Laparoscopic sigmoid colectomy with primary anastomosis for experimental modeling in the nonhuman primate

David J. Leishman[1], Scott H. Oppler[1], Melanie L. Graham[1,2]^, Cyrus Jahansouz[3]

[1]Preclinical Research Center, Department of Surgery, University of Minnesota, Minneapolis, MN, USA; [2]Department of Veterinary Population Medicine, University of Minnesota, St. Paul, MN, USA; [3]Division of Colon and Rectal Surgery, Department of Surgery, University of Minnesota, Minneapolis, MN, USA

Contributions: (I) Conception and design: All authors; (II) Administrative support: ML Graham; (III) Provision of study materials or patients: ML Graham; (IV) Collection and assembly of data: DJ Leishman, SH Oppler, C Jahansouz; (V) Data analysis and interpretation: DJ Leishman, C Jahansouz; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Cyrus Jahansouz, MD. Division of Colon and Rectal Surgery, Department of Surgery, University of Minnesota, 420 Delaware St. SE, MMC 195, Minneapolis, MN 55455, USA. Email: jahan023@umn.edu.

Abstract: Laparoscopic colon surgery is performed frequently in the clinical setting for a multitude of reasons including cancer, infection, and autoimmune disease. As a result, extensive research has been conducted in relation to clinical outcomes after surgery, but more recently, in relation to the impact of surgery and other patient factors on physiologic homeostasis including the host microbiome. Despite this, experimental surgical models for laparoscopic colon surgery are scarce in the literature with most studies utilizing rodents. While rodent studies provide valuable insights into basic mechanistic processes, the translation of novel therapeutic approaches to clinical practice often requires the use of large animal models. In exploring the intricate systems biology linking surgery and medicine, sophisticated models such as nonhuman primates (NHPs) play a pivotal role. By closely resembling human anatomical, physiological, and behavioral characteristics, NHPs facilitate the development and refinement of complex surgical techniques and peri-operative practices. Furthermore, they enable longitudinal studies that comprehensively assess both immediate and long-term outcomes. The availability and utilization of multiple robust models enhance the validity of surgical research, leading to more successful translation to human clinical practice. Here we describe our technique for performing a laparoscopic sigmoid colectomy with a primary anastomosis in an NHP. The entire procedure was well tolerated without significant ventilation or hemodynamic issue. To our knowledge, this represents the first laparoscopic sigmoid colectomy with primary anastomosis performed in an NHP. Furthermore, this demonstrates the feasibility of the technique and provides a relevant, preclinical model for the study of surgical colon disease. Although the surgical colectomy model in NHPs closely resembles the clinical scenario, it is crucial to recognize that a 'model' inherently comes with limitations. The intended use of any model should be carefully evaluated concerning the target patient population with the consideration of potential disparities in anatomy, physiology, environmental factors, and disease to properly interpret results. This model provides an opportunity to study mechanisms, from a systems biology perspective, underlying both innovative surgical treatments and their effects on diseases such as colon cancer, as well as benign conditions like inflammatory bowel disease, diverticulitis, and anastomotic leak, offering high predictive value.

Keywords: Laparoscopic colectomy; nonhuman primate (NHP); colon; experimental surgery

Submitted Feb 01, 2024. Accepted for publication Jun 23, 2024. Published online Aug 14, 2024.
doi: 10.21037/atm-24-25
View this article at: https://dx.doi.org/10.21037/atm-24-25

^ ORCID: 0000-0002-2475-6975.

Introduction

Over 600,000 colectomies are performed in the US each year to treat diseases of the colon including infection, cancer, and inflammatory bowel disease (1). These operations are often performed laparoscopically given improved patient outcomes including shorter length of stay, reduced pain and narcotic use, and decreased morbidity and mortality when compared to the traditional laparotomy (2,3). Bowel anastomoses are often needed to reestablish intestinal continuity. However, despite optimal surgical technique, serious anastomotic complications continue to occur in up to 20% of cases due to inadequate wound healing (4-8). As a result, while clinical outcomes studies have identified various technical issues, patient factors, and comorbidities associated with these complications (9-13), a comprehensive physiologic basis underlying these complications remains limited (6).

