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Effect of prosthetic material on adhesion formation after laparoscopic ventral hernia repair in a porcine model

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Abstract Intraperitoneal placement of prosthetic mesh causes adhesion formation after laparoscopic incisional hernia repair. A prosthesis that prevents or reduces adhesion formation is desirable. In this study, 21 pigs were randomized to receive laparoscopic placement of plain polypropylene mesh (PPM), expanded polytetrafluoroethylene (ePTFE), or polypropylene coated on one side with a bioresorbable adhesion barrier (PPM/HA/CMC). The animals were sacrificed after 28 days and evaluated for adhesion formation. Mean area of adhesion formation was 14% (SD±15) in the PPM/HA/CMC group, 40% (SD±17) in the PPM group, and 41% (SD±39) in the ePTFE group. The difference between PPM/HA/CMC and PPM was significant ($P=0.013$). A new visceral layer of mesothelium was present in seven out of seven PPM/HA/CMC cases, six out of seven PPM cases, and two out of seven ePTFE cases. Thus, laparoscopic placement of PPM/HA/CMC reduces adhesion formation compared to other mesh types used for laparoscopic ventral hernia repairs.

Keywords Laparoscopy · Ventral hernia repair · Adhesions · ePTFE · Spermesh

Introduction

Approximately 115,000 incisional hernia repairs are performed in the United States every year [1]. The

recurrence rate after a primary suture repair without mesh has been estimated at approximately 30–50% [2, 3, 4, 5]. Open mesh repair drops the recurrence rate to 15–25% in most comparative series [6, 7, 8, 9]. Indeed, in the only published randomized clinical trial comparing open suture and open mesh repair of incisional hernias, the recurrence rate fell from 46% for suture repair to 23% for mesh repair [10]. The largest reported series of laparoscopic incisional hernia repairs revealed a recurrence rate of 3.4% [11]. This is lower than in most reports after conventional repairs and would translate into only about 4,000 recurrent hernias per year.

Other comparative studies have also indicated that laparoscopic incisional hernia repair has fewer recurrences than open mesh techniques [12, 13, 14], and likely because of this, the technique is gaining popularity. Additionally, this technique avoids extensive abdominal wall dissection that may contribute to the decreased incidence of wound infections [12, 13, 14, 15, 16, 17]. It also appears to confer some of the other benefits of laparoscopic surgery, such as a quicker recovery [12, 13, 14, 15, 16, 17].

Different types of polypropylene mesh have been evaluated for use in inguinal herniorrhaphy [18]. There, mesh shrinkage and migration, as well as patient discomfort and neuralgia, complicate mesh repair. For ventral hernias, adhesion formation to underlying viscera adds to morbidity of the procedure. Current techniques require that the mesh be placed in an intraperitoneal position. The mesh, along with the tacks used to hold the mesh in place, acts as a foreign body and can incite adhesion formation. This type of response is useful, if not essential, at the interface between the abdominal wall and the mesh. There, it holds the mesh in place, preventing migration and recurrence. Placement of polypropylene mesh (PPM) results in excellent tissue ingrowth at this interface. However, PPM also produces severe bowel adhesions that can lead to obstruction, erosion, and fistulization [19, 20, 21, 22, 23, 24, 25, 26]. Also, these dense adhesions make

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reoperation difficult in those patients who require subsequent abdominal surgery.

Hyaluronic acid and carboxymethylcellulose together (HA/CMC, Seprafilm, Genzyme Corp., Cambridge, Mass. USA) have been shown to decrease adhesion formation after abdominal surgery [27]. A product consisting of polypropylene mesh coated on one side with a bioresorbable adhesion barrier (PPM/HA/CMC, Sepramesh Biosurgical Composite, Genzyme Corp., Cambridge, Mass. USA) was designed to combine the tissue incorporation of PPM with the anti-adhesion effects of HA/CMC. The efficacy of HA/CMC covering PPM, or fused together as PPM/HA/CMC, has been shown in animal models when placed at the time of open surgery [28, 29]. This study evaluates the efficacy of PPM/HA/CMC when placed laparoscopically in the porcine model. Additionally, it compares adhesion formation after the placement of three types of mesh, including the most popular material used for laparoscopic incisional and ventral hernia repairs, expanded polytetrafluoroethylene (ePTFE, DualMesh, W.L. Gore, Flagstaff, Ariz. USA).

