Clear Film Adhesion Barrier Use at Cesarean Section: A Retrospective Analysis

Abstract:

Objective: To evaluate the use of a carboxymethylcellulose-hyaluronate adhesion barrier (Seprafilm) at the time of Cesarean section.

Design: Retrospective cohort study.

Setting: A tertiary care center in Boston, MA, USA.

Population: All women who underwent Cesarean section between the years 2006-2010 and returned for a second pelvic surgical procedure.

Methods: All patients who had a Seprafilm barrier placed at the first (index) Cesarean section were matched on a 2:1 basis to those who had no barrier. Effectiveness and surgical outcomes were compared with Chi Square and Wilcoxon tests. Cofounders were identified and controlled with logistic regression models.

Main Outcome Measures: The location and severity of pelvic adhesions at the follow-up pelvic surgery.

Results: Seventy-seven women who had Seprafilm placed at the index delivery were matched to 154 controls who received no barrier. The two groups had similar rates of any dense adhesions (43% and 42% respectively, p=.78) and those on the anterior uterus (34% and 31%, p=.62) at follow-up surgery. After controlling for all significant confounders, barrier use did not show a significant decrease in any (aOR=0.79, 95% CI 0.43-1.45) or anterior uterine dense adhesion formation (aOR=0.88, 95% CI 0.46-1.65). There were no significant differences in delivery times at follow-up (median 11 minutes in each group, p=.54), or in pelvic infection rate at the index surgery (5% in each group, p=1.0).

Conclusion: Seprafilm use at Cesarean section was not associated with a significant decrease in dense adhesion formation.

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Glossary of Abbreviations: No abbreviations used in this report

Section 1: Introduction

One out of three births in the United States is currently performed by Cesarean section (1). In fact the rate of Cesarean delivery has been climbing steadily since 1996, setting new records year after year, now making it the most common surgery performed in the United States (1). Cesarean sections are known to expose both mother and baby to the risks of major surgery including infection, hemorrhage, placental abnormalities, not to mention risk of uterine rupture with future pregnancy (2). In addition, like other forms of surgical intervention, Cesarean section can result in the formation of adhesions, with reported incidences ranging from 24-73% (2). Adhesions are none other than fibrous, vascular bands of scar tissue that may connect organs or tissues that are normally separated. They are almost always an inevitable result of any form of peritoneal or pelvic surgery. Adhesion-related complications including bowel obstruction, chronic pelvic pain, infertility, and difficult repeat surgery, are estimated to cost $1.2 billion annually (3). It is known that in patients undergoing surgery to the female reproductive tract, almost one-third will experience at least one readmission during the ensuing 10 years, either directly or possibly related to adhesion formation (3). Postoperative adhesion formation represents a significant expenditure for the healthcare system along with important societal costs secondary to lost work force capacity and impaired quality of life. In addition to increased costs to the medical system, adhesions increase the risk of future operative complications such as bleeding, accidental enterotomy or cystotomy, and increased operative time (3). Given these findings, there has been significant interest of pharmaceutical and/or biomedical companies in the application of synthetic barriers to prevent adhesions.

There are many forms of adhesion barriers including physical films, fabrics, gels, or other materials that are applied between tissue layers at the end of a surgery before the incision site is closed. One form of a clear film adhesion barrier, the Seprafilm Adhesion Barrier (Genzyme Biosurgery, Framingham, MA), is an absorbent clear film of hyaluronate and carboxymethylcellulose. It is made of chemically modified sugars, some of which naturally occur in the human body. It is easily adherent to tissues and solely absorbed into the body over a period of 3-7 days. Interceed (Johnson and Johnson Medical Inc., Arlington, TX) is another very similar barrier that like Seprafilm, is composed of modified cellulose that swells and eventually

gels over the injured site of tissue, and is ultimately absorbed by the body over a period of days. Per its package insert: “Seprafilm Adhesion Barrier serves as a temporary bioresorbable barrier separating apposing tissue surfaces. The physical presence of the membrane separates adhesiongenic tissue while the normal tissue repair process takes place…[it] can be expected to reduce adhesions within the abdominopelvic cavity” (Genzyme Biosurgery, Framingham, MA).

