

Preventing Intra-Abdominal Adhesions With Polylactic Acid Film: An Animal Study

Shmuel Avital, M.D.,¹ Thomas J. Bollinger, M.D., M.P.H.,¹
James D. Wilkinson, M.D., M.P.H.,² Floriano Marchetti, M.D.,¹
Michael D. Hellinger, M.D.,¹ Laurence R. Sands, M.D.¹

¹ *Division of Colon and Rectal Surgery, Department of Surgery, University of Miami School of Medicine, Miami, Florida*

² *Department of Epidemiology and Public Health, University of Miami School of Medicine, Miami, Florida*

PURPOSE: The aim of this study was to evaluate the efficacy of an absorbable polylactic acid film (SurgiWrap™) in preventing postoperative intra-abdominal adhesions in an animal model. **METHODS:** Forty-four female Sprague-Dawley rats underwent laparotomy with subsequent cecal wall abrasion and abdominal wall injury. Rats were divided equally between untreated and treated groups. Treated rats had a polylactic acid film (SurgiWrap™) placed between the cecal and abdominal wall defects. Rats in the untreated group received no barrier material. The animals were killed on postoperative day 21. Two blinded observers, using predetermined criteria, graded the cecum-to-abdominal wall adhesions and estimated the percent of cecal surface area involved in the adhesion. The adhesions were classified as absent, moderate, or severe. **RESULTS:** Four rats died postoperatively. Of surviving rats, all of the rats in the untreated group had cecum-to-abdominal wall adhesions, whereas 42.1 percent of rats in the treated group had no adhesions between the cecum and the abdominal wall (two-tailed, $P = 0.001$). Altogether, 28.6 percent and 71.4 percent of untreated rats experienced moderate and severe adhesions, respectively, compared to 47.4 percent and 10.5 percent of treated rats (two-tailed, $P < 0.001$). **CONCLUSIONS:** Strategic placement of polylactic acid film during abdominal sur-

gery is associated with a significantly reduced rate and severity of postoperative intra-abdominal adhesions in this model. A technique for film placement is suggested. [Key words: Abdomen; Adhesions; Animal; Biocompatible materials; Disease models; Polylactic acid; Postoperative complications; Rats]

Intra-abdominal adhesions develop following abdominal surgery as part of the wound-healing process that occurs subsequent to damage to the visceral and parietal peritoneum.¹ Adhesions may cause major clinical problems, such as small bowel obstruction and female infertility, with associated morbidity and mortality. The presence of abdominal adhesions also makes further abdominal surgeries more complicated and less safe.²⁻⁴ Adhesions generally form seven to ten days postoperatively, making this time period crucial for preventing adhesion formation.⁵ Many efforts have been directed toward developing products that can prevent these adhesions; however, products currently available for postoperative abdominal adhesion prevention may be limited in their effectiveness and can be difficult to handle.

One approach to preventing postoperative intra-abdominal adhesions is to place a biocompatible absorbable material in the abdomen that serves as a physical barrier during the period during which postoperative adhesions form.⁶ Polymers of absorbable polylactic acid are currently used as implants in various orthopedic and neurosurgical procedures,⁷ but

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Correspondence to: Laurence R. Sands, M.D., DeWitt Daughtry Family Department of Surgery, Division of Colon & Rectal Surgery (310T), 1474 NW 12th Avenue, Room 3550, Miami, Florida 33136, e-mail: isands@med.miami.edu

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this material has not been studied for use in the abdomen. This study examines the efficacy of an absorbable polylactic acid film (SurgiWrapTM; Macropore Biosurgery, San Diego, CA) with regard to its ability to prevent and reduce the severity of postoperative intra-abdominal adhesions in a rat model.

MATERIALS AND METHODS

This study was performed with assistance from the Division of Veterinary Affairs at the University of Miami School of Medicine. The Animal Care and Use Committee of the University of Miami approved the methods described.

SurgiWrapTM is a 0.02 mm thick, absorbable, transparent film composed of a copolymer of lactic acid. It is flexible and can be sutured to tissues. It is housed in sterile packing and should be stored at a controlled room temperature of 59° to 86°F (15°–30°C).

