The use of Seprafilm Adhesion Barrier in Adult Patients Undergoing Laparotomy to Reduce the Incidence of Post-Operative Small Bowel Obstruction

Erin Call

Follow this and additional works at: http://commons.pacificu.edu/pa

Part of the Medicine and Health Sciences Commons

Recommended Citation
The use of Seprafilm Adhesion Barrier in Adult Patients Undergoing Laparotomy to Reduce the Incidence of Post-Operative Small Bowel Obstruction

Abstract

**Background:** Post-operative adhesions are an expected outcome with nearly every abdominal operation. Adhesions are not always symptomatic, but when they are, they can cause a variety of problems. Small bowel obstructions are a potential complication and are caused by abdominal adhesions in 75% of cases. This complication would be one best avoided, and as a result numerous prophylactic agents have been developed in hopes of decreasing the occurrence of adhesions.

Seprafilm Adhesion Barrier has been used since 1996 and has been largely effective in decreasing the incidence and severity of abdominal adhesions. A thin sheet of Seprafilm placed in the abdominal cavity before closure, keeps the organs from sticking to each other and forming scar tissue as the surgical site heals. The purpose of this systematic review is to evaluate the available research and determine if Seprafilm reduces the incidence of small bowel obstruction after laparotomy, as it does with adhesions.

**Methods:** An exhaustive search of medical literature was completed using Medline-OVID, CINAHL and EBM Reviews Multifile. The keywords *Seprafilm*, *Hyaluronic Acid*, *Carboxymethylcellulose*, *biocompatible materials*, *artificial membranes*, *laparotomy*, *tissue adhesions* and *intestinal obstruction* were used as search terms. The search was limited to articles written in English with human subjects. Only randomized controlled trials were included. Studies with pediatric subjects or gynecological surgeries were excluded.

**Results:** Three articles met the inclusion criteria and were incorporated in this review. Small bowel obstruction as an outcome after laparotomy was explored as well as several study-specific outcomes. The trials used Seprafilm in a randomized treatment group before closing the incision. Post-operative monitoring was completed in order to screen for the incidence of small bowel obstruction between the treatment and control groups. None of the studies found that the use of Seprafilm reduced the incidence of post-operative bowel obstruction, although some positive findings were additionally presented.

**Conclusion:** Although Seprafilm has been proven to decrease the incidence and severity of abdominal adhesions; the research available at this time does not show the same decreased incidence for post-operative small bowel obstructions. Additional large-scale, randomized controlled trials would be beneficial to further investigate this topic.

**Keywords:** *Seprafilm*, *Hyaluronic Acid*, *Carboxymethylcellulose*, *biocompatible materials*, *artificial membranes*, *laparotomy*, *tissue adhesions*, *intestinal obstruction*

**Degree Type**
Capstone Project

**Degree Name**
Master of Science in Physician Assistant Studies

This capstone project is available at CommonKnowledge: [http://commons.pacificu.edu/pa/281](http://commons.pacificu.edu/pa/281)
First Advisor
Mark Pedemonte, MD

Second Advisor
Annjanette Sommers, PA-C, MS

Keywords
Seprafilm, laparotomy, tissue adhesions, intestinal obstruction

Subject Categories
Medicine and Health Sciences

Rights
Terms of use for work posted in CommonKnowledge.
Copyright and terms of use

If you have downloaded this document directly from the web or from CommonKnowledge, see the “Rights” section on the previous page for the terms of use.

If you have received this document through an interlibrary loan/document delivery service, the following terms of use apply:

Copyright in this work is held by the author(s). You may download or print any portion of this document for personal use only, or for any use that is allowed by fair use (Title 17, §107 U.S.C.). Except for personal or fair use, you or your borrowing library may not reproduce, remix, republish, post, transmit, or distribute this document, or any portion thereof, without the permission of the copyright owner. [Note: If this document is licensed under a Creative Commons license (see “Rights” on the previous page) which allows broader usage rights, your use is governed by the terms of that license.]