Currently, both Seprafilm and Interceed are FDA approved for use in certain types of pelvic and abdominal surgery, namely abdominal laparotomy. After gynecologic surgery, intraperitoneal adhesions form in 55-100% of patients, often resulting in infertility, recurrent pelvic pain, small bowel obstruction, and/or difficult reoperative surgery, all of which may escalate healthcare costs as mentioned above (4). The effectiveness of Seprafilm in gynecologic surgery was demonstrated by a randomized trial of Seprafilm placement at the time of abdominal uterine myomectomy, which showed an 85% reduction in anterior uterine adhesion formation (4). Study participants were excluded if they received other adhesion barriers such as Interceed or Preclude (W.L. Gore and Company, Flagstaff, AZ), or if they were administered any anti-adhesion therapy during their initial surgical procedure. Despite the findings from this study, more recent data about Seprafilm has raised safety concerns regarding the safety of its use on patients, with increased rates of bowel anastamosis leak and possibly pelvic abscess (5-6). The package insert warnings state: “An increased potential for abdominal events related to anastomotic leak was identified in a post-approval study when Seprafilm Adhesion Barrier was wrapped directly around a fresh anastomotic suture or staple line” (Genzyme Biosurgery, Framingham, MA). Thus, for its use at Cesarean section, more investigation on Seprafilm regarding its safety is warranted.

Repeat Cesarean sections account for more than 40% of all Cesarean sections performed (1). Conventional wisdom is that repeat Cesarean deliveries are often more difficult because of adhesions that involve the lower uterine segment, which may delay entry into the uterine cavity and therefore delay subsequent delivery of the infant. Furthermore, it is known that the incidence of adhesions increases with each subsequent Cesarean section; and repeat Cesarean delivery is known to increase operative time, time to delivery, and risk of bladder injury. In fact, multiple studies comparing primary and repeat Cesarean sections have documented increased adhesion

formation and delayed infant delivery time with repeat delivery, raising the question of whether an adhesion barrier placed at Cesarean section would be efficacious (7-8). One study reported that 94% of women with a myomectomy incision on the posterior uterine surface had adhesions to the adnexa and that every patient had at least one adhesion at second-look laparoscopy (8). Another major study examining the incidence of adhesions after Cesarean section and impact on delivery time, found that the presence of adhesions increased the time from skin incision to delivery of the infant, and that delivery of the infant took longer with each subsequent Cesarean delivery (7). Adhesions were scored as severe if the operative summary contained the words severe, extensive, or dense. Adhesions were categorized as mild if operative notes used words such as present, mild, few, or some. It is important to note that at the institution where this study took place, peritoneal closure was not routinely performed, which may have resulted in an underestimation of the true incidence of reported adhesions.

While the use of Seprafilm at Cesarean section falls within its approved use at laparotomy, both its effectiveness and safety remain largely unexplored in this field, and the product's package insert notes the lack of specific data in pregnancy (9). The insert clearly states: "The safe and effective use of Seprafilm Adhesion Barrier in pregnancy has not been evaluated…This product is not recommended for use during pregnancy" (Genzyme Biosurgery, Framingham, MA). In addition, One recent systematic review reported that using adhesion barriers at Cesarean delivery is currently "ill-advised" due to limited data to support any meaningful clinical benefit (2). Given the paucity of controlled data for the use of Seprafilm at Cesarean section, this study was designed to evaluate the postoperative course, degree of future adhesive disease, and adhesion-related complications among these patients. We hypothesized that patient's receiving Seprafilm would have decreased dense adhesions at the time of future surgery, similar to the benefit seen with gynecologic surgery.

