Successful Repair of Esophageal Injury Using an Elastin Based Biomaterial Patch

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An esophageal injury with significant tissue loss is very difficult to repair. We conducted an *in vivo* study to test our elastin based acellular biomaterial patch to repair such defect. The patch was made from porcine aorta, by decellularization and sterilization. Collagen fibers were preserved to retain mechanical strength and enhance cellular in-growth. Ten domestic pigs underwent right thoracotomy. A 2 cm circular defect was made on the distal esophagus, excising half its circumference, and was repaired using the biomaterial patch and sutures. Soon after the procedure, the animals resumed oral feeding. They were followed for clinical status, weight gain, barium studies, and endoscopic studies, and were killed after 6 weeks to 4 months. All ten animals survived long term, with a procedure success rate of 100% (10 of 10). With the exception of one pneumothorax, no complications occurred, and all animals resumed oral feeding and gained weight. Endoscopic studies showed mucosal coverage by 6 weeks, with minimal stricture at the repair site. Excised specimens showed complete mucosal coverage with regeneration of all three layers. Our biomaterial patch can be used safely and reliably for repair of esophageal injury with significant tissue loss when repaired immediately as in our experiment. *ASAIO Journal* 2001; 47:342–345.

Repair of major injury to the intrathoracic esophagus with significant tissue loss is a surgical challenge and is associated with significant morbidity and mortality.[1] A small injury, detected early, can be treated by primary closure, usually reinforced with a vascularized flap, such as parietal pleura, pericardium, or the fundus of the stomach.[1–3] Segmental resection and primary end-to-end anastomosis is quite difficult if not impossible and requires extensive dissection to mobilize the esophagus. Tension on the suture line will create less than optimal results, with possible leak and stricture formation. Most of the external injuries are caused by penetrating trauma, such as gunshot wounds, and are almost always associated with injuries to the other intrathoracic organs, such as lungs, heart, and great vessels.[1,4–6] Because of these associated injuries, the patients are very often unstable; therefore, quick, easy, and reliable treatment methods are needed. Even when the injury is recognized early, usually during chest exploration for other associated injuries, diffuse hemorrhage, acute coagulation necrosis, or acute inflammation in the adjacent wall of the esophagus may make it necessary to perform extensive debridement, which will result in a larger defect in the esophageal wall.[1] Primary repair of such an enlarged defect is difficult and may result in stricture, leak, and/or fistula. Diversion and esophageal exclusion have been used for delayed exploration, or when the primary repair was not believed to be feasible. This approach will predispose the patient to gastrostomy tube feeding or hyperalimentation, with later reconstruction of the esophagus using stomach, intestine, or colon.[1,7–9]

If we could develop a technique that can easily, quickly, and reliably close an esophageal injury without compromising the lumen, we can expect much faster recovery with fewer complications and less morbidity and mortality, without need for further reconstruction.

The elastin based heterograft we have developed at the Oregon Medical Laser Center can be used to repair such a defect in the esophagus without compromising the lumen, need for other bowel anastomosis, or extensive resection. In our laboratory, this material was shown to be biologically inert, inducing minimal immunologic response, and to be resistant to infection and hydrochloric acid. Our previous study with a composite heterograft of a pure elastin patch with small intestinal submucosa for a large duodenal wall defect showed reliability of this material, with a success rate of 91.7% while the patch was exposed to active digestive enzymes *in vivo*.[10] We were very encouraged by these results and decided to proceed with application of the elastin based material to repair esophageal injury.

Methods

Elastin Based Acellular Patch

The patch was made from porcine aorta. After harvesting, it was preserved in 80% ethanol for 72 hours, then washed with pH 8.0 Tris buffer for 30 minutes at room temperature on a stirrer plate. The vessel was then immersed in a 1% solution of octylphenoxypolyethoxyethanol (Triton X-100; Sigma) for 4 hours at room temperature with stirring. The solution was changed every hour, and the vessel was rinsed in saline. It was then immersed in DNase at 37°C for 2 hours on a stirrer plate and then rinsed in saline. The vessel was immersed in 1% Triton X-100 solution for 24 hours at 4° centigrade, then in saline three to five times. The patch was packaged and sterilized using gamma irradiation.