Inquiries regarding further use of these materials should be addressed to: CommonKnowledge Rights, Pacific University Library, 2043 College Way, Forest Grove, OR 97116, (503) 352-7209. Email inquiries may be directed to: copyright@pacificu.edu

This capstone project is available at CommonKnowledge: http://commons.pacificu.edu/pa/281
NOTICE TO READERS

This work is not a peer-reviewed publication. The Master’s Candidate author of this work has made every effort to provide accurate information and to rely on authoritative sources in the completion of this work. However, neither the author nor the faculty advisor(s) warrants the completeness, accuracy or usefulness of the information provided in this work. This work should not be considered authoritative or comprehensive in and of itself and the author and advisor(s) disclaim all responsibility for the results obtained from use of the information contained in this work. Knowledge and practice change constantly, and readers are advised to confirm the information found in this work with other more current and/or comprehensive sources.

The student author attests that this work is completely his/her original authorship and that no material in this work has been plagiarized, fabricated or incorrectly attributed.
The use of Seprafilm Adhesion Barrier in Adult Patients Undergoing Laparotomy to Reduce the Incidence of Post-Operative Small Bowel Obstruction

Erin B. Call

A Clinical Graduate Project Submitted to the Faculty of the

School of Physician Assistant Studies

Pacific University

Hillsboro, OR

For the Masters of Science Degree, August 11, 2012

Faculty Advisor: Mark Pedemonte, MD
Clinical Graduate Project Coordinator: Annjanette Sommers, PA-C, MS
Biography

Erin Call was born in Salem, Oregon where she stayed through elementary school until her family moved to Santa Barbara, California. She remained there through college where she received a B.A. in Communication Studies. She worked in Southern California in Dermatology and Plastic Surgery before PA school and then returned to the Northwest to attend Pacific University. She enjoys international travel, mountains, oceans and laughing.
Abstract

**Background:** Post-operative adhesions are an expected outcome with nearly every abdominal operation. Adhesions are not always symptomatic, but when they are, they can cause a variety of problems. Small bowel obstructions are a potential complication and are caused by abdominal adhesions in 75% of cases. This complication would be one best avoided, and as a result numerous prophylactic agents have been developed in hopes of decreasing the occurrence of adhesions.

Seprafilm Adhesion Barrier has been used since 1996 and has been largely effective in decreasing the incidence and severity of abdominal adhesions. A thin sheet of Seprafilm placed in the abdominal cavity before closure, keeps the organs from sticking to each other and forming scar tissue as the surgical site heals. The purpose of this systematic review is to evaluate the available research and determine if Seprafilm reduces the incidence of small bowel obstruction after laparotomy, as it does with adhesions.

**Methods:** An exhaustive search of medical literature was completed using Medline-OVID, CINAHL and EBM Reviews Multifile. The keywords *Seprafilm, Hyaluronic Acid, Carboxymethylcellulose, biocompatible materials, artificial membranes, laparotomy, tissue adhesions* and *intestinal obstruction* were used as search terms. The search was limited to articles written in English with human subjects. Only randomized controlled trials were included. Studies with pediatric subjects or gynecological surgeries were excluded.

**Results:** Three articles met the inclusion criteria and were incorporated in this review. Small bowel obstruction as an outcome after laparotomy was explored as well as several study-specific outcomes. The trials used Seprafilm in a randomized treatment group before closing the incision. Post-operative monitoring was completed in order to screen for the incidence of small bowel obstruction between the treatment and control groups. None of the studies found that the use of Seprafilm reduced the incidence of post-operative bowel obstruction, although some positive findings were additionally presented.

**Conclusion:** Although Seprafilm has been proven to decrease the incidence and severity of abdominal adhesions; the research available at this time does not show the same decreased incidence for post-operative small bowel obstructions. Additional large-scale, randomized controlled trials would be beneficial to further investigate this topic.

