesions and intestinal obstruction after CD by analyzing data from the Swedish Hospital Discharge Registry linked to the Swedish Medical Birth Registry.10 According to their results, women delivered by CS had an increased risk of adhesions (adjusted odds ratio, 2.1 [95% CI 1.8–2.4]) and intestinal obstruction (adjusted odds ratio, 2.0 [95% CI, 1.7–2.4]). The number needed to harm was 360.

In September 2012, recognizing the problem of adhesions at repeat CS, Tulandi and Lyell searched the Medline, PubMed, and Embase databases as well as the Cochrane Database of Systematic Reviews from 1996 through 2011 for all articles pertaining to adhesion scoring after a CD and proposed the first standardized classification of adhesions after CD.11 Recent data have suggested avoidance of bladder flap creation as well as parietal peritoneal closure as techniques for reducing CS adhesions, although the topic is not yet settled.12–14

Recently, we published our results of the use of an absorbable adhesion barrier (Gynecare Interceed™ Absorbable Adhesion Barrier, Gynecare, Somerville, NJ, USA) placed at primary CD in an attempt to reduce abdomino-pelvic adhesions found at repeat CS.15 Despite the information gathered from this pivotal study, issues related to maternal morbidity between the barrier and no-barrier groups were not analyzed. This is the focus of this article.

**Materials and methods**

This is a sub-analysis of our group’s original retrospective medical chart review describing an absorbable adhesion barrier used at time of primary cesarean.15 In that original study, a medical record review of primary and subsequent first repeat cesareans between January 1, 2006 and December 31, 2009 was undertaken to determine whether an adhesion barrier would reduce the incidence and/or grade of adhesions found at subsequent repeat CD. This was an independent, non-funded study.

**Review of original study**15 **premise, design, and endpoints**

Women’s Specialty Center is a single specialty OB/Gyn multi-physician practice in inner city Dallas. Our office maintains a central database of all primary and repeat cesareans performed by its member physicians. This database was queried for patients who underwent primary cesarean and repeat cesarean during that same time frame. Our physicians adopted the use of Interceed barrier at time of cesarean, based on their discretion, beginning in 2006 and continues currently.15 For original inclusion/exclusion criteria for our first published study, the reader is directed to that original text.

The main study endpoint was incidence and grade of adhesions noted at the first repeat cesarean section between the two groups. Affect of parietal peritoneal closure, suture material, and time from skin incision to complete fetal delivery were also reported in that original article.15

The endpoints of this study were: incidence/grade of adhesions found at repeat CS and time interval from skin incision to fetal delivery between the barrier and no-barrier groups.

**Present sub-analysis endpoint**

The focus of this current study was comparison of intraoperative maternal morbidity in the two groups: barrier versus no barrier use at time of first repeat CS.
Blood loss

Overall intraoperative blood loss between groups was compared and further evaluated based on need for adhesiolysis. In our practice group, blood loss at CS is recorded as 1000 mL for routine cases. Increases in blood loss are recorded by increments of 250 mL, as appropriate (ie, 1250 mL, 1500 mL, 1750 mL, etc). Any blood loss over 1250 mL is marked as “excessive.” For our study analyzing blood loss, cases of uterine atony, hysterotomy extensions, and other potential hemorrhage contributors (eg, intravenous magnesium sulfate) were excluded.

“Excessive blood loss” was defined as either blood loss of 1250 mL or more, or transfusion of two or more units of blood either intraoperatively or within the postoperative course.\textsuperscript{5} Intraoperative blood loss during the study period was documented in the operative record after determination of volume based on an automated blood collection system via suction (major determinant) and laparotomy sponge soaking (minor determinant).

Hemoglobin evaluations

Mean differences between postoperative day 2 and preoperative hemoglobin values (mg/dL) were compared between barrier and no-barrier groups for correlation to recorded blood loss.

Metritis evaluations

“Postpartum febrile morbidity” was defined as a temperature of 38.0°C (100.4°F) or higher on any two of the first days after delivery, exclusive of the first 24 hours. Absence of mastitis, breast engorgement, urinary tract infection, or aspiration pneumonitis was required before diagnosis of metritis was made by the attending physician.

Statistical analysis

The Chi-square test was performed to assess blood loss in repeat cesareans between the barrier versus no-barrier group. This test was used to compare blood loss based on adhesiolysis, against the two barrier groups. Fisher’s exact test was used to compare need for adhesiolysis (nonparametric) as well as febrile morbidity (recorded diagnosis of “metritis”) between the two groups (barrier/no barrier). Logistic regression was used in analyzing the relationship between lysis of adhesions and barrier use, to determine if the relationship affected intraoperative blood loss. This was set as a two-exposure (barrier use and adhesiolysis) single-outcome (excessive blood loss) model. Drops in postoperative hemoglobin values are presented as mean ± standard deviation, with significance determined by Student’s t-test (continuous parametric). As described in our first publication,\textsuperscript{13} demographic differences between groups were calculated using the rank-sum test for continuous variables and the Chi-square test for binary data. Significance was set at \( P < 0.05 \). Data were analyzed using GraphPad data analysis and biostatistics software (GraphPad Prism (2009)), (GraphPad Software, La Jolla, CA, USA).