Surgical method

Ten domestic pigs, each weighing 30 to 53 lb, were used. They were anesthetized, intubated, and under sterile technique, underwent right thoracotomy. The mediastinal pleura was opened to expose the distal esophagus. A circular defect 2

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Submitted for consideration July 2000; accepted for publication in revised form December 2000.

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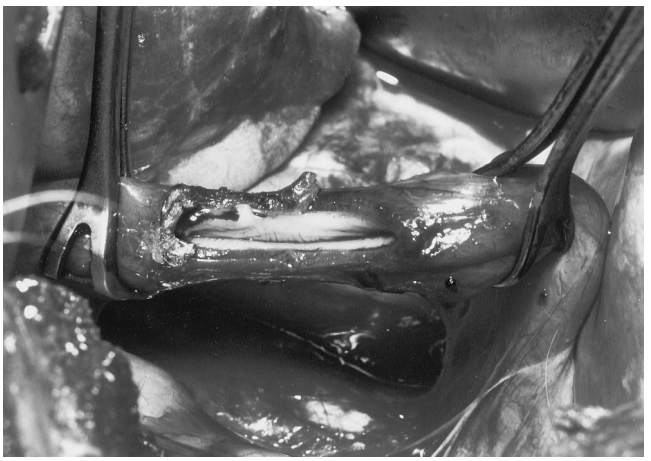

Figure 1. A 2 cm defect was made in the distal esophagus, excising half the circumference.

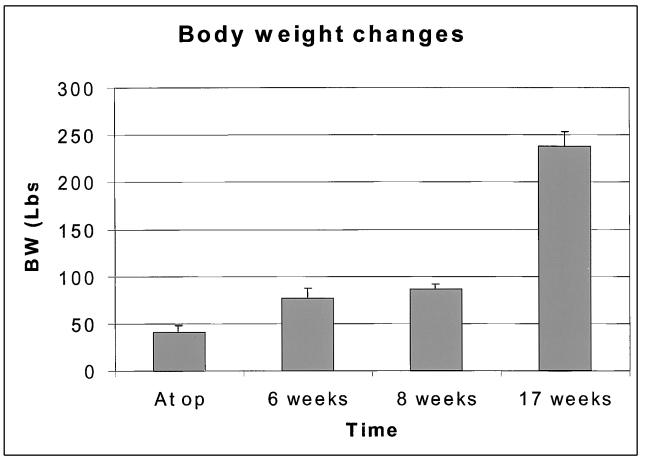

Figure 3. Body weight change after repair. All animals gained weight at a rate that follows the normal growth curve.

cm in diameter was made on the distal esophagus, about 10 cm proximal to the diaphragm, excising half its circumference (**Figure 1**). A circular elastin based patch with a diameter of 2–2.5 cm was sewn in to seal the esophageal defect using 3-0 monofilament absorbable running sutures (**Figure 2**). The mediastinal pleura was closed to cover the repaired site when possible, the thoracotomy closed, while air in the chest was evacuated with a rubber catheter, that was removed at completion of the thoracotomy closure. No chest tube or drain was left in place. Anesthesia was withdrawn, and the animals were extubated and allowed to resume regular feeding soon after the surgery, typically within the first hour after extubation. They were followed by clinical observation, weight gain, endoscopic studies, and barium swallow studies. Six weeks to 4 months after surgery, the animals were killed to obtain the graft specimens, which were submitted for histologic examination. No antibiotics or antacids were given after surgery. Animal experiments were conducted strictly following the guidelines set by the Institutional Animal Care and Use Committee of the Oregon Health Sciences University.

Figure 2. Repair with the elastin based acellular biomaterial patch.