**Keywords:** Seprafilm, Hyaluronic Acid, Carboxymethylcellulose, biocompatible materials, artificial membranes, laparotomy, tissue adhesions, intestinal obstruction
Acknowledgements

To my wonderful parents: Thank you for your never-ending love and support. I appreciate that you are always there for me; whether it is just to share some laughs, or to give advice. Thank you for reminding me that you are proud of me. I could not have made it through all of this without your encouragement. Thanks for believing in me. I love you!
Table of Contents

Biography......................................................................................................................................................... 2
Abstract............................................................................................................................................................ 3
Acknowledgements ............................................................................................................................................... 4
Table of Contents ............................................................................................................................................. 5
List of Tables ..................................................................................................................................................... 6
List of Abbreviations .......................................................................................................................................... 6
Background ....................................................................................................................................................... 7
Methods............................................................................................................................................................. 8
Results ............................................................................................................................................................... 8
Discussion......................................................................................................................................................... 15
Conclusion ....................................................................................................................................................... 20
References......................................................................................................................................................... 21

Table I: Characteristics of Reviewed Studies........................................Error! Bookmark not defined.

Table II: Summary of Findings......................................................................................................................... 24
List of Tables

Table I: Characteristics of Reviewed Studies
Table II: Summary of Findings

List of Abbreviations

ASBO………………………………………………………..…..Adhesive small bowel obstruction(s)
SBO……………………………………………………………….Small bowel obstruction(s)
The use of Seprafilm Adhesion Barrier in Adult Patients Undergoing Laparotomy to Reduce the Incidence of Post-Operative Small Bowel Obstruction

BACKGROUND

Abdominal adhesions are a health concern of many individuals who have previously had surgery. In fact, they are so common that postoperative adhesions are an expected outcome with nearly every abdominal operation. Adhesions are not always symptomatic, but when they are, they can cause chronic abdominal pain and are known to cause problems with fertility. Depending on the size and location, adhesions can also complicate further surgeries. Additionally, small bowel obstructions are caused by abdominal adhesions approximately 75% of the time. Post-operative bowel obstruction is an immense complication for the patient to endure. There is an increase in healthcare costs for the patient due to additional hospitalizations, potential for further complications and the possible need for subsequent surgery to treat the bowel obstruction.

For many years now, the healthcare field has been trying to identify possible prophylactic treatments which could decrease the incidence of abdominal adhesions post-operatively. In 1996, a study was published which found that the use of Seprafilm Adhesion Barrier was largely effective in decreasing the incidence, extent and severity of abdominal adhesions after surgery. Seprafilm is a bioresorbable membrane that is made of sodium hyaluronate and carboxymethylcellulose. A thin sheet of film is placed over the organs in the abdominal cavity before the incision is closed. Seprafilm keeps the organs from sticking to each other and from forming scar tissue as the surgical site heals. The film does not need to be removed, as it conveniently becomes a gel, is absorbed by the body and is excreted naturally within 28 days.
The safety of this product has been established, and research has shown the benefit of using Seprafilm to reduce the incidence of adhesions. The purpose of this systematic review is to evaluate the available research and determine if Seprafilm reduces the incidence of small bowel obstruction after laparotomy, as it does with adhesions.

METHODS

An exhaustive search of available medical literature was completed using Medline-OVID, CINAHL and Evidence-Based Medicine Reviews Multifile. The keywords *Seprafilm*, *Hyaluronic Acid*, *Carboxymethylcellulose*, *biocompatible materials*, *artificial membranes*, *laparotomy*, *tissue adhesions* and *intestinal obstruction* were used as search terms. The literature search was limited to articles written in the English language and with humans as the subject. Studies that included pediatric subjects or gynecological surgeries were excluded. A complete review of references was additionally performed, and a cited reference search was completed in the Web of Science database. After assessing the potential full-text articles, it was determined that randomized controlled trials would be included in this systematic review and all other types of studies would be excluded. Studies were not excluded based on date of publication.

The GRADE criteria was used to assess the validity and the quality of each article. The studies were critically appraised and then placed into categories based on the strength of their evidence. The categories used were high, medium, low and very low and this compiled data can be found in Table I.