Materials and methods

Twenty-one female Yorkshire pigs were randomized to one of three groups for laparoscopic intra-abdominal placement of mesh: one group received PPM, another group received PPM/HA/CMC, and the third group received ePTFE. The veterinary staff picked the animal at random to undergo the procedure. The mesh selection was made at random by the research nurse coordinator.

Twenty-eight days after the placement of the mesh, the animals were euthanized with an intravenous injection of barbiturate solution (120 mg/kg). Animals were taken to the necropsy suite for post mortem examination of the site of mesh placement. The segment of abdominal wall with the attached mesh was examined for the presence of adhesions, hernias, collections, and defects in the mesh. Adhesions were evaluated for the area of mesh involved and which organs were adherent. Images of the abdominal wall in situ and of the excised abdominal wall with adherent tissues were captured with a digital camera (Sony, DCR 100). The surface area of the prosthesis covered by adhesions was calculated using image-analysis software (ImageTool, Version 2.00, UTHSCSA, San Antonio, Tex. USA). The surface area data was compared between groups using one-way ANOVA with Bonferroni post-test, as well as non-paired two-tailed t tests. In all cases, a *P* value <0.05 was considered statistically significant.

Portions of the mesh, both with and without adhesions, were excised and preserved in 10% formalin and subsequently reviewed histologically by a veterinary pathologist who was blinded as to the type of mesh used at the time of surgery.

Operative technique

Pigs were kept without food for 12 h prior to the procedure. After selection by the veterinary staff, the animals were sedated with an intramuscular dose of Telazol (6.6–10 mg/kg) and given intramuscular Atropine (0.02–0.05 mg/kg) in preparation for induction. The animals were intubated by the veterinary staff and general anesthesia maintained with isoflurane and buprenorphine. Animals were monitored with pulse oximetry and ECG by the veterinary staff. Prior to incision, each animal received cefazolin 1 g i.v. The abdomen was prepped and draped in a sterile fashion. A 10-cm midline incision was made caudally from a point 15 cm caudal to

the xyphoid process. The peritoneum was excised from the overlying fascia to create an 8×6-cm defect in the peritoneum. A portion of the small bowel was delivered through the wound, and 80 cm of small bowel was mechanically abraded on each side with 15 strokes of a surgeon's scrub brush. This caused the serosa to become hyperemic with punctate areas of bleeding, so as to induce adhesion formation. The small intestine was then returned to the abdominal cavity. A 12-mm trocar was placed under direct vision in the right upper quadrant. The midline fascia was closed with a running 0 polypropylene suture, and the skin was closed with a running 4-0 absorbable synthetic polyester suture (Biosyn, United States Surgical Corporation, Norwalk, Conn. USA). A CO₂ pneumoperitoneum was established by insufflating through the trocar. The laparoscope was inserted, and three additional 5-mm ports were placed. The mesh was centered over the previously marked center of the peritoneal defect and cut in the shape of an oval measuring 10×15 cm. Six nonabsorbable sutures of 0 polypropylene were placed equidistant around the perimeter of the mesh, approximately 6 cm apart. The mesh was immersed in saline for approximately 5 seconds and then rolled with the HA/CMC layer on the inside of the roll. It was delivered into the abdominal cavity through the 12-mm trocar. A suture passer (Endoclose, United States Surgical Corporation, Norwalk, Conn. USA) was passed through a 2-mm incision in the skin, and, using laparoscopic visualization, both ends of each suture were pulled out of the abdominal cavity and tied down to the fascia through the small incision in the skin. This secured the mesh to the abdominal wall. The edge of the mesh between the sutures was fixed to the abdominal wall using metal tacks (Protacker, United States Surgical Corporation, Norwalk, Conn. USA) that were placed through the mesh into the abdominal wall at 1-cm intervals around the periphery of the mesh. The pneumoperitoneum was desufflated and the trocars removed. The fascia at the 12-mm trocar incision was closed with 2-0 absorbable, coated, braided Lactomer suture (Polysorb, United States Surgical Corporation, Norwalk, Conn. USA). The skin at each incision was closed with subcuticular stitches of 4-0 absorbable synthetic polyester suture. The 2-mm incisions were closed with sterile adhesive strips. The animals were allowed to recover in a warm area away from the other animals for 8 h. Animals were given additional buprenorphine 0.008 mg/kg as needed for signs of pain.

Results

No animals were excluded from the study. All pigs survived for the full 28 days of the study. There were no infections and no hernias in any group. There was only one complication, a hematoma between the mesh and abdominal wall in one pig in the ePTFE group.