Results

All 10 animals survived long-term, with a survival rate of 100% (10 of 10). One animal developed respiratory failure soon after extubation due to a tension pneumothorax, which was recognized promptly and treated appropriately. The pigs showed significant weight gain every month (t-test, $p < 0.05$), following the normal growth curve of domestic pigs (**Figure 3**).

Two animals were killed at 6 weeks, two at 7 weeks, four at 8 weeks, and two at 4 months. Endoscopic studies were performed at the time of surgery, and 3, 4, and 5 weeks after surgery. To avoid traumatic injury to the repair site, we elected not to perform endoscopic studies for the first 3 weeks. The repair site was easily identified in the distal esophagus and easily inflatable by injecting air, allowing the endoscope to pass through the area of repair, suggesting no mechanical obstruction (**Figure 4**).

Upper gastrointestinal contrast studies were also performed to evaluate the function of the esophagus. The repair site showed flat stiffening, but no significant stricture or obstruction to the passage of contrast (**Figure 5**).

Gross specimens from the sacrificed animals showed complete healing of the repair site with mucosal coverage as early as 3 weeks (**Figure 6**). Histologic study of the specimens after 7 weeks showed a completely healed esophageal wall with mucosal regeneration in the center (**Figure 7**). Submucosal tissue had also regenerated, with incomplete regeneration of the muscular layer. Nerves were also found in the center of the regenerated tissue, and there were fragments of elastin fibers identified in the specimen (**Figure 8**).

Discussion

Major esophageal injury with significant tissue loss is a serious injury that is very difficult to manage.[1] It requires innovative surgical techniques and has high morbidity. In treating a trauma victim with penetrating injury to the esophagus, which most likely has coexisting serious associated injuries to the heart, the great vessels, and the lungs, the chances of survival are expected to improve when a more definitive and reliable repair, in a short amount of time, can be done.

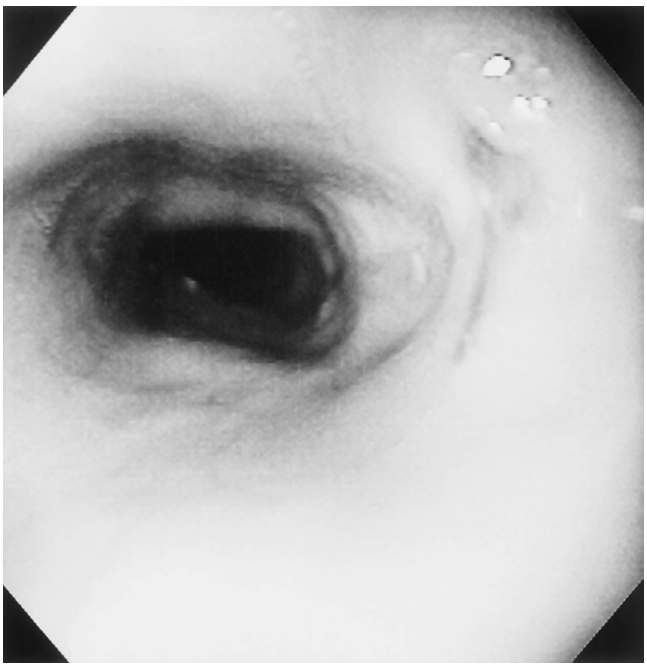

Figure 4. Endoscopic view of the repair site 6 weeks after repair. Mucosal coverage was complete, and minimal to no stenosis is seen.