In summary, adhesion prevention is an important consideration with Cesarean delivery. Synthetic adhesion barriers have been proposed as a preventive measure, but have not been well studied in this clinical setting. From conversations with other obstetricians around the country at major scientific conferences, it is clear that Seprafilm is being placed at the site of hysterotomy to prevent future adhesive disease. In fact, even the Brigham & Women's Hospital Labor and

Delivery Unit has made Seprafilm available for this purpose since 2006, and obstetricians use the barrier at their own discretion. Given the lack of any randomized trials or prospective studies on Seprafilm, the goal of this project was to ultimately guide modern day obstetric practice and inform obstetricians on the efficacy and safety of using the Seprafilm clear film adhesion barrier.

Section 2: Methods

This retrospective cohort study was approved by the Institutional Review Boards at Partners Heatlhcare and Harvard Medical School. Individual informed consent was waived, given anonymous abstraction and removal of identifiers at the conclusion of our data collection.

We identified all patients who had a Seprafilm barrier placed during a Cesarean delivery at Brigham & Women's Hospital between the years 2006-2010, and selected those who returned for a second pelvic surgical procedure. All subjects had a sheet of Seprafilm placed over the anterior uterus. Control subjects were matched to the Seprafilm cohort on a 2:1 basis according to hysterotomy type (low transverse or vertical) and whether the initial surgery was a primary or repeat Cesarean section. We also matched subjects based on the primary attending surgeon. If an exact match by surgeon could not be made within the other two constraints, then a different surgeon from the same practice group was selected. When multiple exact matches were available, we selected controls whose Cesarean section took place in the same year as the Seprafilm subject. Patients who underwent hysterectomy or who had alternative adhesion barriers placed at time of index Cesarean were excluded.

All data were abstracted from operative notes, labor and delivery records, and electronic medical records of patients' first (index) and second surgical procedures. For all subjects, we collected patient demographic data (maternal age, parity, and race) and relevant data from their medical and surgical history. We also collected the basic characteristics of each surgery and complications at the index surgery, including major hemorrhage (blood loss greater than 1200cc or description of major bleeding requiring operative intervention), visceral organ injury, postoperative ileus or bowel obstruction, infection, and hysterotomy extensions. We also

recorded any additional pelvic procedures performed with the index Cesarean section, including any arterial devascularization procedures (uterine artery ligations or embolization). Operating times were obtained from an electronic labor and delivery record.

Our primary outcome of interest was the presence, severity, and location of adhesions at the time of the patient's second surgical procedure. Adhesions at either surgery were characterized based on a previously validated "Adhesion Scoring Data Sheet" as described in Lyell et al (10). We characterized adhesions as either simple ("filmy," "minimal") or dense ("extensive," "vascular,") Adhesions that altered the surgical approach or required surgical intervention were categorized as dense. The location of the adhesions on the uterus and/or other pelvic structures was noted. Secondary outcomes included occurrence of immediate surgical complications, uterine rupture or scar dehiscence (documented as complete dehiscence, uterine "window", or absent myometrial tissue in the prior uterine scar) at the second surgical procedure, and delivery times with repeat Cesarean section. Delivery time was recorded from the time of initial skin incision. In order to control for individual patient factors that could affect surgical time (such as body habitus or abnormal anatomy), we additionally calculated a "delta-delivery time," defined as the difference (in minutes) between the delivery times at the first and second cesarean sections.

Statistical analyses were performed using SAS software, Version 9 (Copyright © 2002-2008, SAS Institute, Inc). Categorical variables were analyzed with Chi Square or Fisher's Exact tests. Continuous variables were analyzed with Wilcoxon tests for nonparametric data. Univariate analyses were used to define factors associated with adhesion formation and with Seprafilm placement. We then controlled for multiple confounding variables with logistic regression models, excluding subjects with missing data. Variables associated with either the exposure or the outcome were retained in the models if they changed an odds ratio by more than 10%. With the number of Seprafilm subjects available for our analysis (77), a 2:1 ratio of controls to Seprafilm subjects, and an alpha of .05, we had 90% power to detect a 50% reduction in adhesions, using a baseline adhesion rate of 42% (11).