Average mesh size was 121 cm². Two pigs in the ePTFE group had no adhesions, while one pig in the PPM/HA/CMC group had no adhesions (Fig. 1). All pigs with plain PPM had adhesions. None of the pigs in the PPM/HA/CMC group had more than 50% of the mesh covered with adhesions, yet four pigs with ePTFE and one pig with PPM had more than 50% of the mesh covered with adhesions.

The adherent viscera were cut away from the mesh at necropsy and digital photographs were taken to use for image analysis (Fig. 2). Mean area of adhesions covering the mesh was 14% (SD ± 14) in the PPM/HA/CMC group, 40% (SD ± 17) in the PPM group, and 41% (SD ± 39) in the ePTFE group (Fig. 3). The difference between PPM/HA/CMC group and the PPM group was statistically significant (*P* = 0.01). The

Fig. 1 In situ abdominal wall from each subject at necropsy grouped by type of mesh placed intra-abdominally. Each group is organized by increasing percentage of mesh covered by adhesions

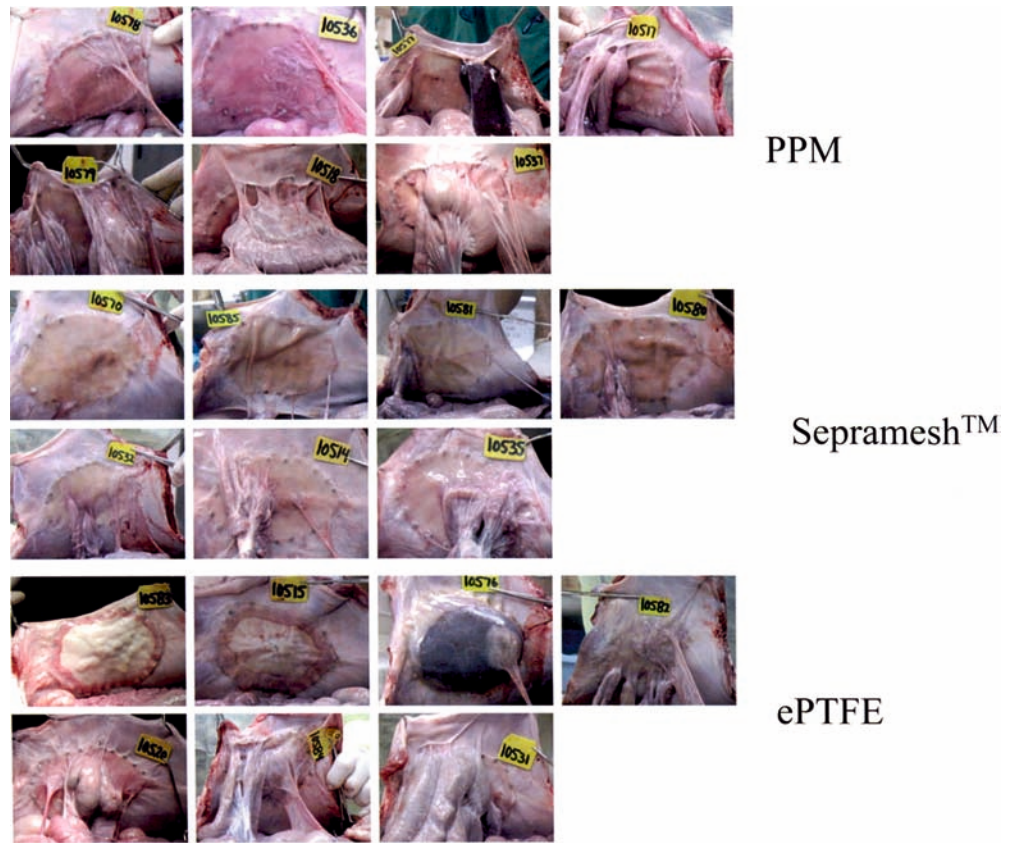
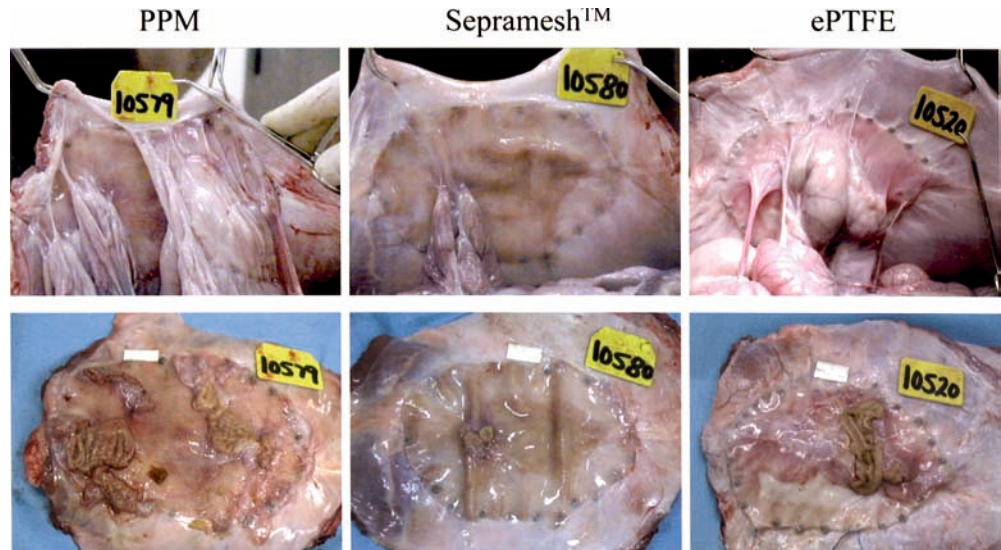


