

Review Article

Patch Repair for Intestinal Perforation Closure in an *Ex-Vivo* Porcine Model with Burst Pressure Characterization

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Abstract

Background: Bowel perforation is the loss of intestinal wall integrity and can occur by several mechanisms including infection, obstruction, inflammation, trauma and iatrogenic causes. Incidences of bowel perforation range from 1-7% in pediatric trauma patients and 0.02-8% in adults. There is no specific classification for gastrointestinal perforations, but several methods have been used to describe perforations based on etiology, including systemic, inflammatory, medication, neoplastic and instrumentation-induced perforations. We assessed the feasibility of closing small intestine perforations with a mesh patch instead of sutures only.

Methods and Findings: Nine porcine *ex-vivo* small intestine specimens were incised 0.5 cm to simulate bowel perforations. Control group perforations were sutured closed without mesh. The two experimental groups were closed by mesh sewn to the outside (first group) or inside (second group) of the bowel wall. Each specimen was submerged in normal saline and insufflated until air bubbles leaked from the perforation. That insufflation pressure was recorded as the burst pressure. The control group burst at 78.0±17.9 mmHg. The “patch outside” group burst at 54.7±9.1 mmHg. The “patch inside” group burst at 32.0 ±4.6 mmHg. Only the “patch inside” group had statistically significant inferiority, but both groups trended towards inferiority.

Conclusions: Preliminary research indicates that patch repair of intestinal perforations is likely inferior to sutures alone, although repair with the patch outside the bowel wall cannot be completely excluded because of the high variability of the data. Further research may try alternate patch types or different variations to find a non-inferior closure method. A sample size of n=9 each would give 80% power to detect a minimal detectable difference of 20 mmHg.

Keywords: Bowel Perforation; Perforation Repair; *Ex-Vivo*; Small Intestine; Surgery; Gastroenterology; Swine; Burst Pressure; Suture; Mesh

Introduction

Bowel perforation is the loss of intestinal wall integrity and can occur by several mechanisms including infection, obstruction, inflammation, trauma and iatrogenic causes. Incidences of bowel perforation range from 1-7% in pediatric trauma patients and 0.02-8% in adults [1,2]. The most common etiology, namely ulcerative disease, accounts for up to 15% of duodenal perforations [1,2]. Additionally, the increasing use of diagnostic and therapeutic endoscopy has resulted in increased incidence of disease, including perforation. There is no specific classification for gastrointestinal perforations, but several methods have been used to describe perforations based on etiology, including systemic, inflammatory, medication, neoplastic and instrumentation-induced perforations.

Treatment for acute endoscopic perforations was traditionally open surgical repair which is associated with high morbidity (25-36%) and mortality (7-10%), but continual efforts toward less invasive methods may provide better outcomes [3]. In contrast to surgery, benefits of endoscopic closure include no requirement for general anesthesia and decreased leakage of gastrointestinal contents into the peritoneal cavity, which carries the potential to reduce both morbidity and mortality. Given the potential benefits of endoscopic approaches, novel modalities may prove beneficial for rapid resolution of perforations [4,5].

In this report, we compared burst pressure performance between suture only and sutured mesh (patch) repair in *ex-vivo* porcine models of perforation of the small intestine. We hope this study can provide further insight into opportunities and challenges in developing endoscopic approaches for the repair of bowel perforations.

Materials and Methods

Specimen Preparation

Nine porcine *ex-vivo* small intestine specimens roughly 10 cm in length were obtained. In each specimen, a simulated bowel perforation was created with a 0.5 cm longitudinal, transmural, linear incision using a #11 scalpel blade.

To prepare the specimen for insufflation, the distal end of the specimen was sealed by suturing in a purse-string fashion a 1/4-inch (0.635 cm) barb end plug, preventing leakage distally. The proximal end of the specimen was sutured to one end of a 1/4-inch hose barb coupling, to which the other end of the hose barb was connected to rubber tubing that led to the pressure measurement apparatus (Fig. 1).

Three specimens each were allocated to the control group, experimental group 1 and experimental group 2. The control group consisted of primary repair of the perforation by sutures alone, without the presence of a mesh (patch). In both experimental groups, the perforation was closed with an oval-shaped mesh 2 cm x 2.5 cm graft created from a commercially available Phasix ST Mesh patch (BD, Becton, Dickinson and Company) surgical graft material intended for soft tissue repair. The graft was secured to the tissue with four simple interrupted 3-0 silk sutures on the long and short axes of the oval-shaped graft. In the first experimental group ("patch outside"), the mesh was placed on the outside of the bowel wall (Fig. 1), while in the second experimental group ("patch inside"), the mesh was placed inside the bowel wall i.e., adjacent to the mucosa (Fig. 1).