Section 3: Results

We identified 378 women who had Seprafilm placed at cesarean section, 77 of whom returned for a second pelvic surgery prior to July 2013. Theses subjects were matched to 154 control patients who did not have a barrier placed at the index delivery. Controls were matched to the exact surgeon 78% of the time, while the other 22% were matched to a different surgeon in the same practice group.

As shown in Table 1, the two groups were highly similar in terms of maternal age, rate of nulliparity, number of prior Cesarean sections, and endometriosis history, while those receiving Seprafilm had a higher rate of current or past fibroids (21% vs. 10% in the control group, p=.02). Subjects in the Seprafilm group were also more likely to report their race as black (21% vs. 9%, p =.01), while race information was missing for two subjects in the control group.

When evaluating the index Cesarean sections, we found no significant difference between the two groups in relation to gestational age, hysterotomy type, estimated blood loss, surgical time, and rate of peritoneal closure. Subjects in the Seprafilm group were significantly more likely to have dense pelvic adhesions present at the index delivery (22% vs. 11% in the control group, p =.02), and were less likely to have labored before their cesarean section (27% vs. 41%, p =.04). Both groups showed similar rates of hysterotomy extensions, infection, and major hemorrhage. Only one subject in the Seprafilm group experienced an organ injury, while one subject in the control group developed a postoperative pelvic hematoma. Five subjects in the Seprafilm group underwent a uterine artery devascularization procedure, including four uterine artery ligations and one intraoperative uterine artery embolization, while no control subjects had such a procedure (Table 1).

For the second surgical procedure, at which time the primary outcome was measured, 71 Seprafilm patients (92%) and 147 control patients (95%) underwent a repeat Cesarean delivery. Of the thirteen who had an alternate pelvic surgery, eleven underwent gynecologic pelviscopies, one had an abdominal hysterectomy, and one had an abdominal myomectomy. The median time

between the first and second procedures was 27.9 months and did not significantly vary between the groups.

Overall, 42% of subjects had dense pelvic adhesions present at the follow-up pelvic surgery, and we evaluated predictors of this outcome (Table 2). We observed the highest rates of dense adhesion formation among those with three or more prior Cesarean sections (62%), vertical hysterotomy at the index delivery (58%), Black or Asian race (73% and 61%, respectively), presence of dense adhesions at the index delivery (74%), a history of endometriosis (67%), prior postoperative pelvic infection (67%), hysterotomy extensions at index delivery (60%), and prior performance of an arterial devascularization procedure (80%). Neither a history of fibroids nor laboring prior to the index delivery was associated with dense adhesion formation, with 42% and 43% adhesion rates, respectively. Of the above factors, race, hysterotomy type, hysterotomy extensions, and dense adhesions at the index delivery were statistically significant predictors of dense adhesions at follow-up surgery.

Our primary analysis is detailed in Table 3. Forty-three percent of patients who received Seprafilm had dense adhesions at follow-up, while this rate was 42% in the control group (p=.78). Because Seprafilm was placed over the anterior uterus, and thus was expected to prevent adhesions at this location, we separately evaluated dense anterior uterine adhesions as an endpoint. Again, we found no significant association, with a 34% dense uterine adhesion rate in the Seprafilm group and a 31% rate in the control group (p=.62).

After evaluating multiple variables, black race, the presence of adhesions at the index surgery, and use of a prior devascularization procedure were significant confounders in the association, altering the odds ratio by 10% or more. After controlling for all of these factors, there remained no significant reduction in the formation of any (aOR=0.79, 95% CI=.43-1.45) or anterior uterine dense adhesions (aOR=0.88, 95% CI=.46-1.65).