RESULTS
A total of three articles\textsuperscript{4, 5, 7} that met the inclusion and exclusion criteria mentioned above were appraised in this systematic review. Outcomes of small bowel obstruction (SBO) after open abdominal surgery were explored along with several additional outcomes specific to each study. One study by Hayashi et al\textsuperscript{4} researched participants who were being treated for gastric cancer and would be undergoing gastrectomy. The primary endpoint in this study was the incidence of bowel obstruction while secondary endpoints looked at morbidity and mortality both intraoperatively and postoperatively. The second study, conducted by van der Wal et al\textsuperscript{5}, presented the 10-year follow-up results from original research published in 2001 by Vrijland et al.\textsuperscript{6} This study monitored patients with sigmoid diverticulitis or obstructed rectosigmoid who would be having Hartmann’s procedure, a type of colorectal surgery. The third study by Fazio et al\textsuperscript{7} published delayed results from research started by Beck et al.\textsuperscript{8} This report focused on a large population undergoing intestinal resection. The research monitored the overall rate of SBO after surgery and the incidence of adhesive small bowel obstruction (ASBO), which required reoperation.

**Hayashi et al**

Hayashi et al\textsuperscript{4} was a randomized controlled trial which took place in Japan. Adult patients with gastric cancer who were scheduled to have gastrectomy were entered into the study between August 2003 and September 2006. A total of 150 patients were enrolled into the study. Subjects were excluded if they were older than 80 years of age, pregnant, had a past history of small bowel obstruction, ascites, metastasis or liver or renal dysfunction. Patients who ended up having laparoscopic surgery, a transverse incision or peritoneal carcinomatosis were also excluded. Written informed consent was
obtained and subjects were randomized into the Seprafilm treatment group or the control group using the minimization technique. Prognostic differences were present between groups with the amount of experience of the surgeons differing and the individual procedures being performed were not equal. The patients in the control group were also in surgery for a longer duration and the estimated blood loss was greater in the control group than in the treatment group. The Seprafilm group consisted of 70 participants and the control group totaled 74 people after six subjects were excluded. The patients were blinded to their assigned group and study evaluators were also blinded to whether or not Seprafilm had been used.4

Various surgeries which required an upper midline abdominal incision were performed. Those in the Seprafilm treatment group received two sheets of Seprafilm between the fascia of the abdomen and the surface of the small intestines before closure. It was not revealed in the operative report if Seprafilm had been used.4

Patients were followed post-operatively to measure the incidence of SBO, which was identified by clinical symptoms, physical examination, radiographs, or a combination of such. If small bowel dilatation was seen on abdominal x-ray or CT, patients received a nasoenteric tube for up to five days. Those who did not show signs of improvement underwent an additional surgery for post-operative SBO.

SBO occurred in four patients in the Seprafilm group and in seven patients in the control group. None of the SBO patients in the Seprafilm group required surgery but one patient in the control group required reoperation for SBO that did not resolve with the placement of the nasoenteric tube. A second patient in the control group had two separate episodes of SBO during follow-up, although it was managed non-surgically.
The results of this study were not statistically significant and confidence intervals were not discussed. The Seprafilm group experienced SBO at a rate of 5.7% while the control group incidence was 9.5% (P= 0.534). The cumulative incidence of SBO was lower in the Seprafilm group throughout the follow-up period, but was not found to be significant with a P-value of 0.378.4

van der Wal et al

The report by van der Wal et al5 discussed long-term results from a study which began ten years prior. The original single-blinded study, which was conducted between 1996 and 1998 and published by Vrijland et al,6 researched patients who were scheduled for the two-part Hartmann’s procedure for sigmoid diverticulitis or an obstructed rectosigmoid. There were eight hospitals in the Netherlands that participated and initially 71 patients enrolled, but only 42 could be evaluated. The patients were randomized into the Seprafilm treatment group or control group at the time of surgery. The treatment and control groups were not equal with respect to prognostic factors. There were patients in the treatment group who had the peritoneum sutured, while no suturing of the peritoneum occurred in the control group. Also, there were more patients in the Seprafilm group with adhesions present at the time of the first surgery than in the control group.6

Randomization was obtained by a computer-generated list and then sealed envelopes were opened in surgery to direct the surgeon to either use Seprafilm before closure or not.6 During the first surgery, Seprafilm was placed under the midline incision and in the pelvic cavity just before the laparotomy wound was closed. A mean of 1.9 units of Seprafilm was used under the incision and a mean of 1.3 units was used in the pelvis.5 The second-stage surgery was done laparoscopically and at this time, the midline
incision was visualized and the incidence and severity of developing adhesions was evaluated in all 42 subjects. The initial results of this study were published in 2002 and reported that there were significantly less severe adhesions present at the time of the laparoscopic procedure in the Seprafilm group when compared to the control group.\textsuperscript{5, 6}

