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Development of a critical-sized ventral hernia model in the pig

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ABSTRACT

Background: The pig is commonly used as a preclinical model for ventral hernia repair. However, no study has verified that an unrepaired surgically induced hernia (control) in the pig does not heal spontaneously but rather develops a persistent hernia. Without such verification in any given model, one cannot draw conclusions on the efficacy of the repair technique investigated.

Materials and methods: Three surgically induced hernia models with increasing severity were created in eight pigs. These included 10-cm retrorectus partial-thickness (model 1) and 15-cm preperitoneal full-thickness (model 2) incisional defects and an 8 × 8 cm preperitoneal full-thickness excisional defect (model 3). Postoperative management included use of an abdominal binder, and in some cases, suction drainage, for 2 wk to support the repair and prevent seroma. Models were evaluated for persistence of hernia at 5 wk using clinical and radiographic assessments.

Results: All pigs developed clinical hernias after 2 wk of defect creation, but only models 1 and 3 had clinically persistent hernias at 5 wk. At 5 wk, the average defect area was 97 cm^2 in model 1, 66 cm^2 in model 2, and 245 cm^2 in model 3. Dense fibrotic scarring was observed in the models with resolved hernias.

Conclusions: Our results highlight the need to verify an unrepaired hernia injury model does not heal spontaneously prior to using it for hernia repair studies. The partial-thickness incisional model 1 and full-thickness excisional model 3 formed persistent hernias in pigs at 5 wk and should be further explored as models for investigating hernia repair strategies.

Introduction

A common strategy for evaluating the effectiveness of meshes for hernia repair involves assessment in animal hernia models. Small animal models like the rat are used to assess mesh biocompatibility, whereas large animal models like the pig are used to study functional outcomes such as repair integrity, hernia formation, and biomechanics. The pig is the most commonly used large animal model for hernia repair as it is anatomically and physiologically similar to humans with respect to size, bulk and blood supply of the abdominal wall, and healing characteristics.[1] The size of the ventral abdominal wall in the pig allows creation and repair of hernia defects of clinically relevant dimensions using surgically relevant

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techniques and mesh sizes.[2-8] Indeed, several models of hernia injury and repair in the pig model have been reported in the peer-reviewed literature.[4-20]

However, many of the clinically relevant features of hernia patients (e.g., advanced age, presence of comorbidities, chronic nature of hernias, associated contamination, and infection) are challenging, if not impossible, to reproduce in animal models. As porcine subjects are generally young and healthy, surgically-induced, acute injuries in porcine models are often associated with robust wound healing and scar tissue formation in a manner not encountered in human patients.[10,19] Hence, when developing a porcine model for hernia injury and repair, it is of paramount importance to first verify that the unrepaired surgically induced hernia (control) is "critical-sized". In other words, in the absence of repair, the injury model must not heal spontaneously but rather go on to form a persistent hernia. In prior studies using porcine models to investigate hernia repair, the absence of healing an unrepaired defect and/or the persistence of a hernia at a postacute time point were not verified.[4-20] Without such verification in any given model, one cannot conclude that the subsequent repair technique investigated was truly effective in-and-of-itself. Therefore, it is difficult to interpret the results from the current body of surgical literature evaluating outcomes in porcine models of hernia repair.

The aim of this study was to investigate the absence of healing and persistence of a hernia in three surgically induced hernia models with increasing severity of injury in the pig. We hypothesized that injury severity would correlate with formation of a persistent hernia.

Methods

We created three surgical models of ventral hernia injury in a porcine model, wherein the abdominal wall defect was made increasingly larger or more severe. Each injury model was followed for 5 wk and evaluated for the formation of a persistent hernia using clinical and radiographic assessment.

Eight female Yorkshire pigs (30-40 kg, 3-4-month old, Michael Fanning Farms, Howe, IN) were used in the study. All animal experiments complied with the Animal Research: Reporting In Vivo Experiments (ARRIVE) guidelines, the National Institutes of Health guide for the care and use of Laboratory animals (NIH Publications No. 8023, revised 1978), and were approved by the Institutional Animal Care and Use Committee at the Cleveland Clinic.

Preoperative care and anesthesia

The pigs were housed under standard conditions and fed twice daily (Teklad Vegetarian Pig/Sow Grower Diet, 2%-4% of body weight) throughout the study. Animals were acclimated for 1 wk and fasted for 12 h before surgery. General anesthesia was induced with intramuscular (IM) ketamine (20 mg/kg) and xylazine (2 mg/kg) and maintained by inhalational isoflurane (1%-3%) throughout the procedure. Perioperative medications included intravenous (IV) isotonic saline, IV cefazolin (20 mg/kg, every 2 hours), IM famotidine (0.5-1 mg/kg), and IM buprenorphine (0.005-0.01 mg/kg). Standard abdominal preparation, with abdominal shaving and 70% alcohol and betadine washes, was performed, and sterile drapes were placed.

Surgically induced ventral hernia models

Three ventral hernia models were investigated wherein the abdominal wall defect was made increasingly larger or more severe by modulating the defect dimensions, depth (partial *versus* full thickness), and extent of myofascial resection. All surgeries were performed by team members experienced in clinical and/or animal surgery (M.J.R., S.S., I.N.H., and A.R.B.) following a standardized surgical protocol.

Model 1: partial-thickness, retrorectus incisional defect (n = 2)
A 12-cm midline skin incision was made, and 1-cm wide skin flaps were raised bilaterally through the avascular prefascial plane. The anterior rectus sheath was exposed, and 10-cm incisions were made bilaterally on the anterior rectus sheath along the medial edge of the rectus abdominis muscles to enter the retrorectus space. A 12 × 12 cm retrorectus space was developed by dissecting bilaterally to the lateral edge of the rectus muscles and extending the incisions medially to connect the two spaces across the midline. The posterior rectus sheath and underlying layers were not compromised. The resulting incisional defect was almond-shaped and approximately 10 × 5 cm (Fig. 1A, $n = 2$ pigs).

Model 2: full-thickness, preperitoneal incisional defect (n = 2)
A 15-cm midline incision was made through the skin, subcutaneous fat, aponeurotic layers, and the visceral peritoneum. A 12 × 12 cm preperitoneal space was developed by dissecting the visceral peritoneum away from the preperitoneal tissues. The peritoneum was closed across the midline using a running 2-0 Vicryl suture. The resulting incisional defect was almond-shaped and approximately 15 × 7.5 cm (Fig. 1B, $n = 2$ pigs).

Model 3: full-thickness, preperitoneal excisional defect (n = 4)
A 10-cm midline incision was made through the skin, subcutaneous fat, and aponeurotic layers, and 5-cm wide skin flaps were raised bilaterally. An 8 × 8 cm region was marked on the rectus abdominis-fascial surface. An 8-cm midline incision was made through the linea alba without violating the parietal peritoneum, and 4 × 8 cm sections of rectus abdominis muscles were resected bilaterally using electrocautery. The resulting excisional defect was rectangular and approximately 11 × 10 cm in the craniocaudal and transverse directions respectively (Fig. 1C, $n = 4$ pigs).

Radiopaque marker placement

To permit computed tomography (CT)–based monitoring of the hernia defect size over the postoperative period, radiopaque markers were placed around the defect edge as well as on the underlying tissue layer (Fig. 1). Eight interrupted radiopaque polypropylene suture tags (Radiopaque Marker, USP-0, Viscus Biologics, Cleveland, OH) were used to mark the defect edge. Five 1.6-mm diameter tantalum beads (Tilly Medical Products, Lund, Sweden) were affixed to the underlying tissue layer (posterior rectus sheath in model 1 or visceral