Results

Patient demographics are shown in Table 1. No significant sociodemographic differences were noted between the barrier and no-barrier groups at repeat CS.

A total of 262 primary cesareans were performed, with 43% (\( N = 112 \)) undergoing repeat CD during the study period. These 112 patients comprised the study group. A barrier was used in 53 of these patients at first CD (barrier group) and was not used in 59 (no-barrier group).

The following restates our previous published results from the original study:

In our original publication, barrier use in the index surgery resulted in a 74% adhesion free outcome compared to 22% adhesion free without it (\( P = 0.011 \)). Additionally, barrier use resulted in lesser grades of adhesions; no severe adhesions were found in the barrier group (\( P = 0.02 \)). In the first study, choice of suture material did not affect adhesion formation, although parietal peritoneal closure seemed to favor adhesion free outcome. Logistic regression revealed barrier use to have an odds ratio of 0.54, controlling for peritoneal closure; peritoneal closure had

| Table I Patient characteristics at repeat cesarean section (CS) |
|------------------|------------------|------------------|
| Age, median (range) | Barrier | No barrier, N (%) |
| Race, n (%) | | | P value |
| Hispanic | 28 (19–38) years | 26 (18–43) years | 0.5 |
| African-American | 39 (74) | 42 (710) |
| Caucasian | 10 (18) | 12 (20) |
| EGA, n (%) | | | |
| <37 | 4 (8) | 5 (9) |
| ≥37 | 53 (100) | 59 (100) |
| Diabetes (any class), N (%) | 1 (1.8) | 0 (0) | NA |
| Insurance, n (%) | | | |
| Medicaid | 49 (9) | 55 (93) | 0.8 |
| Private | 5 (9) | 4 (7) | 0.9 |
| Reason for repeat CS, n (%) | | | |
| Elective | 53 (100) | 59 (100) | NA |

Note: A \( P \) value of <0.05 was considered statistically significant. 
Abbreviation: EGA, estimated gestational age.
an odds ratio of 0.49 for adhesion formation, controlling for barrier use.15

Blood loss between groups at repeat cesarean
Table 2 presents the blood loss in the two groups. Although the overall difference in mean blood loss between the two groups was not statistically significant (P = 0.89), more women in the no-barrier group had excessive blood loss (P = 0.04).

Blood loss and lysis of adhesions
All cases of excessive blood loss (n = 7) had documented lysis of adhesions. In the barrier group, one lysis of grade 2 adhesions was undertaken, while in the no-barrier group, one lysis was undertaken for grade 2 adhesions and five for grade 3 adhesions. All procedures were performed for anterior uterine serosa involvement.

Based on logistic regression (two-variable exposure, single-outcome model), individuals in whom a barrier was used had an odds ratio of excessive blood loss of 0.92 (P = 0.01; 95% CI, −2.9 to −0.59) compared with those in whom a barrier was not used, controlling for lysis of adhesions, while adhesiolysis had an odds ratio of 2.3 (P = 0.04; 95% CI, 1.5−3.3) for excessive blood loss.

Overall, 42/112 patients underwent adhesiolysis (37.5%). Significantly more patients in the no-barrier group (35/59 [59.3%]) underwent lysis of adhesions than in the barrier group (7/53 [13.2%]) (P = 0.03) (Table 3).

Comparison of hemoglobin changes
No statistically significant differences were noted between groups in this regard. The mean drop in hemoglobin was −0.9 mg/dL in the barrier group and −1.2 mg/dL in the no-barrier group (P = 0.98). When analyzed in terms of excessive blood loss (n = 7), those in the no-barrier group who experienced excessive blood loss (n = 6) had a statistically greater drop in mean hemoglobin values (1.5 ± 0.3 mg/dL) than those in the barrier group (n = 1; 0.9 mg/dL) (P = 0.04).

Table 3 Need for adhesiolysis, per group, by adhesion grade

<table>
<thead>
<tr>
<th>Grade</th>
<th>All cases, n (%)</th>
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<th>No barrier, n (%)</th>
</tr>
</thead>
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<tr>
<td></td>
<td>LOA</td>
<td>LOA</td>
<td>LOA</td>
</tr>
<tr>
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<td>52 (46)</td>
<td>39 (74)</td>
<td>13 (22)</td>
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<td>31 (28)</td>
<td>6 (11)</td>
<td>25 (41)</td>
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<td>13 (23)</td>
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<tr>
<td></td>
<td>12 (92)</td>
<td>NA</td>
<td>12 (93)</td>
</tr>
</tbody>
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Note: Overall evaluable cohort: N = 112 (barrier group: n = 53; no-barrier group: n = 59).
Abbreviation: LOA, lysis of adhesions.