With regards to our secondary endpoints, we saw no reduction in the delivery time at follow-up Cesarean section between the two groups. The median time from incision to delivery was 11 minutes in both the Seprafilm (interquartile range 9-17) and control group (interquartile range 8-

15), p=.54. We adjusted for patient-specific factors by calculating a delta-delivery time (defined as the difference in delivery time between the follow-up Cesarean and index Cesarean deliveries). Again we saw no significant reduction in the delta-time for the Seprafilm group, in which the follow-up Cesarean delivery took an additional 3.5 minutes (IQR 0-6) vs. 2 extra minutes (IQR 0-6) in the control group, p=.53. The time variables were dichotomized in order to control for race, preexisting dense adhesions, and uterine devascularization, and the resulting odds ratios remained non-significant for delivery times (aOR = 0.86, 95% CI = 0.47-1.59) and delta-delivery time (aOR = 1.16, 95% CI = 0.64-2.08) (Table 3).

In terms of surgical complications, we observed identical rates of pelvic infection following the index surgery (5% for both the Seprafilm and control groups, p=1.0, Table 1). There was no significant difference in the rate of major hemorrhage at follow-up surgery (8% of those who had received Seprafilm and 3% who had not, aOR = 1.33, 95% CI = 0.28-6.44 (Table 3). Two subjects in the control group experienced bowel injuries at follow-up surgery, while there were no organ injuries in the Seprafilm group (p = 0.55). No uterine ruptures, bowel obstruction, or cases of postoperative ileus occurred.

We observed an increased incidence of hysterotomy dehiscence in the Seprafilm group, though this outcome was too rare to show statistical significance (6% in the Seprafilm group vs. 4% in the control group, OR=1.71, 95% CI=0.51-5.80). This observation remained after controlling for race, dense adhesions at index delivery, prior devascularization, and history of fibroids (aOR=2.37, 95% CI=0.68-8.26). Notably, none of the patients who experienced hysterotomy dehiscence had undergone a prior uterine artery devascularization procedure.

Section 4: Discussion, Limitations, Conclusions, and Suggestions for Future Work

Main Findings: We hypothesized that women receiving Seprafilm at Cesarean section would have significantly fewer dense adhesions at follow-up surgery. After controlling for multiple potential confounders, we found no significant association between Seprafilm use and dense uterine adhesion formation. Notably, the adjusted odds ratio of 0.88 did not come close to the 85% adhesion reduction seen when Seprafilm was studied at myomectomy (4), nor to the 50%

reduction that we predicted. Similarly, we saw no significant differences in delivery times or operative complications at either the index Cesarean section or follow-up surgery.

Strengths and Limitations: We recognize the potential for confounding with a nonrandomized study design, and we therefore matched subjects on factors that we considered potentially important in adhesion formation: Hysterotomy type, surgeon, and whether the index delivery involved a primary or repeat Cesarean section. We considered hysterotomy type to be important because the low transverse incisions may lead to different adhesion patterns compared to uterine incisions for abdominal myomectomy. One study looking at the effectiveness of Seprafilm at the time of abdominal myomectomy suggested that the location of the uterine incision (vertical versus low transverse) might play a role in its future adhesive potential (4).

We matched for the surgeon performing the operation, believing that variations in surgical technique may affect adhesion formation. Adherence to Halstedian principles of surgery - avoidance of infection, tissue damage, and tissue desiccation - has been shown to reduce adhesions (12). Given these findings, individual surgeons' techniques can potentially lead to variation in postoperative adhesion formation, and can be difficult to identify and specifically control. For 22% of our cases we had to match for a surgeon in the same group practice rather than to the exact surgeon. We believe that surgical practice was well controlled in our study, as the total operating time, estimated blood loss, and rates of peritoneal closure and hysterotomy extension were balanced between the comparison groups.