Primary repair is feasible only in relatively small injuries. Esophageal exclusion techniques will predispose the patient to requiring further extensive reconstruction procedures, such as a gastric pull-up or colonic interposition.[1,7–9] Although the mortality has decreased recently, owing to improvement in intensive care and antibiotics, the morbidity and cost of care remains high, and patients suffer prolonged disability. The esophageal patch repair we developed can be performed very easily, quickly, and reliably. The elastin based acellular aortic patch is designed to provide a reliable barrier for 1 to 2 weeks while tissue growth and regeneration into the adventitial collagen layer takes place. The material is sterilized by gamma irradiation, and it is similar to the product used for porcine heart valve prostheses, which has been implanted in human hearts for decades. Therefore, we believe the material to be quite safe for human use. Unlike a duodenal injury that leaves an ulcerated lesion over an extended time,[10] an esophageal injury seems to heal very quickly, with complete mucosal coverage in as little as 3 weeks. This is probably because of the lack of digestive enzymes in the esophageal lumen, provided that the subject has no gastroesophageal reflux. Once mucosal regeneration has taken place, underlying muscular tissue seems to slowly regenerate within the fibrous scar, leaving minimal stricture without functional or anatomic obstruction. The majority of the elastin based biomaterial used degenerates while mucosal regeneration takes place, with only a very small amount of elastin fiber fragments remaining in the scar tissue.

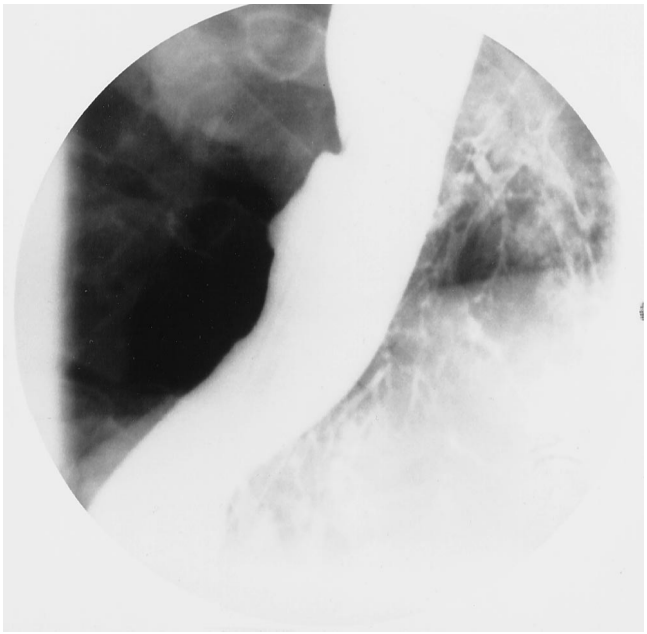

Figure 5. X-ray contrast study using barium. The repair site shows some flat stiffening, without significant stricture or obstruction.

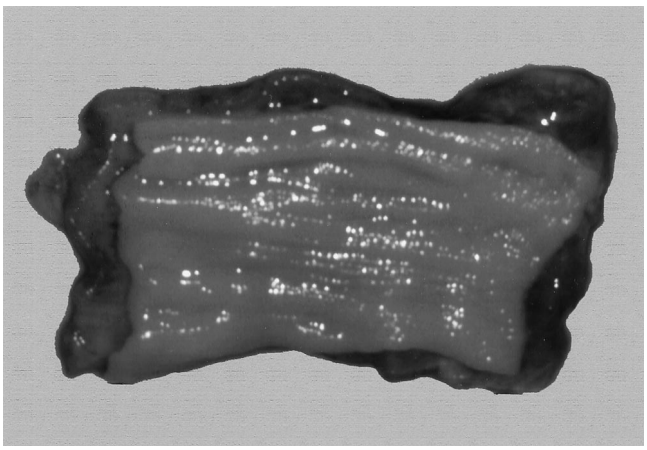

Figure 6. Gross specimen of the healed repair site. Mucosal coverage is complete, and minimal scar was seen from the outside.

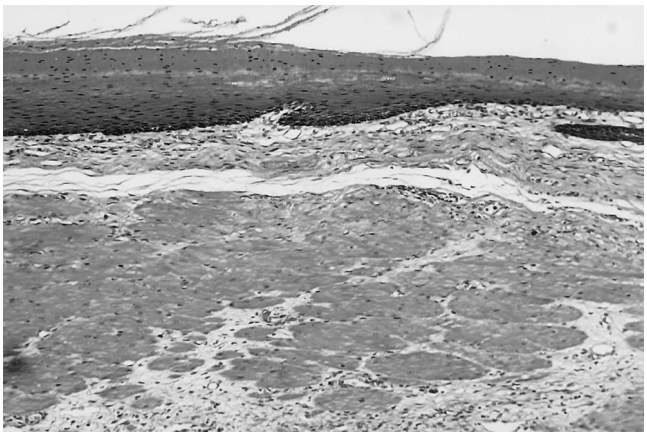

Figure 7. Histology of the healed repair site. Complete regeneration of the mucosa and submucosa is seen. Muscular regeneration was also seen but still was incomplete.