Forty-four Sprague Dawley female rats weighing 180 to 220 g were used in this study. The rats were housed in an environment of alternating 12-hour light and dark cycles with food and water available *ad libitum*. Surgical procedures were performed under general anesthesia achieved with isoflurane at least three days after the rats were placed in this environment. All rats received one dose of subcutaneous ampicillin (50 mg/kg) prophylaxis before surgery. Postoperative analgesia was achieved with buprenorphine injection (0.01–0.05 mg/kg twice a day for 2 days).

Operative Technique

The rat cecal abrasion model is designed to create adhesions between the rat's cecum and abdominal wall.⁸ In this model, a midline laparotomy incision measuring 3 cm was created, and the cecum was identified. The ventral side of the cecum was then abraded with surgical gauze until an area of approximately 1.5 cm² was deserosalized as evidenced by punctate bleeding. Hemostasis was not attempted. Next, an injury of approximately 1.5 cm² was created with a scalpel in the right lateral internal abdominal wall. First, four superficial incisions were made in the parietal peritoneum in a selected area. Next, six perpendicular incisions were made. Finally, this entire area was scratched with the scalpel tip. Again, bleeding was observed, and hemostasis was not attempted.

This particular model was developed after an initial pilot study was conducted that involved 24 rats. In

that study, only the ventral surface of the rat cecum was abraded with gauze, as described above. Preliminary results demonstrated failure of the model to produce adhesions consistently, with cecum-to-abdominal wall adhesions being observed in only 25 percent of control rats. The expected rate of adhesiogenesis was 86 percent in other studies.⁸ In addition, the pilot study demonstrated that most of the polylactic acid film was absorbed by 21 days. However, small fragments of material remained in areas of the abdomen remote to the intervention, suggesting migration of the material. Therefore, it was decided that to better test SurgiWrap'sTM efficacy in preventing adhesions the model would have to be highly adhesiogenic, and the material would need to be fixed in place to prevent migration. Thus, the model was modified, and the rate of adhesiogenesis increased dramatically in control subjects.

The rats were randomized to untreated and treated groups as they were brought to the operating room. In animals assigned to the untreated group, the cecal and abdominal wall defects were approximated with a 3/0 Vicryl[®] (Ethicon Endo-Surgery, Inc., Cincinnati, Ohio, USA) suture placed in the cecal serosa and abdominal wall inferior to the respective injuries. Specific care was taken not to puncture the cecal wall with this suture. The purpose of the suture was to approximate the injuries and to fixate the floppy rat cecum. This suture remained intact throughout the entire study period. Treated rats received a 2.0 cm² SurgiWrapTM film, which was placed between the abrasions and incorporated into the suture. Following the procedure, the laparotomy incision was closed with a 3/0 Vicryl[®] running suture.

Evaluation

The animals were euthanized *via* carbon dioxide inhalation on postoperative day 21. The abdominal wall was then raised as a flap by incising the left upper and lower abdominal walls. Two board-certified surgeons, working concurrently, were blinded to the rats' study status and used predetermined criteria to assign an adhesion grade to the cecum-to-right lateral abdominal wall adhesions.⁸ The percentage of injured cecal surface area incorporated into the adhesion was also assessed. A third observer documented the surgeons' findings.

Grade and area of involvement parameters were combined, and adhesion severity was classified (Table 1). "Absent adhesions" were defined as a com-

Table 1.
Adhesion Severity Based on Adhesion Grade and Percent of Injured Cecal Surface Area

Severity	Grade	% Area Involved
Absent	0	0
Moderate	1	1–100
	2	1–100
	3	< 100
Severe	3	100

0 = no adhesions; 1 = thin, filamentous, easily separated adhesions; 2 = thick adhesions, difficult to dissect, do not tear organ when separated; 3 = thick adhesions, not dissectible, tears organ when separated.

plete lack of cecum-to-abdominal wall adhesions. “Moderate adhesions” included all Grade 1 and 2 adhesions as well as any Grade 3 adhesions involving less than 100 percent of the abraded wall of the cecum. “Severe adhesions” were defined as Grade 3 adhesions that involved 100 percent of the abraded wall of the cecum (Fig. 1).

Statistical Analysis

The population for analysis included only subjects alive for follow-up evaluation. Data were plotted, and frequency distributions were calculated. Ordinal variables were described by median and range. Categorical variables were described by frequencies. Group means were compared using Student’s *t*-test for two independent samples. Binomial variables were compared using chi-squared analysis with Fisher’s exact test for small expected cell values. Binomial and ordinal variables were analyzed for trend using the Wilcoxon rank-sum test. All tests were two-tailed. Significance level was set at $\alpha = 0.05$. All analyses were performed using an SPSS (v. 11) statistical software package (SPSS, Chicago, IL).