The number of previous Cesarean sections plays a role in the rate of future adhesion formation, as multiple studies have shown that the number and severity of adhesions will increase with each subsequent Cesarean delivery (7-8, 11). We matched subjects based on whether they underwent a primary or repeat Cesarean for the index delivery, and found that in doing so the groups were well matched in terms of specific Cesarean order.

The retrospective nature of our study forced us to rely on the surgeons' dictations and patients' medical records. Surgeons may have failed to report or specifically detail the nature of adhesions found at the index or follow-up operations. However, we feel that clinically insignificant (filmy)

adhesions are more likely to be underreported in the operative notes, while those adhesions altering the surgical procedure – the primary outcome of our study – are more likely to be mentioned. Additionally, only a subset of our hospital's obstetricians is represented in this study. It is unclear whether the cohort represented in these obstetric practices well reflects the obstetric population as a whole.

Interpretation: We are aware of two other studies that evaluated the use of carboxymethylcellulose adhesion barrier at the time of Cesarean delivery. The first found a found a significant benefit in time to delivery, duration of surgical procedure, and incidence of adhesions in patients receiving Seprafilm during prior Cesarean sections (13). However, the study had several limitations in its design and subsequent analysis. First, the study was conducted in Japan, and subjects were of primarily Asian descent. Our study, with a multi-racial population, suggested that Asian women have a higher overall rate of adhesion formation than their white or Hispanic counterparts (61% vs. 34% and 38%, respectively), suggesting that the effect of Seprafilm may vary based on maternal race and underlying genetic factors. In addition, the study did not adjust for potential confounders associated with dense adhesions, or comment on the severity or location of the subsequent adhesion formation, raising questions about the clinical significance of their outcome variable.

In a recent retrospective study by Edwards et al, carboxymethylcellulose adhesion barrier placement at primary cesarean section was not associated with decreased time to delivery, operative complications, or decreased adhesion formation.(14) In addition, authors noted a statistically significant rate of hospital readmission in the group who received the adhesion barrier. Unlike both of these studies, our study design focused on the severity and location of the adhesions, using a previously published scoring system for adhesions at cesarean section.(10) We felt that clinically relevant adhesions are those that may alter the course of the follow-up surgery, either by requiring additional procedures or changing the type and/or location of the hysterotomy. The Fushiki et al study did not focus on clinical relevance of adhesions in their cohort. The Edwards et al study used a surrogate clinical variable - time to delivery at the next cesarean delivery – as their primary outcome, but did not otherwise characterize the adhesions at follow-up. Our study adds to the findings by Edwards et al, in that the adhesion barrier

placement was associated with neither the prevention of dense uterine adhesions nor a reduced time to delivery in the subsequent cesarean section. Additionally, our study looks at barrier use at the time of repeat cesarean delivery and in the presence of preexisting adhesions, and did not show a benefit in these settings.

We found one randomized trial investigating Seprafilm use during open uterine myomectomies (4). This study showed a significant benefit to using Seprafilm after myomectomy, with an 85% reduction in the rate of anterior uterine adhesions after placement (from 39% with no barrier to 6% with Seprafilm). This contrasts with the lack of effect found with our study. Cesarean sections are generally of short duration (median operative time in our study group was 47 minutes at the index delivery), which may produce less tissue desiccation. Other factors, such as the alkaline environment created by amniotic fluid and the fundal hysterotomy location at myomectomy, could also explain the discrepancy in findings.

In an earlier study of gynecologic cancer surgery, a trend towards increased pelvic abscesses was noted in patients receiving Seprafilm (6). Our analysis revealed no difference in major morbid outcomes among patients who received Seprafilm and those who did not. We observed the same 5% rate of postoperative infection in the Seprafilm and control groups, which promotes the safety of the barrier in the immediate postpartum period.