In recent years, the collective knowledge of the gut microbiome and its physiologic effects has improved, leading scientists and surgeons to investigate its interactions with anastomotic tissue healing and related complications. Indeed, ongoing research has focused on various aspects that impact the microbiome (antibiotics and medications, surgical bowel preparations, host diet, etc.) and how that influences anastomotic healing (7,14-18). Currently, most studies utilize a mouse model for colon resection and anastomosis via open approach to study the impacts on anastomotic healing and anastomotic leak (AL) (7,19-21). The advantages of this model are related to their wide availability, ease of handling and maintaining, as well as their less fragile digestive system in comparison to strict herbivores (22). While appropriate for initial soft-screening of novel therapies and mechanistic modeling, the mouse model is unable to recapitulate the clinical surgical technique, such as laparoscopy, and lacks proper prediction of the human/primate immune response. The use of multiple animal models is often necessary to address specific questions related to intestinal disease, allowing researchers to capture the complexity of the disease process and evaluate various aspects such as pathogenesis, immune responses, and therapeutic interventions. While different animal models have been extensively reviewed (23), each presenting its own strengths and limitations, establishing a colectomy model in the nonhuman primate (NHP) model opens the possibility to properly apply this model within the context of the research question. Here, we demonstrate our surgical technique of a laparoscopic sigmoid colectomy with primary stapled anastomosis in an NHP (*Video 1*). The rationale behind choosing an NHP model is multi-fold: (I) the animal has adequate size to allow for standard laparoscopic techniques and equipment used clinically, (II) the anatomy and physiology of NHPs is closest to that of humans including its gastrointestinal system in comparison to other animals, (III) the immune system, a major factor in wound and tissue healing, is most similar between NHPs and humans (24,25) to more accurately model anastomotic healing after colectomy, (IV) diet, environment, and medications can be strictly controlled, allowing for investigation of the gut microbiome on host immune activation and healing while limiting confounding factors. The goal of this technique is to provide a framework for performing a laparoscopic colectomy with an anastomosis in NHPs to allow researchers to utilize an animal model that is both clinically relevant and translatable. We present this article in accordance with the SUPER reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-24-25/rc).

Highlight box

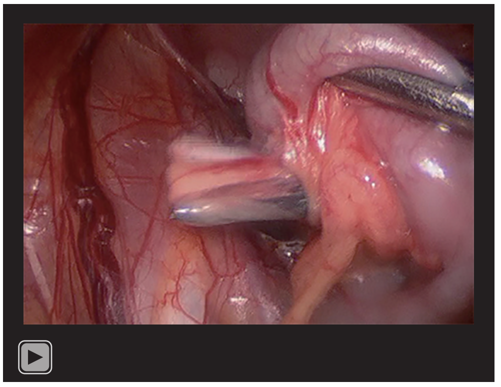
Surgical highlights
- The close resemblance of nonhuman primate (NHP) intestinal anatomy and physiology to humans permitted the development of a laparoscopic sigmoid colectomy model with primary anastomosis that effectively mirrors the clinical scenario, thereby enhancing the model validity.

What is conventional and what is novel/modified?
- The entire surgery is performed using conventional techniques and standard equipment that are used on a regular basis in the clinical operating room.
- Given the size of the NHP, an air-leak test which is a critical part of intraoperative anastomotic evaluation can be performed.

What is the implication, and what should change now?
- This novel NHP model of laparoscopic sigmoid colectomy serves as a valuable tool for uncovering underlying mechanisms, particularly in immunology, pertinent to surgical therapies for intestinal disease or innovative interventions aligned with the minimally invasive surgery clinical standard.

Preoperative preparations and requirements

Experiments were performed under a project license (No. 2103-38932A) granted by the University of Minnesota Institutional Animal Care and Use Committee (IACUC), in compliance with the Animal Welfare Act, adhered to principles stated in the NIH Guide for Care and Use of



Video 1 Laparoscopic sigmoid colectomy in the nonhuman primate.

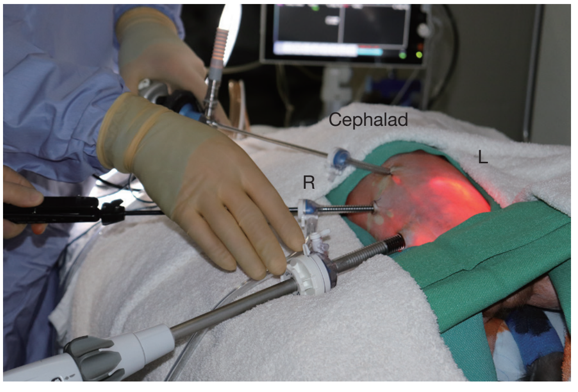


Figure 1 Animal positioning and trocar placement. The animal is placed in a modified lithotomy position making sure to have clear access to the anus after sterile draping. A 5 mm camera port is placed supraumbilical, and 5 and 12 mm working ports are placed in the right upper and right lower quadrant, respectively. R, right; L, left.

Laboratory Animals (26), and were performed and reported in compliance with the ARRIVE guidelines. The selection of candidate animals for this procedure should mimic the clinical situation. As with human patients, significant obesity in the animal can make laparoscopy much more challenging. The increased subcutaneous adipose tissue can make safe entry into the abdomen much more difficult and may limit the degrees of freedom of the trocars, while the increased visceral adiposity limits the intraabdominal working space and can obscure the surgeon's view (27,28). Therefore, it is advisable to avoid overweight or obese NHPs, if possible, to circumvent these challenges, unless attempting to model the obese clinical patient. One should also bear in mind that the pelvis of a male macaque is narrower than that of a female macaque (29), which may make dissection of the rectosigmoid junction and subsequent anastomosis creation more challenging, especially in those with limited laparoscopic experience.