Fig. 2 Representative specimens from each group of mesh are shown. The in situ abdominal wall is shown in comparison to the cut section from which the area of adhesions was calculated for each subject



difference between PPM/HA/CMC and ePTFE approached but did not reach statistical significance ($P=0.13$). Intestinal adhesions (small bowel and colon) covered 8.6% of the mesh in the PPM/HA/CMC group, 9.6% in the ePTFE group, and 17.0% in the PPM group. There were no statistically significant differences between the intestinal adhesions between groups. Only one pig overall had an adherent solid organ. This pig was in the PPM group and had 24% of

the mesh covered with adherent spleen. All other adhesions to the mesh in each group were omentum.

Histology of the abdominal wall with attached mesh revealed a marked inflammatory response at the mesh-abdominal wall interface in three pigs from the ePTFE group and one pig in the PPM/HA/CMC group. Additional histologic examination revealed a layer of cells overlying the mesh (similar to a mesothelial layer) present in all pigs in the PPM/HA/CMC group, six of

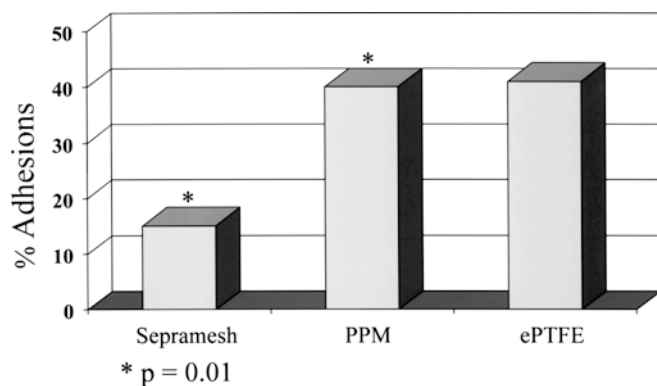


Fig. 3 Percent of mesh covered with adhesions in each group. There was a statistically significant difference in adhesion formation between PPM/HA/CMC and PPM ($P=0.01$). PPM = polypropylene mesh; PPM/HA/CMC = polypropylene mesh coated on one side with a bioresorbable adhesion barrier

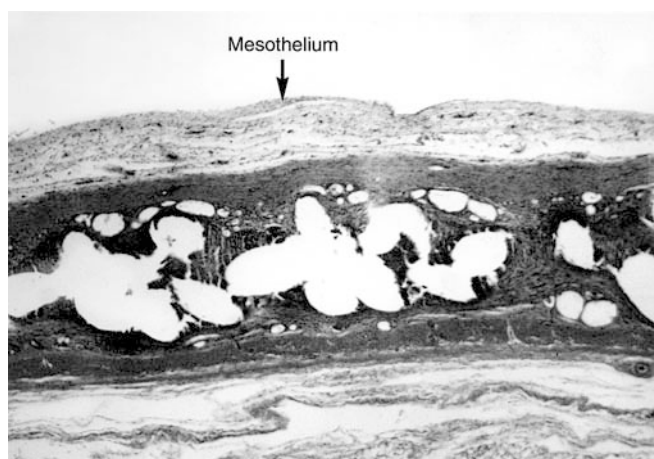


Fig. 4 Photomicrograph stained with hematoxylin and eosin of a section of the abdominal wall from a pig at necropsy after PPM/HA/CMC placement. The *empty spaces* represent polypropylene, surrounded by a matrix of proliferating fibrous connective tissue, blood vessels, and inflammatory cell infiltrate. The *arrow* depicts a layer of collagen and fibroblasts overlying this matrix representing the new mesothelial lining. PPM/HA/CMC = polypropylene mesh coated on one side with a bioresorbable adhesion barrier

the seven pigs in the PPM group, and two of the pigs in the ePTFE group (Fig. 4). The two pigs in the ePTFE group with the mesothelial layer were the two pigs with no adhesions to the mesh.