In a prospective trial examining post-operative bowel obstructions after abdomino-pelvic surgery, an increased rate of bowel anastamosis leak was noted in patients who had Seprafilm placed directly over their bowel anastamoses (13.5 % vs. 5.1%, $p<0.001$) (5). This finding led to a revision in the Seprafilm package insert, warning users that Seprafilm "should not be wrapped directly around a fresh anastamotic suture or staple line"(9). We observed a non-significant increase in the rate of hysterotomy dehiscence in patients who received Seprafilm compared to those who did not. However, the small size of this study and rarity of the outcome does not allow us to draw conclusions regarding the effects of Seprafilm on hysterotomy healing.

Conclusions: We were unable to show that the adhesion reduction demonstrated with Seprafilm at gynecologic surgery can be extrapolated to Cesarean section. Given the potential for residual

confounding, results of randomized trials are needed to understand whether or not Seprafilm is an effective adhesion barrier at Cesarean delivery. We also believe that larger studies are needed to assess whether Seprafilm placement compromises hysterotomy scar formation, analogous to what has been shown when the product is placed over a fresh bowel anastamosis (5).

Given the lack of data demonstrating a clear benefit to Seprafilm at time of Cesarean, and the lack of adequate data regarding the effects on hysterotomy scar formation, any decision for the routine use of Seprafilm during Cesarean delivery should await the results of randomized trials.

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Role of the Student:

1. Independently conducting review of literature to construct background information about the research project
2. Determining research question and primary/secondary outcomes of interest with mentor
3. Designing methodology of research study with guidance from principal investigator
4. Leading and executing a retrospective chart review (both electronic and paper records) of all patients
5. Developing a standardized data collection tool with principal investigator and statistician to collect clinical information from electronic medical records in a manner that facilitates ease of data entry and analysis
6. Managing and entering patient data in the form of a secure, electronic database with only de-identified patient information
7. Working with mentor and statistician to utilize statistical computer programs (SAS) to perform descriptive data analysis and eventually help with comparative univariate and multivariate data analysis

8. Writing the first draft of the manuscript fit for publication with weekly meetings with other co-authors to review concepts, assess need for further editing, assess progress on overall timeline, and discuss both short-term and long-term goals.

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Table I. Patient and Operative Factors at the Time of Index Surgery.

Variable	Seprafilm (n=77)	No Barrier (n=154)	p-value[a]
Maternal age, years[b]	32.3 (30.2-35.6)	32.9 (30.9-35.6)	.43
Gestational age, weeks[b]	39.1 (38.7-39.6)	39.1 (38.0-40.0)	.89
Nulliparous	43 (56%)	87 (56%)	.92
Number of prior C-sections			.96
0	48 (62%)	95 (62%)	
1	24 (31%)	51 (33%)	
2	4 (5%)	7 (4%)	
3	1 (1%)	1 (1%)	
Race			.12
White	52 (68%)	113 (74%)	.35[c]
Black	16 (21%)	14 (9%)	.01[c]
Hispanic	5 (6%)	11 (7%)	1.0[c]
Asian	4 (5%)	14 (9%)	.43[c]
Not available/Other	0	2 (1%)	
Presence of labor	21 (27%)	63 (41%)	.04
Endometriosis history	3 (4%)	9 (6%)	.76
Fibroid history	16 (21%)	15 (10%)	.02
Type of Hysterotomy			.97
Classical	10 (13%)	20 (13%)	
Low vertical	8 (10%)	14 (9%)	
Low transverse	59 (77%)	120 (78%)	
Adhesions Present			
None	56 (73%)	127 (83%)	