All animals should be fasted for at least 6–8 hours to avoid regurgitation or aspiration of gastric contents during the procedure. The NHP model also offers the opportunity to mimic pre-operative bowel preparation conditions such as surgical bowel preparation [mechanical bowel preparation (MBP) with antibiotics] or MBP alone. Unlike other animal models, NHPs can be trained to cooperate and participate with their care (30,31), allowing them to ingest bowel preparation or other drugs as in the clinical situation. In this study, we chose to model the condition of fasting without the use of any bowel preparation.

As with clinical surgery, the procedure should be performed in a dedicated operative suite under sterile conditions with hemodynamic monitoring, ventilation, and general anesthesia capabilities. To aid in exposure, a surgical bed with Trendelenburg positioning is necessary to facilitate movement of the omentum and bowel into the upper abdomen, out of the surgical field. The bladder should also be emptied to allow visualization within the pelvis; this can be accomplished using a pediatric feeding tube as a urinary catheter connected to a gravity feeding bag for collection. A surgical assistant is also required to assist with the camera and creation of the anastomosis. In addition to standard laparoscopic equipment, a 5 mm laparoscopic Harmonic ultrasonic scalpel for dissection, an EndoGIA stapler, and an end-to-end anastomosis (EEA) circular stapler for resection and anastomosis creation are used. A laparoscopic suction-irrigator and endoscope with insufflation capabilities are used for performing an air-leak test of the anastomosis.

Step-by-step description

Positioning and preparation

The animal is sedated under general anesthesia and is intubated using direct laryngoscopy. The animal is then placed supine in a modified lithotomy position with rolled towels under the thighs (*Figure 1*) facilitating passage of the EEA stapler and endoscope later. A urinary catheter or pediatric feeding tube is inserted into the urethra and the bladder is decompressed. The hair from the abdomen, groin, and perianal area is clipped. A chlorhexidine surgical scrub is applied and the abdomen is draped in the usual

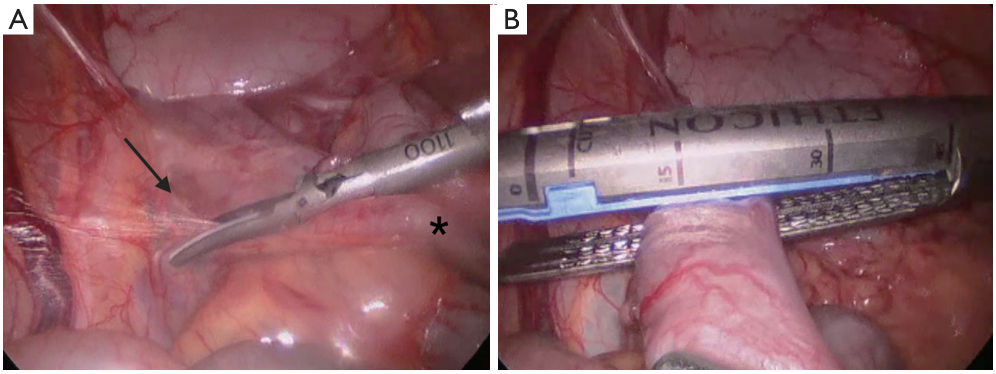


Figure 2 Laparoscopic dissection and transection of the distal sigmoid colon. (A) Colon (asterisk) is retracted medially, and the left lateral peritoneal attachments (arrow) are taken down with energy. (B) The lower jaw of the laparoscopic linear stapler is guided through the created mesenteric window and the colon is transected at the rectosigmoid junction.

sterile fashion, allowing for ease of access to the anus under the drapes. The surgeon stands on the animal's right side with the assistant on the animal's left side.

Abdominal access and port placement

A supraumbilical 5 mm incision is made and carried down to the level of the fascia. The fascia is incised along the linea alba and the peritoneal cavity is entered. A 5 mm trocar is placed through the incision under direct visualization as a camera port and is connected to insufflation tubing with pneumoperitoneum established to 10 mmHg. Every 10–15 minutes, the insufflation is paused for 30 seconds to allow for maintenance of normal physiology. A 5 mm 45° laparoscope is inserted, and visual inspection of the peritoneal cavity is performed to assess for injuries. Under direct visualization with the laparoscope, a 5 mm port is placed in the right upper quadrant and a 12 mm port is placed in the right lower quadrant as working ports (*Figure 1*).

Mobilization of the colon

Using a grasper in the left hand, the sigmoid colon is identified and retracted medially to expose the white line of Toldt (lateral peritoneal reflection). The colon is then mobilized in a lateral to medial fashion using the Harmonic ultrasonic scalpel to incise the white line of Toldt inferiorly (*Figure 2A*) and then tracing it superiorly toward the splenic flexure, releasing the colon from its lateral attachments. This mobilization should create sufficient length to allow the proximal transection margin to reach the pelvis without tension.