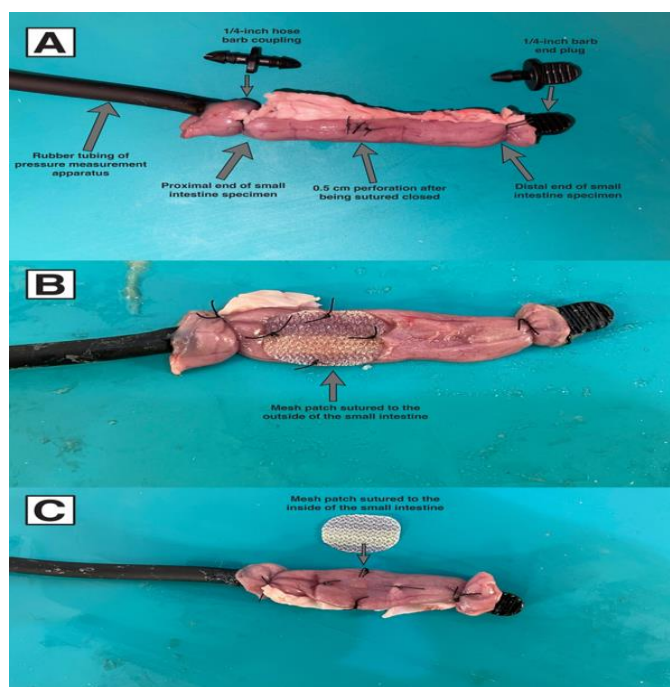


Figure 1: Porcine intestinal specimens after closure of perforation, but before insufflation. The setup components are labeled in (A), but present in all subfigures. (A) Example control (perforation repaired with sutures only). (B) Example of specimen with patch sutured to the outside of bowel wall. (C) Example of specimen with the patch sutured to the inside of the bowel wall.

Pressure Measurement Apparatus

The pressure measurement apparatus consisted of a T-configuration of rubber tubing, with one end leading to the inside of the bowel specimen, a second end connected to an aneroid manometer with a pressure range of 20-300 mmHg and a third end connected to a bulb insufflator with an adjustable valve (Fig. 2).

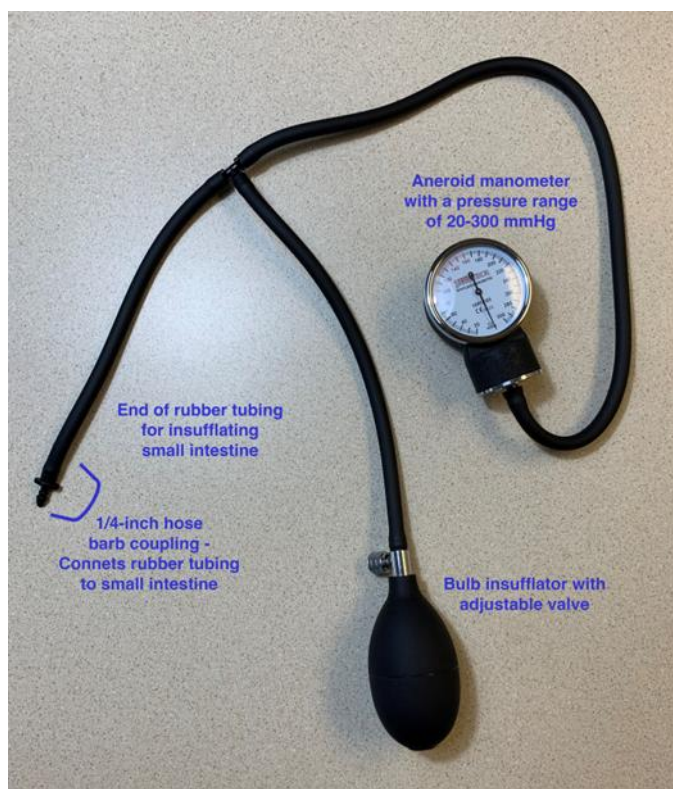


Figure 2: Pressure measurement apparatus.

Testing of Burst Pressure

Each specimen was submerged in normal saline and insufflated with room air to the minimum pressure that caused an appearance of air bubbles from the site of artificial perforation. If this site of the specimen was not the first to fail (2 cases), the sample was repaired in a way as to ensure that the site of artificial bowel perforation was the first location of integrity failure, detected by visualization of air bubbles emanating only from this area of the specimen. All trials were recorded in slow motion and videos were reviewed after the experiment. Upon review, the minimum pressure at which the burst occurred was recorded for each specimen. An example video can be seen in supplementary File. 1.