RESULTS

Of the 44 study animals, 22 (50 percent) were randomized to the treatment condition, with the remaining animals randomized to the control condition. Four animals died before postoperative day 21. The only rat to sustain an iatrogenic cecal perforation and repair survived the postoperative period. Mortality for the treatment group was 13.6 percent (three animals) and for the control group 4.5 percent (one animal). The difference was not statistically significant (Fisher’s exact test, two-tailed, $P = 0.357$). Observers involved

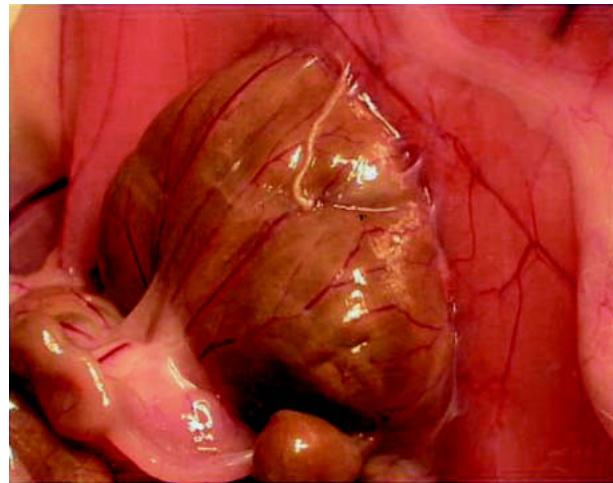


Figure 1. Grade 3 adhesion between the cecum and the abdominal wall in an untreated rat.

Table 2.
Frequency and Classification of Cecum-to-Abdominal Wall Adhesions in the Two Treatment Groups

Treatment Group	No.	%
Control		
Rats without adhesions	0	0
Rats with adhesions		
Moderate	6	28.6
Severe	15	71.4
Total	21	100.0
Treated		
Rats without adhesions*	8	42.1
Rats with adhesions		
Moderate	9	47.7
Severe	2	10.5
Total	11	57.9

in the study did not determine the causes of death; rather, deaths were reported to the observers by the veterinary staff. There were reports that some animals had chewed on their incision line sutures, causing evisceration. The veterinary staff made no reports of documented sepsis.

As shown in Table 2, 57.9 percent of treated rats had adhesions between the cecum and the abdominal wall, which was significantly less than the proportion found in the untreated rats (100 percent; Fisher’s exact test, $P = 0.001$).

Trend analysis indicated that untreated rats were significantly more likely to have more severe cecum-to-abdominal wall adhesions than the treatment group (Wilcoxon rank-sum test, $P < 0.001$). Altogether, 28.6 percent of untreated rats and 47.4 percent of treated rats displayed moderate adhesions between the cecum and the abdominal wall, whereas 71.4 per-