Transection of the inferior mesenteric artery (IMA) and rectosigmoid junction

The mobilized colon is retracted medially, and the IMA is identified and traced to its base within the retroperitoneum. Care must be taken to identify the left ureter and gonadal vessels to prevent injury to these structures. Once these structures are safely identified, the IMA is dissected circumferentially at its base, then sealed and transected using the Harmonic ultrasonic scalpel. The point at which the tinea coli splay distally is identified as the rectosigmoid junction and a window in the mesentery is made at that point. The Harmonic ultrasonic scalpel is removed and replaced with a laparoscopic EndoGIA stapler with a blue staple load. The lower jaw is inserted through the window ensuring the colon lies flat and untwisted before closing and firing the stapler jaws to transect the colon (*Figure 2B*). The stapler is removed and using the Harmonic ultrasonic scalpel, the mesentery of the colon is transected along the course of the IMA proximally to isolate the sigmoid colon.

Extracorporeal division of the sigmoid and anvil insertion

The abdomen is desufflated and the supraumbilical camera port incision is extended to facilitate the passage of the colon. The distal colon staple line is delivered through the incision and the entire sigmoid colon is extracorporealized. The proximal end of the isolated sigmoid colon is transected with the Harmonic ultrasonic scalpel and the specimen is passed off the field (*Figure 3A*). The remaining colon end is incised, and a stay stitch is placed to facilitate passage of the anvil. A small colotomy is made more proximally on the

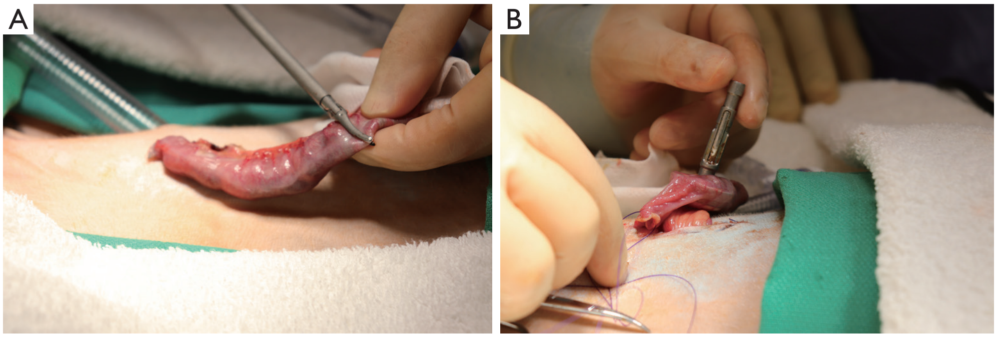


Figure 3 Extracorporeal sigmoid resection and anvil placement. (A) The distal sigmoid colon staple line is extracorporealized through the supraumbilical incision and the resection is completed by transecting the proximal sigmoid colon. (B) The EEA stapler anvil center rod is guided into the proximal transection margin and through a more proximal antimesenteric side colotomy 5 cm proximal to the cut colon edge ensuring that the until the remaining anvil body is intraluminal. A purse-string stitch is then placed at the base of the anvil at the side colotomy for fixation. EEA, end-to-end anastomosis.

antimesenteric side of the colon. The center rod of the anvil is inserted in the open colon end and directed through the side wall colotomy while the body of the anvil is advanced until entirely intraluminal (*Figure 3B*). The proximal end is then staple closed thus facilitating an end (rectum) to side (colon) anastomotic configuration. The distal colon end is then reinserted into the abdomen and the camera trocar is replaced with nylon or prolene suture used to reapproximate the incision temporarily to allow for reinsufflation.

Air-leak test and colorectal anastomosis creation

With the abdomen reinsufflated, one surgeon moves to the foot of the operative table to perform endoscopy and insertion of the EEA stapler. The anus is identified under the drapes and an endoscope is carefully passed into the anal canal. The endoscope is advanced into the rectal stump and insufflated to directly visualize the staple line for obvious defects (*Figure 4A*). With the suction irrigator, the assistant fills the pelvis with saline until the rectal stump staple line is completely submerged. An air-leak test is performed as the surgeon insufflates the rectal stump and the staple line is laparoscopically visualized for bubbling which would indicate a stump leak. After ensuring there is no leak, the endoscope is removed, lubrication is applied to the EEA stapler and it is carefully inserted into the anal canal. The stapler is gently passed into the rectal stump ensuring no resistance until it is visualized laparoscopically. The surgeon then deploys the pin of the EEA stapler through the corner of the staple line ensuring there is no twisting of the stump (*Figure 4B*). Using a laparoscopic grasper, the assistant grasps the center rod of the anvil and facilitates insertion of the stapler pin into the rod (*Figure 4C*). Once the anvil and stapler are connected and the colon and rectal stump are approximated, another check of the colon length is performed ensuring there is no tension on the anastomosis. The stapler is then fired and once completed, it is removed from the anus and the anastomotic tissue rings of the stapler are checked to for proper circumferential stapling, confirmed by the presence of two complete rings (proximal and distal). The endoscope is then reinserted into the anus for direct visualization of the anastomosis and another air-leak test is performed (*Figure 4D*) with the assistant gently clamping the colon proximal to the anastomosis to achieve adequate intraluminal pressure.