The results of the van der Wal\textsuperscript{5} study, published in 2011, are more applicable to this systematic review as the primary goal was to determine the long-term effects of Seprafilm in reducing SBO and chronic abdominal pain after surgery. In order to follow-up with the 42 patients who completed the two-part Hartmann’s procedure nearly ten years earlier, researchers contacted the medical providers of the enrolled patients and asked them to complete a questionnaire about their patient and also indicate if the patient was deceased. Of the original 42 patients from the study, seven were lost to follow-up with 35 remaining for evaluation. Of the original sample size, 83\% were still available for follow-up, 16 in the Seprafilm treatment group and 19 in the control group. The patients that were willing and able to do so were also given some questionnaires to complete. The information from the questionnaires, along with reviewed hospital and medical records, provided data that were helpful in determining the number of post-operative SBO and abdominal pain complaints after surgery.\textsuperscript{5}

Hospital records showed that there were two readmissions for post-operative SBO in the control group during the follow-up period and none in the Seprafilm group. Although there were fewer incidences of SBO in the treatment group, this finding was not statistically significant. There were results of significance that were found when analyzing the patient questionnaires. The patients in the Seprafilm group reported significantly fewer abdominal complaints, defined as pain, nausea and obstipation, when
compared to the control group: “6 patients (35%) in the Seprafilm group experienced at least 1 episode of abdominal complaints of 3 months or longer, whereas 14 patients (78%) in the control group went through at least 1 episode of abdominal complaints of 3 months or longer (P = 0.018).”  

**Fazio et al**

Fazio et al\(^7\) was a prospective, randomized, controlled study that involved 83 surgeons from 22 centers throughout the United States, Europe and Canada. Patients entered into the study between June 1998 and November 2000 (for the complete details of this study’s methodology, the original article published by Beck et al\(^8\) was reviewed). Subjects who were eligible to participate were adults under 85 years of age who were going to have a surgery for colorectal resection. Patients having lysis of adhesions for SBO were initially included in the sample population, but were ultimately removed, evaluated in a separate group and not included in the results. Exclusion criteria included pregnancy, patients with active cancer or cancer within five years of enrollment in the study, those undergoing laparoscopic surgery, patients with abdominal trauma, intra-abdominal infection, history of severe allergy, history of pulmonary embolism or deep vein thrombosis within one year of surgery and patients with any other medical condition for which they were not expected to survive at least five years.\(^7,8\)

There were 1701 patients who met the eligibility criteria and were scheduled to have open resection of the small intestines, colon or rectum. Written consent was obtained from the patients at least 30 days prior to surgery. As surgery was completed, just before the abdomen was closed, the patients were randomized into the Seprafilm treatment group or the non-treatment control group. Randomization was performed “with
a table of random numbers…used to balance the distribution of patients scheduled for
two-stage surgical procedures across treatment groups and participating surgeons.”7

There were prognostic differences between groups as the control group consisted of
sicker patients with history of diabetes and deep vein thrombosis. There were also fewer
patients in the treatment group that received perioperative steroids when compared to the
control group. This was a patient-blinded study as the patients were not aware to which
group they were assigned, but the information was available to the surgeons and
researchers.7

The Seprafilm treatment group consisted of 840 patients and there were 861
patients in the control group. Surgeons who placed the Seprafilm before abdominal
closure applied three to ten sheets to the surfaces of abdominal organs and tissue that had
been manipulated and was thought to be adhesiogenic. Patients who had a future
procedure as a two-part surgery were given an additional sheet of Seprafilm at the time of
the subsequent surgery. The patients in the Seprafilm group received a mean of 4.4
sheets while those in the control group did not receive Seprafilm or a placebo.7, 8

The paper presented by Beck et al8 in 2003 was focused on the safety results of
Seprafilm. Fazio et al7 published the results for the incidence and severity of SBO in
2006 after an extended follow-up period with a mean of 3.5 years. To maintain the SBO
data, clinical personnel followed-up with the patients by telephone at set intervals.
Hospital and surgical records were also reviewed after hospitalization in order to evaluate
for potential bowel obstruction. Post-operative patients with suspected bowel
obstructions were classified into three categories:

Class Ia consisted of adhesive or nonadhesive bowel obstruction confirmed by
surgery or autopsy…Class Ib included bowel obstruction confirmed by contrast
enhanced CT scan or small bowel follow-through with oral contrast. Class II was defined by the presence of clinical symptoms (at least 3 of the following: nausea, vomiting, abdominal pain, abdominal distention, or the absence of stool or flatus in the previous 24 hours) in addition to documented suspected or confirmed bowel obstruction in the medical record and a plain x-ray or CT scan showing or failing to rule out bowel obstruction, with an onset of 11 days or more after initial surgery. This time interval was chosen to minimize the number of patients with prolonged ileus in this category.7

There were no significant differences between classes and the total number of patients in each of the three classes were similar in the treatment and control groups. Furthermore, Fazio et al7 found that there was no difference in the incidence of first post-operative bowel obstruction when all three categories were combined. The treatment and control groups each had an incidence of 12%. The number of SBO caused by adhesions that required surgery were lower than anticipated. However, during an analysis of the subgroups, statistically significant results were found in subgroup Ia showing that the Seprafilm treatment group suffered fewer SBO caused by adhesions. The Seprafilm group was affected at a rate of 1.8% while 3.4% of the control group experienced ASBO post-operatively. These results were statistically significant with a P-value of less than 0.05 and a confidence interval of 95% (see Table II). It was concluded that the use of Seprafilm provided a reduction in the risk of developing ASBO post-surgically and the Seprafilm was determined to be the only variable that predicted this outcome.7

DISCUSSION

Although prior research2 has proven that Seprafilm Adhesion Barrier reduces the incidence of post-operative abdominal adhesions, this systematic review did not reach the same conclusion when reviewing the outcome of post-operative small bowel obstructions. These three studies4, 5, 7 did not produce statistically significant results that
the use of Seprafilm decreases the incidence of SBO as it does adhesions. Still, the studies identified some benefits to using Seprafilm, some with statistically significant findings and others without (see Table II). Abdominal adhesions and subsequent SBO after laparotomy is a prevalent problem in medicine which often leads to additional hospitalizations, potential for more surgery, further complications and increased health care costs. Finding a safe and effective prophylactic treatment to decrease the incidence of SBO would be very useful and beneficial to many different types of surgical patients.

As suggested by van der Wal et al,\textsuperscript{5} there is benefit to performing a study with a long follow-up period when investigating the incidence of SBO after the use of a product like Seprafilm. This lengthy follow-up is important, because SBO are not always an immediate complication after surgery; they can take many years to become apparent. It would be of great utility to have a large, well-done, randomized controlled trial completed in the future with this specific long-term endpoint in order to better understand what benefit post-surgical patients can expect from Seprafilm.

The three studies\textsuperscript{4, 5, 7} that are analyzed in this systematic review were all randomized controlled trials, so by default they began as high quality evidence according to the GRADE criteria.\textsuperscript{9} Each study was composed of a Seprafilm treatment group and a control group. The process of randomizing was discussed in detail more in the van der Wal\textsuperscript{5} article than in the other two studies. Hayashi et al\textsuperscript{4} did not describe their randomization process by minimization, which suggests that it may have not been well randomized. Fazio et al\textsuperscript{7} stated that patients were randomized, but this did not happen until the end of surgery. The subjects remained in their assigned groups through the remainder of the trials and no crossover occurred between groups.
Additionally, all studies were blinded in some fashion. All articles\textsuperscript{4, 5, 7} stated that patients remained blinded to their assigned group, but the surgeons were not blinded. Only Hayashi et al\textsuperscript{4} additionally mentioned that the researchers, as well as the patients, were blinded.