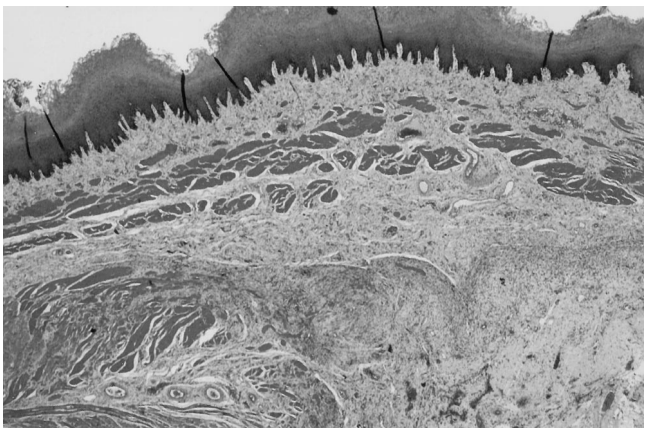

Figure 8. Histology of the healed repair site. Fragments of elastin fibers were identified. Nerves were also found in the center of the regenerated tissue.

In our previous experiment using a duodenal implant, one critical problem we faced with our pure elastin patch was that the material was quite fragile, lacking in mechanical strength, which made it technically difficult to suture. By preserving the collagen fibers in the adventitia, we could obtain a fairly strong material, which was much easier to handle. The mechanical strength of the new material was compared with the pure elastin patch. 3-0 Vicryl suture (Ethicon, Inc., Somerville, NJ) was passed through a 1 × 2 cm patch, 3 mm from its edge, and a Chatillon V-1,000 mechanical tester (Largo, FL) was used to measure the gram force needed to pull the suture through the material. It was 23.8 ± 4.3 (n = 4) for the single layer elastin patch, 78.13 ± 8.93 for a double layer elastin patch, and 459.6 ± 35.1 (n = 5) for the cellular aorta patch, which was used for this experiment. The patch also has the theoretical advantage of preserving the collagen as a scaffold for tissue regeneration, which was provided by small intestinal submucosal patch in our previous study.[10]

One of our major concerns was the development of leak or fistula. From our experience thus far, we encountered no significant leak, fistula, or abscess formation, and this finding was very encouraging. We should, however, note that we conducted this experiment in a clean injury without any other associated injuries, repairing the defect at the earliest stage possible. We could, on the other hand, demonstrate that the patch repair is durable, and quite reliable even without antibiotics, enzyme inhibitors, or nutritional supplements in this setting.

Surgical experiments were typically performed in 50 minutes from skin to skin. The actual time required for the esophageal repair itself was less than 15 minutes. No other bowel resection or anastomosis is required, and our animals can resume oral feeding immediately after they recover from anesthesia. For trauma victims with penetrating injury to the esophagus, this is a potentially ideal treatment in that the surgery time is minimal and recovery is fast, eliminating the need for prolonged hospitalization with antibiotics and intravenous hyperalimentation.

Conclusion

Our new elastin patch material provides a reliable way to repair a major tissue defect in the esophagus. By preserving the adventitial collagen layer of this patch, we could obtain a fairly strong material, which is resistant to infection and digestive enzymes, while allowing the tissue to heal without leak or obstruction.

Acknowledgment

This Program is supported by a grant from the United States Army Medical Research and Material Command. The authors thank Ms. Vicki E. Feldmann. for her dedicated technical assistance during our experiments.

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