Statistical Analyses

Both experimental groups were compared against the control using a null hypothesis of noninferiority. For each comparison, this was tested with a one-tail, two-sided, unpaired t-test with assumption of equal variance. The significance threshold (α -value) was set as $p \leq 0.05$. Mean and Standard Errors of the Mean (SEM) were created for each group and for the intergroup differences.

Results

The control group had a mean burst pressure of 78.0 ± 17.93 mmHg (10.4 ± 2.39 kPa, mean $\pm$ SEM). The first experimental group (patch outside the intestines) had a mean burst pressure of 54.7 ± 9.06 mmHg (7.3 ± 1.21 kPa). The second experimental group (patch inside the intestines) had a mean burst pressure of 32.0 ± 4.58 mmHg (4.27 ± 0.61). The mean of both patch groups combined was 43.3 ± 6.81 mmHg. The results are summarized in Table 1.

	Group	Trial data			Mean	±	SEM	Difference from		
	Control (sutures only)	110	76	48	78.00	±	17.926	control ± SEM.		
	Patch outside	67	60	37	54.67	±	9.062	-23.33	±	20.086
*	Patch inside	26	41	29	32.00	±	4.583	-46.00	±	18.502
Perforations were repaired with either sutures only (controlled), patch sutured inside the bowel, or patch sutured outside the bowel. All units in mmHg. N=9 (3/group). SEM: Standard error of mean. * The “patch inside” group had p=0.033 in 1 tail t test compared to control.										

Table 1: Minimal pressure to burst repaired specimen perforations.

Discussion

In this study, artificial bowel perforations were created in ex-vivo porcine bowel specimens and repaired using either sutures only (control), a mesh patch sutured to the inside of the bowel wall, or a mesh patch sutured to the outside of the bowel wall. Preliminary results were taken to assess general feasibility and generate avenues for further research.

These results indicated a trend towards inferiority for the patch options. While only the “patch inside” group had a statistically significant difference, we suspect that this might be due to a small sample size. Further researchers may better characterize the difference using a larger sample size. Using our results, we predict from a power analysis that to achieve a power ≥ 0.8 , a per-group sample size of n=28 is needed to detect an effect size of 10 mmHg, n=14 for 15 mmHg and n=9 for 20 mmHg assuming one-tail t tests. These become n=36, n=17 and n=11 for two-tail t tests. Alternatively, continued efforts in this regard may be futile. Proven inferiority by statistical significance of one of the groups as well as a subjective review of the overall data suggests that mesh patches will not realistically be adequate for repair.

One hypothesis for a better seal resulting from sutures only may be that this method approximates the bowel layers with minimal disruption. Another possible mechanism for this result may be that the suture-only repair allows for a tighter, more uniform seal between the edges of the artificial perforation. For example, when introducing a mesh patch to seal a perforation, it is technically challenging to place sutures in the exact locations as the suture-only trials, resulting in sutures farther away from the perforation margins leading to an ineffective seal.

It is also important to note that these trials were completed on short segments of ex-vivo porcine bowel specimens and the external validity of these studies remains unclear. However, while many devices exist to aid in the repair of bowel perforation a traditional repair with simple interrupted sutures, if this is technically feasible intraoperatively, may lead to the highest probability of success, although further studies on this topic would likely be beneficial [6-10].

Conclusion and Limitations

Our findings are preliminary and as such are limited by the small sample size. Secondly, as this is in an *ex-vivo* porcine model, we cannot truly know how translatable the results are to human medicine. *In-vivo* animal studies would partially, but not completely, bridge this gap by keeping the tissue alive and connected to the body. However, human and porcine tissue might still react differently. This is especially true as, in real-world clinical situations, the tissue is often diseased and thus can be inflamed and friable. In addition, it is possible that the experimenters' skill in suturing factored into the results. However, we have low suspicion that that would have changed the final results as the same experimenter sutured all specimens. Furthermore, the suturing involved in an *ex-vivo* model, especially for the “patch inside” group, is significantly less challenging than the endoscopic or laparoscopic suturing that may be involved in human studies. Thus, if experimental skill confounded the results, it would have artificially improved the patch group results; however, the patch results are lower than the control despite any possible confounding help. Another limitation is that the burst pressure model only considers immediate closure strength and does not consider how the wounded tissue may change in the coming days after closure. Furthermore, our findings involve one mesh type and it is theoretically possible that a different patch may have different results and be non-inferior to suturing alone. Finally, the perforations here were simulated with 0.5 cm transmural linear scalpel incisions. Real-world perforations are rarely so clearly defined and, additionally, it is unknown how our results would apply to perforations of different sizes and shapes.

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Supplementary File

File 1: Example video of burst pressure trial for one of the control specimens (<https://athenaeumpub.com/wp-content/uploads/Additional-File-1-Sutures-only-trial.mp4>).

Conflict of Interest

The authors have no conflict of interest to declare.

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