Closing

After the anastomosis is checked for patency and leak, the peritoneal cavity is inspected once more for hemostasis. Once confirmed, the abdomen is desufflated and trocars are removed. The fascia of the supraumbilical and 12 mm trocar incision is primarily closed with 3-0 Vicryl suture and the skin of all the incisions are closed with a buried 5-0 Monocryl Plus suture and skin glue.

Postoperative considerations and tasks

As this study was exploratory in nature, the animal underwent humane euthanasia following successful completion of the procedure. For chronic studies, there are some basic postoperative considerations researchers

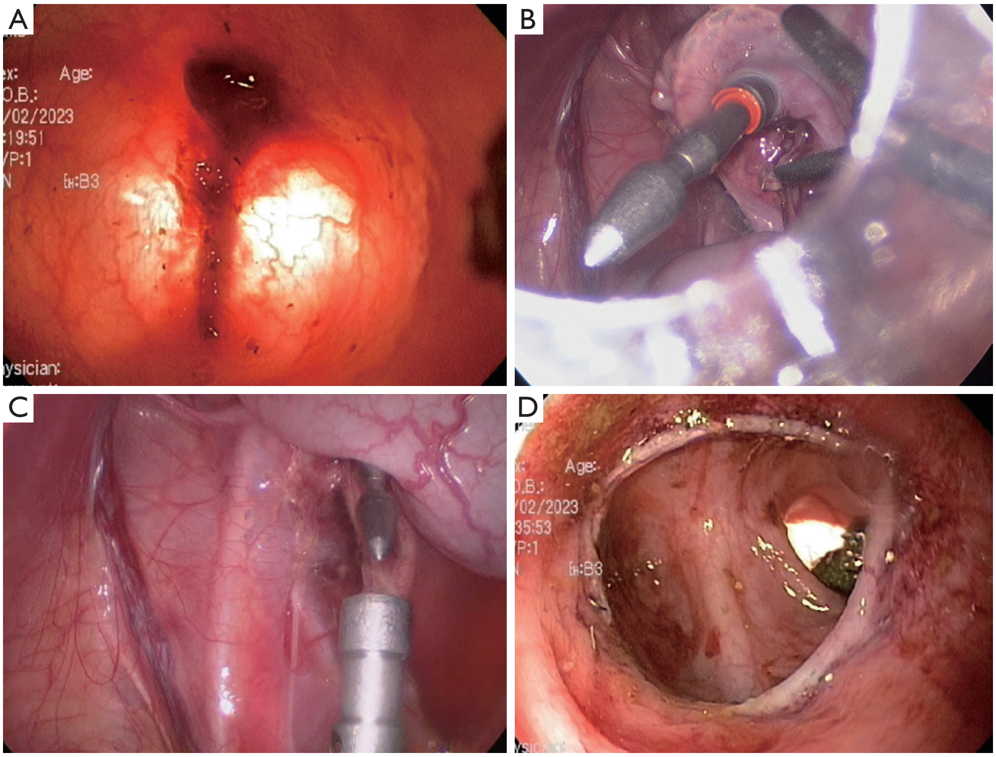


Figure 4 Colorectal anastomosis creation and endoscopic evaluation. (A) Endoscopic view of intact rectal stump staple line without evidence of leak prior to anastomosis. (B) Deploying of stapler pin through rectal stump corner. (C) Guiding of stapler pin into anvil center rod for anastomosis creation. (D) Endoscopic evaluation of newly created circular stapled colorectal anastomosis demonstrating patency without evidence of leak.

performing this technique should consider. In general, early mobility after surgery is encouraged with the recommendation that the animal return to normal species-typical behavior without restriction on the day of surgery. After the effects of general anesthesia have worn off, early intake of fluids and solid foods are encouraged as there should be little concern for ileus or oral intake intolerance after this procedure. The animal should receive adequate analgesia with a multi-modal approach to limit the need for opioids which should also aid in early return of function and gut motility. While early postoperative blood spotting of stool may be seen, this should not persist and suggests bleeding from the anastomosis. This is usually self-limited, and may require repeat colonoscopy for evaluation to achieve hemostasis.

Fever and significant abdominal pain to palpation may be indicative of infection or possible AL. General malaise, fatigue, anorexia, and elevated heart rate may also be signs and symptoms of intraabdominal infection in NHPs.

Tips and pearls

During insufflation, the hemodynamic and respiratory status of the animal should be closely monitored—if needed, the insufflation pressure can be reduced or intermittent breaks in insufflation can be employed to allow for proper compensation by the animal.

