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# Urinary bladder matrix scaffolds strengthen esophageal hiatus repair

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ABSTRACT

*Background:* Laparoscopic repair of the hiatal hernia is associated with a recurrence rate between 12% and 42% depending on the defect size. Although the impact of hiatal reinforcement on long-term recurrence remains controversial, the main limitation of this approach has been the risk of adverse events related with the use of synthetic materials in the vicinity of the esophagus.

*Methods:* A total of 14 female domestic pigs underwent laparoscopic primary hiatal hernia repair of a simulated defect in the esophageal hiatus. Seven of the hiatal repairs were reinforced with an extracellular matrix (ECM) scaffold, whereas the remaining seven served as primary repair controls. Animals were survived for 8 wk. At necropsy, after gross morphologic evaluation, samples were sent for mechanical testing and histology.

*Results:* The repaired defect site reinforced with ECM scaffolds showed a robust closure of the crura in all cases with a smooth peritoneal-like structure covering the entire repair. Average load at failure of the treated group was found to be significantly stronger than that of the controls (185.8 ± 149.7 g *versus* 57.5 ± 57.5 g, $P < 0.05$). Similarly, the stiffness was significantly higher in the treated animals (57.5 ± 26.9 g/mm *versus* 19.1 ± 17.5 g/mm; $P < 0.01$). Interestingly, there was no difference in elongation at failure (7.62 ± 2.02 mm *versus* 7.87 ± 3.28 mm; $P = 0.44$).

*Conclusions:* In our animal survival model, we have provided evidence that the addition of an ECM to augment a primary hiatal repair leads to tissue characteristics that may decrease the possibility of early failure of the repair. This may translate to decreased recurrence rates. Further study is necessary.



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## Introduction

Laparoscopic repair of the hiatal hernia is associated with a recurrence rate between 12% and 42% depending on the defect size.[1-3] As a result, many surgeons have attempted reinforcement of the esophageal hiatus using a tension-free synthetic mesh, such as those that have been successfully used in the repair of groin hernias and abdominal wall hernias.[3,4] Although the impact of such reinforcement on long-term recurrence remains controversial, the main limitation of this approach has been the risk of adverse events related with the use of synthetic materials in the vicinity of the esophagus. There are several reports of polypropylene or polytetrafluoroethylene mesh esophageal intrusion leading to devastating conditions with disabling symptoms such as dysphagia and food intolerance. Treatment of these complications can present serious surgical challenges.[5-8]

Extracellular matrix (ECM) scaffolds have been recently used for reinforcement of surgical soft-tissue repairs in a wide variety of clinical applications, including hiatal hernia repair. Preclinical and clinical reports describe that these devices are remodeled at variable rates depending on the source of the ECM and placement of the device. Ultimately, the goal is for these scaffolds to be replaced by the patient's own tissue, which would overcome the problem of esophageal intrusion in the case of hiatal hernia repair.

The first clinical reports of the use of ECM scaffolds in this setting of reinforcement of a hiatal hernia repair were encouraging with little or no adverse events and a reduction in the short-term recurrence rate of the hiatal hernia.[9] However, in the long term, the difference in recurrence rate with or without reinforcement tends to dissipate.[10] This finding may be influenced by different factors, with integrity of hiatal closure being just one of them. Detection of the failure mechanism is not always possible in a clinical setting and can only be specified when the patients need reoperation due to that failure, which only happens 3%-5% of the time according to several reports.[11,12] Therefore, the specific contribution of ECM scaffolds to the reinforcement of the hiatal closure remains unstudied. The objective of the present study was to assess the contribution of an ECM scaffold, specifically porcine urinary bladder matrix (UBM; MatriStem Surgical Matrix PSMX; ACell, Inc, Columbia, MD). The contribution of UBM was assessed through investigation of the mechanical properties, gross morphology, and histologic appearance of the esophageal hiatus after primary hiatal hernia repair with and without reinforcement in a preclinical porcine model.

## Materials and methods

A total of 14 female domestic pigs, weighing between 40 and 60 kg, underwent laparoscopic primary hiatal hernia repair of a simulated defect in the esophageal hiatus. Seven of the hiatal repairs were reinforced with an ECM scaffold, whereas the remaining seven served as primary repair controls. Animals were survived for 8 wk. At this time, the scaffolds have a complete disappearance from the implant site, and it was proved by the authors in previous publications.[13] At necropsy, after gross morphologic evaluation, samples were sent for mechanical testing and histology.

All animal procedures were performed in compliance with the 1996 Guide for the Care and Use of Laboratory Animals.

### *Surgical procedure*

Each animal was preanesthetized with xylazine 20 mg/kg and ketamine 50 mg/kg by intramuscular administration, and anesthesia was maintained by orotracheal intubation (isoflurane and intravenous propofol 5 mg/kg). Then, animals were placed in a supine position, and laparoscopic approach was performed using standard surgical equipment. The retroesophageal space was reached through a window created in the pars flaccida of the lesser omentum. The esophageal hiatus was dissected using harmonic scalpel (Ultracision, Johnson & Johnson) until the esophagus was completely free of attachments. A hiatal defect was created by sectioning the fascia between the crura. Primary repair was performed using 2.0 Prolene (Ethicon; Johnson & Johnson) sutures to the crura. UBM scaffolds were implanted with a U shape in an onlay fashion and secured with titanium tackers (ProTack; Covidien; Fig. 1).

### *Postsurgical care*

The pigs were recovered from anesthesia, extubated, and monitored in the recovery room until they were resting comfortably in sternal position and were kept in a cubicle specially designed for this kind of animal, were they can stay awake. The pigs were given prophylactic antibiotics consisting in a combination of G penicillin (20.000 UI/kg) and streptomycin (sulfate 2 g) via intramuscular administration. After surgery, the pigs received fentanyl (20 mcg/kg IM) for analgesia as needed and were fed with a high-protein balanced food. Vital signs and wound care were checked every day. The weight was checked every 7 d.

### *Gross morphology*

Euthanasia was achieved with an anesthesia overdose with xylazine/ketamine by intramuscular administration and a propofol IV bolus.

Through a midline abdominal incision, the hiatal area was carefully inspected before tissue harvesting. Presence of sliding hernias or weak areas at the repair site was recorded. Particular attention was given to esophageal intrusion or strong adhesions to the hiatoplasty. After inspection, the esophageal hiatus and crura were harvested en bloc and submitted to mechanical testing and histologic processing.

### *Biomechanical testing*

Briefly, 1 strip of tissue from the hiatoplasty was obtained using a 10-mm long by 3-mm wide biopsy punch with a dog-bone shape (Fig. 2A and B). The samples were excised taking care of including the center of the hiatoplasty without de prolene sutures and a small portion of each crura. Each test sample was immersed in saline (37°C) bath for tensile testing to failure. The elongation rate was set to 25 μm/s (1.5 mm/