Discussion

A combination of chemically modified sodium hyaluronate and carboxymethylcellulose (HA/CMC) has been clinically proven to reduce adhesion formation following abdominal surgery [27]. HA/CMC reduces adhesion formation to PPM in a rat model for open incisional hernia repair [28]. A recent study by Kramer et al. has shown adhesion prevention in an animal model if HA/CMC is placed in proximity to PPM during laparoscopic

placement of the mesh on the anterior abdominal wall [30]. However, no studies to date have shown the effectiveness of PPM/HA/CMC when placed laparoscopically.

One of the concerns about placing PPM/HA/CMC laparoscopically was that the HA/CMC might separate from the PPM. To evaluate the effect of rolling PPM/HA/CMC and passing it through a trocar, we felt that the size of the mesh and the size of the trocars should be similar to those used for human surgery. We chose the porcine model because the peritoneal cavity of a pig is similar in size to that of most human patients. We found that we could effectively roll PPM/HA/CMC and pass it through a 12-mm port without separating the HA/CMC from the PPM. Using proper surgical technique, the PPM/HA/CMC will remain intact.

Although HA/CMC is known for its difficult handling, it is easier to apply in association with PPM, as in this PPM/HA/CMC mesh. In the clinical setting, pieces of mesh larger than used in this study may be needed. If any of the bioresorbable coating should become separated from the PPM, HA/CMC may be placed laparoscopically to cover the denuded section [30].

The decision to use a laparotomy was made to create the most adhesiogenic model. In preliminary studies, abrasion of the bowel laparoscopically did not always result in significant adhesion formation in the pig, even when using PPM. For that reason, a laparotomy with removal of some of the peritoneum was used to incite adhesions. The laparotomy was closed prior to placing the mesh laparoscopically.

In this study, laparoscopic placement of PPM/HA/CMC resulted in statistically significantly fewer adhesions than laparoscopic placement of PPM. Although the laparoscopic placement of PPM/HA/CMC did not result in a statistically significant reduction in adhesions compared with ePTFE, there was a trend towards fewer adhesions here as well. The choice of number of animals was based on an estimated 25% variability in adhesion formation in the ePTFE group; however, the variability in the ePTFE group was higher than that. Because of this increased variability in adhesion formation in the ePTFE group, more animals would be needed in each group to show a statistically significant difference. The PPM/HA/CMC seemed to inhibit adhesion formation more uniformly than ePTFE.

As stated previously, bowel adhesions to mesh may induce bowel obstruction, erosion, and fistulization. In this study, we documented a reduction in bowel adhesions to PPM/HA/CMC when compared to PPM, although the difference was not statistically significant. The omentum formed most of the adhesions, just as we typically see in human patients. There were relatively fewer adhesions to the metal tacks on the periphery of the mesh in the PPM/HA/CMC group than there were to the tacks in the other two groups. The HA/CMC coating forms a gelatinous substance shortly after intra-abdominal placement, and we hypothesize that it may

migrate over the metal tacks and prevent adhesion formation to the tacks as well.

Microscopic examination of the abdominal wall revealed a mesothelial-like lining in all the pigs in the PPM/HA/CMC group. This mesothelial layer was not unique to the pigs in the PPM/HA/CMC group. It was also seen in most of the pigs in the PPM group, but only in two of seven in the ePTFE group. These two cases in the ePTFE group had no adhesions to the mesh. This suggests that this remesothelialization of the mesh may be an important component of adhesion prevention.

Only the extent of adhesions, based on percent of surface area, was evaluated in this study, and the study was designed with this outcome in mind. Since typical adhesion-severity grading scales use ordinal data for comparison, evaluation of these specimens would likely not show a significant difference between these groups with relatively small subject numbers. Therefore, the severity of the adhesions was not evaluated.

We conclude that PPM/HA/CMC reduces adhesion formation to the mesh in a laparoscopic incisional hernia repair model. It can be placed safely and easily with conventional laparoscopic techniques.

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