An additional 5 mm assistant port can be placed in the left lower quadrant to facilitate retraction and visualization by the surgical assistant.

Finger dilation of the anus may help in facilitating safe passage of the circular stapler.

An esophagogastroduodenoscopy (EGD) endoscope may be used to assess the colorectal anastomosis rather than the larger colonoscope in the NHP.

If endoscopy is not available, an air-leak test can by inserting a Toomey syringe in the anal canal and insufflating the rectum until it is clearly distended.

Discussion

Laparoscopic sigmoid colectomy with primary anastomosis in an NHP can be performed similarly as in the clinical setting and represents a useful preclinical model for studying the effects of various experimental conditions on physiology, host immune-microbiome interactions, and tissue healing. As an experimental model, NHPs have been used to further our knowledge on multiple diseases such as diabetes, Parkinson's disease, venous thrombosis, and asthma while also accurately simulating the surgical scenario for metabolic surgery, transplantation, and medical device validation (32-37). In the context of anastomotic healing, the NHP model has the advantage of closely mimicking the clinical situation from pre-operative ingestion of bowel preparation and antibiotics to the surgical technique including the use of standard equipment, as well as post-operative management and testing. With the shift in surgical training toward minimally invasive techniques such as laparoscopy rather than open surgery, a model capable of embracing current surgical practices is vital for translational benefit. The NHP model also allows for removal of major confounders including comorbidities, diet, smoking and alcohol use, all of which are known to impact the gut microbiome and host immunity (15,38). In contrast, the variability in these confounders is difficult to control in human patients making interpretations of microbial and immune studies challenging.

While patient management and surgical techniques have improved, anastomotic complications and surgical site infection (SSI) still impact 14–27% of colorectal operations (39,40), resulting in significant morbidity and cost to the patients and healthcare system. In recognition of these problems, numerous strategies have been tried to improve these outcomes with the most recognized protocol being surgical bowel preparation using a concomitant mechanical bowel preparation (MBP) and oral antibiotics (OA) prior to colon surgery (41). The proposed role of MBP is to reduce fecal impaction at the anastomosis thus reducing tension and possibly ischemia, while OA reduce intestinal bacterial density. Multiple studies have demonstrated decreased rates of AL and SSI with their use (42-45). Despite this, the underlying mechanisms behind the efficacy of SBP is unknown and represents a fundamental gap in knowledge. This presents a unique opportunity to gain valuable mechanistic insight into investigating a therapy that is clinically efficacious with the help of a proper experimental model, such as the NHP model. Aside from the obvious physical constraints in experimental surgery, the mouse model is unable to capture the complex interplay between the host immune system, microbiome, diet, drug and antibiotic interactions necessary for understanding the pathophysiology of AL and SSI in colon surgery. The NHP model can capture this with the potential for scalability and translation to the clinical setting.

Despite the strengths of this animal model and technique for experimental colon surgery, there are limitations in relation to costs and the researcher's experience level. Having a functional operating suite for experimental surgery has significant initial costs related to procuring the proper equipment. In addition, having laparoscopic as well as endoscopic capabilities is another substantial cost that the researcher should thoroughly investigate prior to initiating studies of this kind. There are some ways to minimize these equipment costs: performing a hand-sewn or linear stapled anastomosis rather than utilizing a more expensive circular EEA stapler or performing an air-leak test by injecting air into the anal canal with a syringe rather than an endoscope. As with any surgery, there is a learning curve to performing a safe and productive procedure. While many experimental surgeons have some degree of familiarity with open approaches, laparoscopic surgery is not as common in the experimental setting and does take time to familiarize with the equipment and techniques. Furthermore, the research and surgical team must also have a significant understanding of the equipment and procedures to adequately assist in real time.

Conclusions

Laparoscopic sigmoid colectomy with primary anastomosis can be performed in an NHP model using techniques and equipment that mirror the surgical and perioperative approach in human patients. However, as with any experimental surgical model, this NHP laparoscopic colectomy model must be carefully considered before applying it to a clinical problem, ensuring it has the capability to answer the research question and identifying any discrepancies in relevant physiology, anatomy, or environmental factors. In the correct context, this model can be used to study various diseases of the colon and their surgical therapies with high predictive value and applicability to the clinical situation.

Acknowledgments

The authors gratefully acknowledge the excellent and expert

contributions of the University of Minnesota's Preclinical Research Center team.
Funding: This study was funded by the Goodale Chair Endowment awarded to Principal Investigator M.L.G. at the University of Minnesota.