Discussion
Recently, the increased morbidity due to postoperative adhesions arising from CDs has received renewed attention. The unique nature of anterior uterine adhesions was recently addressed by Levin and Tulandi.14 Previously, Tulandi et al described the increased adhesion frequency as cesarean number increased with adhesion frequencies of 24% at second CD, 43% at third, and 48% at time of the fourth CD.4 For this reason, we sought to investigate the clinical utility of an absorbable adhesion barrier at time of primary CD for reduced adhesion propensity at repeat cesarean. These results were published recently;15 however, that study design did not incorporate consideration of maternal morbidity at repeat cesarean related to adhesion presence. Thus, the present study has sought to consider this.

For blood loss determination, we used visual estimation of loss based on automated collection containers and visual inspection of blood-soaked gauges. Overall, the difference in mean blood loss between those in whom a barrier was used at first CD and those in whom a barrier was not used was not statistically significant. However, excessive blood loss...
(defined as >1250 mL) and adhesiolysis were more likely in those in whom a barrier was not used at first CD. The drop in mean hemoglobin values was also more pronounced in those with adhesiolysis without preceding barrier use. This is probably due to the higher grade of adhesions found in those in whom an adhesion barrier was not used, which required more adhesiolysis. However, it is important to disclose that the large confidence intervals reported with excessive blood loss based on adhesiolysis reflect the otherwise small sample size of that group.

Despite its inter-observer variability, visual estimation is the most frequently practiced method of determining blood loss during childbirth in the USA. Interestingly, Duthie et al reported a significant underestimation of blood loss during cesarean births when compared with a laboratory method of measurement. We attempted to improve the accuracy of blood loss determination by using an automated suction blood collection system, as well as catch pouches per standard cesarean patient drapes. Similar reporting techniques have been previously utilized in delivery blood loss estimations. Similarly, Nelson et al used under-buttocks drapes with a pouch to collect blood/fluid at the time of birth as well as blood-soaked sponges to determine blood loss. In that study, blood in the sponges was calculated by direct weight, with 1 g converted to 1 mL. We elected not to weigh surgical laps or sponges, as weight calculations are not able to separate amniotic fluid from blood or other debris (vernix caseosa, meconium, etc). We included hemoglobin and hematocrit values for a more objective study of blood-loss status, which we consider a benefit of our design. Similarly, Stafford et al compared visual estimation to a calculated blood loss using postoperative hematocrit. The calculated blood loss was derived by multiplying the calculated maternal blood volume (based on height and weight) by the percent of blood volume lost (based on pre- and post-birth hematocrit levels). We agree with these authors’ statements that these calculations can be inaccurate depending on the hydration status of the woman, especially with the intravenous loading conducted with regional anesthesia or with pregnancy-induced hypertension. They also acknowledged that maternal physiologic blood volume changes might alter the hematocrit values. These factors were not analyzed in our study.

No differences in febrile morbidity were noted between the two groups. This may be the result of the biologically inert nature of the barrier chosen — oxidized regenerated cellulose. Significant visceral injury was not encountered in the total evaluable population (N = 112), barring one superficial deserosalization of the bladder dome during adhesiolysis for grade 3 adhesions. However, our study was not powered to detect visceral injury and we cannot exclude that this deserosalization reflects sample bias, as we had a limited number of evaluable cases (N = 112). A larger sample size would be required to report on the true frequency of such an injury. The increased propensity for visceral injury, specifically cystotomies at repeat CD due to adhesions, has been well described. In a 25-year review of more than 7000 CDs, Rahman and colleagues found significantly more intraoperative bladder injuries directly due to adhesions in women who had prior cesareans or other abdomino-pelvic surgery. Such injury not only affects morbidity but also health care costs overall.

A limitation of this study is its retrospective design. We are aware that some physicians may not have dictated or reported otherwise “mild” adhesiolysis, which may have reduced the overall number of adhesiolysis procedures actually performed. Our study focused on immediate intraoperative morbidity differences as well as postoperative fever. Differences in longer-term morbidity differences, such as chronic pelvic pain, infertility, or small bowel obstruction, which were outside the scope of our current research, will require larger sample sizes and longitudinal study for proper evaluation.

**Conclusion**

As far as we are aware, this is the first study of its kind evaluating morbidity at first repeat CD based on prior adhesion barrier use. Although limited by the overall sample size, our study serves as a pilot investigation for potential risks and implications of adhesiolysis during repeat cesareans. An increased need for adhesiolysis, resulting in increased in blood loss, was noted in those in whom a barrier had not previously been used. This reflects the higher incidence and grade of adhesions in that group. The absence of noted metritis in the barrier group is also reassuring. It is concluded, therefore, that use of an oxidized regenerated cellulose adhesion barrier at primary CS may reduce some aspects of maternal morbidity at subsequent repeat CS.

**Disclosures**

Hector Chapa serves as a medical consultant to Ethicon, Inc, and Conceptus, Inc. He has received honoraria for medical education lectureships on the subject of adhesion prevention for Ethicon, Inc. This study was conducted independently of any industry funding or editorial assistance. Gonzalo Venegas has no conflicts of interest, financial or otherwise, to declare in relation to this work.
References