Each article claimed that prognostic factors were equal between the treatment and control groups, but upon further analysis it seems that unequal prognostic factors with no statistical adjustment could have led to inconsistency among results. For example, Hayashi et al\textsuperscript{4} stated that characteristics between both groups were equal, but failed to mention that the experience of the surgeons differed and the procedures performed in each group were not equal. The patients in the control group appear to have been sicker, and therefore the treatment effect could have been underestimated when compared to the results of the control. Vrijland et al\textsuperscript{6} stated that groups were equal with respect to preoperative data, medical history and preoperative physical exam, although, based on prognostic data included in their tables, it seems that there were some differences. These differences may have distorted the results. There were patients in the treatment group who had the peritoneum sutured, while no suturing of the peritoneum occurred in the control group. Sutures are known to be a common cause for adhesion formation and this variable should have been included in their discussion of the results, as it could be an important factor leading to skewed results. Also, there were more patients in the Seprafilm group with adhesions present at the time of the first surgery than in the control group. Prognostic factors between the treatment and control groups in Fazio et al\textsuperscript{7} also appear to be unequal, although this was not discussed in their paper. The control group consisted of more patients with history of diabetes and history of deep vein thrombosis.
Fewer patients in the treatment group received perioperative steroids when compared to the control group. Had the treatment group received equal amounts of steroids during the procedure, it is possible that the incidence of SBO would have, in turn, produced statistically significant results.

One additional limitation in the van der Wal et al study was the use of subjective data through questionnaires to determine some of the long-term outcomes being researched in the article. It is difficult to compare this data to other studies that used more scientific methods for identifying abdominal pathology. It is evident that pain to one person may be described as simply an ache to someone else. Therefore, although their long-term follow-up period was helpful in some aspects, the way in which it was conducted made it susceptible to bias and some of their results cannot be used for comparison in the future.

Another example of inconsistency in each of these three studies is due to the differing number of sheets of Seprafilm used between studies and between patients within each study group. Surgeons in the Fazio et al study placed between three and ten sheets of Seprafilm for patients in the treatment group. Hayashi et al used a pre-determined number with all patients in the treatment group receiving two sheets of Seprafilm. Lastly, van der Wal et al did not discuss the exact number of Seprafilm sheets used in the treatment group, but reported the mean quantity of units applied under the midline incision as 1.9 sheets and 1.3 sheets in the pelvis. None of the studies gave an explanation or reasoning for the differing amounts of Seprafilm used, but it is possible that patients who received more Seprafilm healed better and with fewer complications.
Indirectness was not a problematic issue in the studies\(^4,5,7\) used for this systematic review. The questions being researched in these papers were the same as the outcomes and patient important outcomes were evaluated. Precision, however, was lacking. The sample size in the van der Wal\(^5\) study was very low with 42 patients total. The number of participants was large in Fazio et al\(^7\) with the study following 1701 people and there was an adequate sample size in Hayashi et al\(^4\) with 144 subjects. Only the Fazio et al\(^7\) and van der Wal et al\(^5\) studies included 95% confidence intervals; Hayashi et al\(^4\) did not discuss confidence intervals throughout their paper. None of the P-values were less than 0.05 for the primary outcomes in these studies, meaning that the results were not statistically significant. Table II summarizes which other P-values were significant among these three trials.\(^4,5,7\)

There was potential for publication bias from the Fazio et al\(^7\) study. This research was supported by a grant from the manufacturer of Seprafilm, the Genzyme Corporation. Additionally, a number of the same authors have overlapped and have helped to publish many of the articles currently available on Seprafilm and its utility in decreasing post-operative adhesions and SBO.

All studies\(^4,5,7\) used in this systematic review were critically appraised and the quality of evidence was assessed using the GRADE criteria.\(^9\) For all of the shortcomings discussed above pertaining to blinding, precision, inconsistency, lack of similar prognostic factors and publication bias, the quality of evidence of these articles was adjusted from high to either low or very low (see Table I). Results from future research would be very likely to have an important impact on the continued use of Seprafilm and the confidence with which surgeons recommend its use to their patients.
CONCLUSION

Although Sepraﬁlm has been proven to decrease the incidence and severity of abdominal adhesions, the research available at this time does not show the same decreased incidence for post-operative small bowel obstructions. Sepraﬁlm has shown other beneﬁts for the surgical patient such as decreased post-operative abdominal complaints and fewer re-operations required for adhesive small bowel obstructions. Additional large-scale, randomized controlled trials with similar prognostic factors between groups and long-term follow-up will be needed to further investigate the potential beneﬁt of using Sepraﬁlm for laparotomy patients to reduce the incidence of small bowel obstruction.
References