Footnote

Reporting Checklist: The authors have completed the SUPER reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-24-25/rc

Peer Review File: Available at https://atm.amegroups.com/article/view/10.21037/atm-24-25/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-24-25/coif). M.L.G. holds the endowed Robert and Katherine Goodale Chair in Minimally Invasive Surgery which was appointed by the Department of Surgery at the University of Minnesota. The endowment is to be used at the Chairperson's discretion, therefore M.L.G. used it to fund this work. There is no third-party interest. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Experiments were performed under a project license (No. 2103-38932A) granted by the University of Minnesota Institutional Animal Care and Use Committee (IACUC), in compliance with the Animal Welfare Act, adhered to principles stated in the NIH Guide for Care and Use of Laboratory Animals, and were performed and reported in compliance with the ARRIVE guidelines.

References

1. Society of Gastrointestinal and Endoscopic Surgeons. Colon resection surgery patient information from SAGES. 2015 [Jan 2024]. Available online: https://www.sages.org/publications/patient-information/patient-information-for-laparoscopic-colon-resection-from-sages/
2. Guller U, Jain N, Hervey S, et al. Laparoscopic vs open colectomy: outcomes comparison based on large nationwide databases. Arch Surg 2003;138:1179-86.
3. Steele SR, Brown TA, Rush RM, et al. Laparoscopic vs open colectomy for colon cancer: results from a large nationwide population-based analysis. J Gastrointest Surg 2008;12:583-91.
4. Chai N. Endoscopy and Endosurgery in Nonhuman Primates. Vet Clin North Am Exot Anim Pract 2015;18:447-61.
5. Krarup PM, Nordholm-Carstensen A, Jorgensen LN, et al. Association of Comorbidity with Anastomotic Leak, 30-day Mortality, and Length of Stay in Elective Surgery for Colonic Cancer: A Nationwide Cohort Study. Dis Colon Rectum 2015;58:668-76.
6. Guyton KL, Hyman NH, Alverdy JC. Prevention of Perioperative Anastomotic Healing Complications: Anastomotic Stricture and Anastomotic Leak. Adv Surg 2016;50:129-41.
7. Boatman S, Kaiser T, Nalluri-Butz H, et al. Diet-induced shifts in the gut microbiota influence anastomotic healing in a murine model of colonic surgery. Gut Microbes 2023;15:2283147.
8. Tonini V, Zanni M. Impact of anastomotic leakage on long-term prognosis after colorectal cancer surgery. World J Gastrointest Surg 2023;15:745-56.
9. Kumar A, Daga R, Vijayaragavan P, et al. Anterior resection for rectal carcinoma - risk factors for anastomotic leaks and strictures. World J Gastroenterol 2011;17:1475-9.
10. Davis B, Rivadeneira DE. Complications of colorectal anastomoses: leaks, strictures, and bleeding. Surg Clin North Am 2013;93:61-87.
11. Bakker IS, Grossmann I, Henneman D, et al. Risk factors for anastomotic leakage and leak-related mortality after colonic cancer surgery in a nationwide audit. Br J Surg 2014;101:424-32; discussion 432.
12. Zarnescu EC, Zarnescu NO, Costea R. Updates of Risk Factors for Anastomotic Leakage after Colorectal Surgery. Diagnostics (Basel) 2021;11:2382.
13. He J, He M, Tang JH, et al. Anastomotic leak risk factors following colon cancer resection: a systematic review and