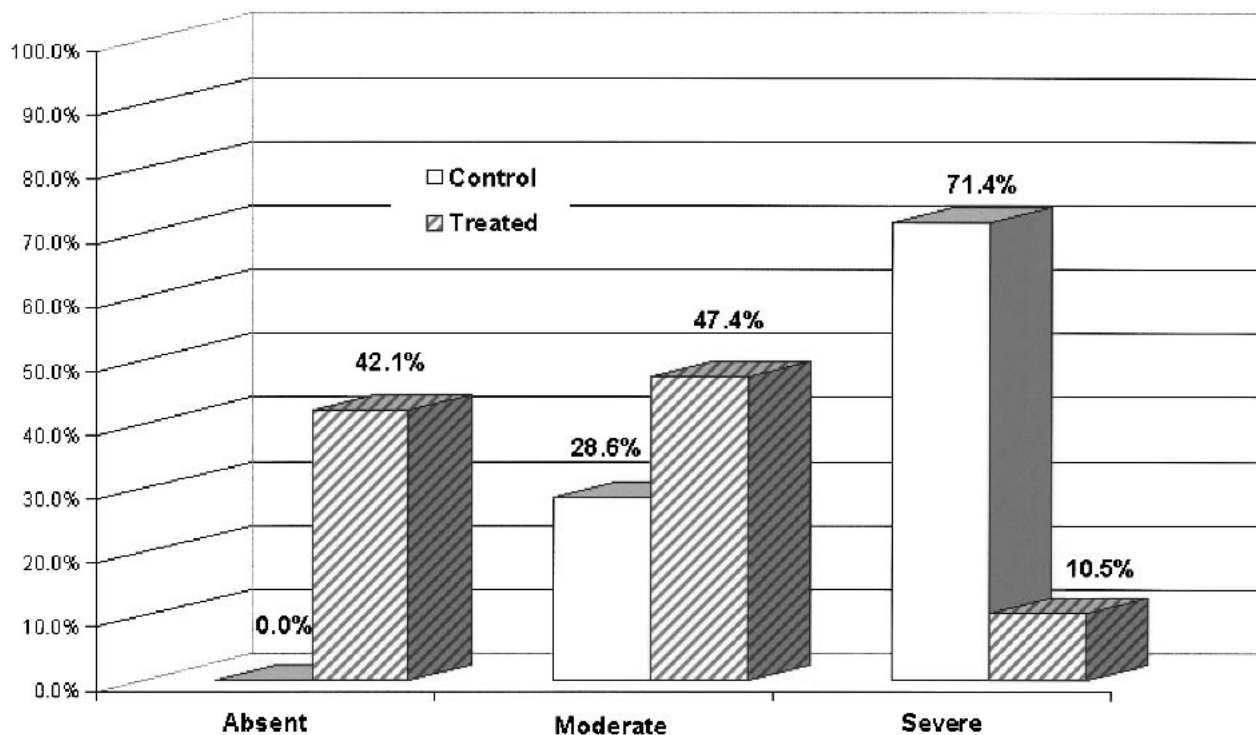


Figure 2. Severity of postoperative intra-abdominal adhesions in two groups of rats.

cent of rats in the untreated group had severe adhesions compared to 10.5 percent of treated rats (Table 2, Fig. 2).

DISCUSSION

Postoperative adhesions in the abdominal cavity are a major source of morbidity that may cause bowel obstruction and complicate further operations with increased surgical time and increased risk for organ injury during adhesion dissection.^{2,3,9}

Several methods have been studied for adhesion prevention, including the use of anti-inflammatory agents, antioxidants, anticoagulants, and fibrinolytics¹⁰⁻¹²; however, absorbable physical barriers are the most commonly used method employed in current surgical practice. These barriers may reduce adhesion formation by limiting tissue apposition during the time following surgery when adhesions usually form.¹³

Absorbable polylactic acid is composed of a copolymer of two forms of lactic acid (L-lactide and D,L-lactide). By varying ratios of these copolymers during production, the manufacturer can manipulate the strength and degradation characteristics of the material.¹⁴ The polymer is degraded in the body by hydrolysis followed by liver metabolism.¹⁴ These polymers,

widely used in cranial and orthopedic surgery as absorbable plates, screws, tacks, and sheets, produce minimal tissue reaction.^{15,16} In a neurosurgical model, polylactic acid film was demonstrated to create a dissection plane and a reduction in tissue adherent to the dura.¹⁷ Although it is not known how polylactic acid film and its degradation products affect the extent of coagulation, epithelialization, and fibrinolysis that is central to adhesion formation, the material's efficacy appears to be achieved by preventing the apposition of two damaged surfaces during the critical time of adhesion formation.¹⁸

Unique qualities of SurgiWrapTM that make it amenable for use in the abdomen are derived from its physical characteristics. It is a flexible material that does not readily fold or crumple. Also, it can be handled easily with wet gloves. Consequently, the material does not readily adhere to the abdominal wall or to organs. Fortunately, the material is relatively strong and can be fixed with a suture without causing damage to its structure.

Use of polylactic acid film is associated with significantly reduced rates of adhesion formation and severity in this model. However, the fact remains that the material could have rotated around this single point of attachment or could have broken free, limiting the material's efficacy at the site of placement.

CONCLUSIONS

SurgiWrap™ is a promising new material that should be studied for use in humans to prevent intra-abdominal adhesions. Use of the film in this model was associated with a significant 42.1 percent reduction in postoperative intra-abdominal adhesions and a significant reduction in adhesion severity. It is noteworthy that these findings were achieved in a model that created adhesions in 100 percent of the untreated group rats. Perhaps further investigation, in which the material is fixed at more than one point of attachment, could demonstrate even greater efficacy in preventing severe adhesions.

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