Table I: Characteristics of Reviewed Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Study type</th>
<th>Randomization</th>
<th>Blinding</th>
<th>Limitations</th>
<th>Publication Bias</th>
<th>Inconsistency</th>
<th>Similar prognostic factors</th>
<th>Precision (CI, P-values)</th>
<th>GRADE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hayashi et al⁴</td>
<td>RCT</td>
<td>Randomization using minimization technique</td>
<td>Patients and evaluators blinded</td>
<td>Minimization technique not described; Confounders underestimated the treatment effect</td>
<td>No</td>
<td>2 sheets</td>
<td>Seprafilm</td>
<td>No CI; no significant P-values</td>
<td>Very low</td>
</tr>
<tr>
<td>van der Wal et al⁵</td>
<td>RCT</td>
<td>Computer-generated randomization and sealed envelopes used</td>
<td>Patient blinded</td>
<td>Small sample size; lack of binding of evaluators; some outcomes measured subjectively</td>
<td>No</td>
<td>Mean 1.9 units</td>
<td>Seprafilm abdominal; 1.3 units pelvic</td>
<td>95% CI; P-value 0.018 for significantly lower chronic abdominal complaints in treatment group</td>
<td>Low</td>
</tr>
<tr>
<td>Fazio et al⁷</td>
<td>RCT</td>
<td>Randomization with random number assigned by table</td>
<td>Patient blinded</td>
<td>Lack of binding of researchers</td>
<td>Potentially</td>
<td>3-10 sheets</td>
<td>Seprafilm at 1st procedure and additional sheet at 2nd procedure</td>
<td>95% CI; P-value &lt; 0.05 incidence of reoperation for ASBO in treatment group</td>
<td>Low</td>
</tr>
</tbody>
</table>

● Downgraded 3 levels for lack of explanation of randomization, differences between prognostic factors and lack of confidence intervals and significant P-values.

○ Downgraded 2 levels for small sample size and differences between prognostic factors.

■ Downgraded 2 levels for potential publication bias and differences between prognostic factors.
### Table II: Summary of Findings

<table>
<thead>
<tr>
<th>Author</th>
<th># in treatment group</th>
<th># in control group</th>
<th>Length of follow-up</th>
<th># Lost to follow-up</th>
<th>Statistics</th>
<th>Significant P-values</th>
<th>1.</th>
<th>2.</th>
<th>Secondary results</th>
</tr>
</thead>
</table>
| Hayashi et al\(^4\)     | 70                   | 74                 | 28 months treatment group, 27 months control group | 0                  | RR: 0.6  
RRR: 0.4  
ARR: 0.038  
NNT: 27 | None                          | No                | Cumulative incidence of SBO was slightly lower in treatment group | No    | No   | Cumulative incidence of SBO was slightly lower in treatment group. |
| van der Wal et al\(^5\) | 16                   | 19                 | median 126 months treatment group, 128 months control group | 7 out of 42         | RR: 0  
RRR: 1  
ARR: 0.105  
NNT: 10 | P = 0.018 incidence of chronic abdominal complaints | No                | Significantly fewer chronic abdominal complaints in treatment group; no subjects in treatment group were readmitted due to SBO | No    | No   | Significantly fewer chronic abdominal complaints in treatment group; no subjects in treatment group were readmitted due to SBO. |
| Fazio et al\(^7\)       | 840                  | 861                | mean 3.5 years      | 0                  | RR: 0.53  
RRR: 0.47  
ARR: 0.016  
NNT: 63 | P < 0.05 incidence of reoperation for ASBO | No                | Significantly fewer patients in treatment group requiring reoperation for ASBO | No    | No   | Significantly fewer patients in treatment group requiring reoperation for ASBO. |

\(^\boxtimes\) according to P-values, results are not statistically significant  
\(\bullet\) statistics measured secondary outcome of incidence of ASBO. Primary outcome with RR= 1  
\(\#\) statistics measured overall incidence of SBO  
\(\checkmark\) statistics measured occurrence of readmission due to SBO