Variable	Seprafilm (n=77)	No Barrier (n=154)	p-value[a]
Any	21 (27%)	27 (18%)	.08
Dense adhesions only	17 (22%)	17 (11%)	.02[d]
Peritoneal closure	16 (21%)	20 (13%)	.12
Estimated blood loss, ml[b]	800 (600-800)	700 (500-800)	.51
Total surgical time, min[b]	50 (42-62)	47 (40-59)	.13
Complications			
Postpartum pelvic Infection	4 (5%)	8 (5%)	1.0
Hysterotomy extensions	12 (16%)	23 (15%)	.90
Major Hemorrhage	5 (6%)	10 (6%)	1.0
Vascular or organ injury	1 (1%)	0	.33
Pelvic hematoma	0	1 (1%)	1.0
Devascularization	5 (6%)	0	<.01
Time between surgeries, mos[b]	28.3 (21.9-34.3)	27.6 (21.1-33.3)	.74

[a]Chi Square unless otherwise indicated

[b] Reported as median (25-75% Interquartile range)), p-value from Wilcoxon test

[c] When compared to all other groups in that category

[d] When compared to those with no adhesions or simple adhesions only

Table II. Predictors of Dense Adhesions at the Follow-up Surgical Procedure.

Predictor	Dense Adhesions n=96 (42%)[a]	No Dense Adhesions n=135 (58%)[a]	P Value (X^2)
Prior C-sections			.18
1	54 (38%)	89 (62%)	.14[b]
2	34 (45%)	41 (55%)	
3+	8 (62%)	5 (38%)	.15[b]
Race			<.01
White	57 (34%)	108 (65%)	<.01[b]
Black	22 (73%)	8 (27%)	<.01[b]
Asian	11 (61%)	7 (39%)	.09[b]
Hispanic	6 (38%)	10 (62%)	.80[b]
Medical/Surgical History			
Endometriosis	8 (67%)	4 (33%)	.08
Fibroids	13 (42%)	18 (58%)	.96
Index Surgery Factors			
Presence of Labor	36 (43%)	48 (57%)	.76
Any Adhesions	31 (65%)	17 (35%)	<.01
Dense Adhesions	25 (74%)	9 (26%)	<.01
Peritoneal closure	13 (36%)	23 (64%)	.47
Vertical Hysterotomy	30 (58%)	22 (42%)	<.01

Hysterotomy Extensions	21 (60%)	14 (40%)	.02
Arterial Devascularization	4 (80%)	1 (20%)	.16
Postoperative Infection	8 (67%)	4 (33%)	.08

[a]Column percentages reflect the dense adhesion rate by predictor

[b]When compared to all other groups in that category

Table III. Surgical Outcomes as a Function of Seprafilm Placement.

Outcome at Follow-Up Surgery	Seprafilm (n=77)	No Barrier (n=154)	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Dense Adhesions				
Any	33 (43%)	64 (42%)	1.08 (.62-1.88)	0.79 (.43-1.45)[a]
Anterior Uterine	26 (34%)	47 (31%)	1.16 (.65-2.08)	0.88 (.46-1.65)[a]
Other Outcomes				
C-sections only	***(n=71)***	***(n=147)***		
Delivery time (min)[b]	11 (9-17)	11 (8-15)	1.08 (.61-1.90)	0.86 (.47-1.59)[a]
Delta-delivery time (min)[b]	3.5 (0-6)	2 (0-6)	1.05 (.59-1.86)	1.16 (.64-2.08) [a]
Hemorrhage	6 (8%)	4 (3%)	2.13 (.52-8.79)	1.33 (.28-6.44)
Organ injury [c]	0	2 (1%)	N/A	N/A
Hysterotomy dehiscence	5 (6%)	6 (4%)	1.71 (.51-5.8)	2.37 (.68-8.26)[d]

[a]Adjusted for black race, prior dense adhesions, and arterial devascularization at index surgery

[b]Expressed as median (Interquartile range)). Differences were non-significant by Wilcoxon tests (p=.54 for delivery times and p=.53 for delta-delivery times). Results were dichotomized to perform logistic regressions.

[c]Unadjusted p-value = .55 by Fisher's Exact test

[d]Adjusted for black race, prior dense adhesions, arterial devascularization at index surgery, and history of fibroids.