meta-analysis. Langenbecks Arch Surg 2023;408:252.
14. Boatman S, Kohn J, Jahansouz C. The Influence of the Microbiome on Anastomotic Leak. Clin Colon Rectal Surg 2023;36:127-32.
15. Nalluri-Butz H, Bobel MC, Nugent J, et al. A pilot study demonstrating the impact of surgical bowel preparation on intestinal microbiota composition following colon and rectal surgery. Sci Rep 2022;12:10559.
16. Williamson AJ, Alverdy JC. Influence of the Microbiome on Anastomotic Leak. Clin Colon Rectal Surg 2021;34:439-46.
17. Guo MY, Liu J, Balmes P, et al. Effects of diet and antibiotics on anastomotic healing: A mouse model study with varied dietary fiber and fat, and pre-operative antibiotics. Am J Surg 2024;S0002-9610(24)00274-5.
18. Hajjar R, Gonzalez E, Fragoso G, et al. Gut microbiota influence anastomotic healing in colorectal cancer surgery through modulation of mucosal proinflammatory cytokines. Gut 2023;72:1143-54.
19. Komen N, van der Wal HC, Ditzel M, et al. Colorectal anastomotic leakage: a new experimental model. J Surg Res 2009;155:7-12.
20. Pommergaard HC, Achiam MP, Rosenberg J. Colon anastomotic leakage: improving the mouse model. Surg Today 2014;44:933-9.
21. Slieker JC, Vakalopoulos KA, Komen NA, et al. Prevention of leakage by sealing colon anastomosis: experimental study in a mouse model. J Surg Res 2013;184:819-24.
22. Zamorano D, Ivulic D, Viver T, et al. Microbiota Phenotype Promotes Anastomotic Leakage in a Model of Rats with Ischemic Colon Resection. Microorganisms 2023;11:680.
23. Jiminez JA, Uwiera TC, Douglas Inglis G, et al. Animal models to study acute and chronic intestinal inflammation in mammals. Gut Pathog 2015;7:29.
24. 't Hart BA, Bogers WM, Haanstra KG, et al. The translational value of non-human primates in preclinical research on infection and immunopathology. Eur J Pharmacol 2015;759:69-83.
25. Estes JD, Wong SW, Brenchley JM. Nonhuman primate models of human viral infections. Nat Rev Immunol 2018;18:390-404.
26. National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals. Guide for the Care and Use of Laboratory Animals. 8th edition. Washington, DC, USA: The National Academies Press; 2011.
27. Afors K, Centini G, Murtada R, et al. Obesity in laparoscopic surgery. Best Pract Res Clin Obstet Gynaecol 2015;29:554-64.
28. Briggs A, Goldberg J. Tips, Tricks, and Technique for Laparoscopic Colectomy. Clin Colon Rectal Surg 2017;30:130-5.
29. Schultz AH. Sex differences in the pelves of primates. Am J Phys Anthropol 1949;7:401-23.
30. Graham ML, Rieke EF, Mutch LA, et al. Successful implementation of cooperative handling eliminates the need for restraint in a complex non-human primate disease model. J Med Primatol 2012;41:89-106.
31. Palmer S, Oppler SH, Graham ML. Behavioral Management as a Coping Strategy for Managing Stressors in Primates: The Influence of Temperament and Species. Biology (Basel) 2022;11:423.
32. Blesa J, Trigo-Damas I, Del Rey NL, et al. The use of nonhuman primate models to understand processes in Parkinson's disease. J Neural Transm (Vienna) 2018;125:325-35.
33. Myers DD Jr. Nonhuman primate models of thrombosis. Thromb Res 2012;129 Suppl 2:S65-9.
34. Nugent JL, Singh A, Wirth KM, et al. A nonhuman primate model of vertical sleeve gastrectomy facilitates mechanistic and translational research in human obesity. iScience 2021;24:103421.
35. Oppler SH, Hocum Stone LL, Leishman DJ, et al. A bioengineered artificial interstitium supports long-term islet xenograft survival in nonhuman primates without immunosuppression. Sci Adv 2024;10:eadi4919.
36. Phillips KA, Bales KL, Capitanio JP, et al. Why primate models matter. Am J Primatol 2014;76:801-27.
37. Shin JS, Kim JM, Kim JS, et al. Long-term control of diabetes in immunosuppressed nonhuman primates (NHP) by the transplantation of adult porcine islets. Am J Transplant 2015;15:2837-50.
38. Zádori ZS, Király K, Al-Khrasani M, et al. Interactions between NSAIDs, opioids and the gut microbiota - Future perspectives in the management of inflammation and pain. Pharmacol Ther 2023;241:108327.
39. Wick EC, Hobson DB, Bennett JL, et al. Implementation of a surgical comprehensive unit-based safety program to reduce surgical site infections. J Am Coll Surg 2012;215:193-200.
40. Young H, Knepper B, Moore EE, et al. Surgical site infection after colon surgery: National Healthcare Safety Network risk factors and modeled rates compared with published risk factors and rates. J Am Coll Surg 2012;214:852-9.

41. Nichols RL, Broido P, Condon RE, et al. Effect of preoperative neomycin-erythromycin intestinal preparation on the incidence of infectious complications following colon surgery. Ann Surg 1973;178:453-62.
42. McSorley ST, Steele CW, McMahon AJ. Meta-analysis of oral antibiotics, in combination with preoperative intravenous antibiotics and mechanical bowel preparation the day before surgery, compared with intravenous antibiotics and mechanical bowel preparation alone to reduce surgical-site infections in elective colorectal surgery. BJS Open 2018;2:185-94.
43. Midura EF, Jung AD, Hanseman DJ, et al. Combination oral and mechanical bowel preparations decreases complications in both right and left colectomy. Surgery 2018;163:528-34.
44. Scarborough JE, Mantyh CR, Sun Z, et al. Combined Mechanical and Oral Antibiotic Bowel Preparation Reduces Incisional Surgical Site Infection and Anastomotic Leak Rates After Elective Colorectal Resection: An Analysis of Colectomy-Targeted ACS NSQIP. Ann Surg 2015;262:331-7.
45. Hansen RB, Balachandran R, Valsamidis TN, et al. The role of preoperative mechanical bowel preparation and oral antibiotics in prevention of anastomotic leakage following restorative resection for primary rectal cancer - a systematic review and meta-analysis. Int J Colorectal Dis 2023;38:129.

Cite this article as: Leishman DJ, Oppler SH, Graham ML, Jahansouz C. Laparoscopic sigmoid colectomy with primary anastomosis for experimental modeling in the nonhuman primate. Ann Transl Med 2024;12(5):93. doi: 10.21037/atm-24-25

