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End-to-End Compression Anastomosis of The Rectum: A Pig Model

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Abstract

Background: Generations of investigators have attempted to achieve compression bowel anastomosis by a sutureless device, providing temporary support to the tissue and facilitating the natural healing process. The biocompatibility of nickel–titanium alloy has made it attractive for use in medical implants and devices, and several studies have described the creation of a side-to-side compression anastomosis in colon surgery with a nickel–titanium clip. We evaluated the feasibility and safety of a newly designed gun for applying a nickel–titanium compression anastomosis ring (CAR) to create an end-to-end colorectal anastomosis in a porcine model.

Materials and methods: A segment of the proximal rectum was resected in 25 pigs. The bowel ends were anastomosed transanally by an end-to-end CAR device. The animals' *follow-up continued for up to 8 weeks, and included general health status, weight gain, blood tests, and abdominal X-ray. They were then sacrificed. The anastomoses were studied for burst pressure, anastomotic index, and histopathology.*

Results: One pig died due to iatrogenic bowel injury unrelated to the CAR device. There was no other morbidity/mortality. The other animals recovered and gained weight. Burst pressure studies demonstrated a minimum pressure of 160 mmHg at time point 0 that escalated quickly to >300 mmHg. The mean anastomotic index after 8 weeks was 0.81. Histologic evaluation revealed minimal inflammation and minimal fibrosis at the anastomosis site.

Conclusion: The principles of compression anastomosis are better executed with the use of memory shape alloys. The promising results of this novel technique should encourage further studies of this technology.

The quality of a colorectal anastomosis is a major factor in determining the rates of morbidity and mortality of colorectal bowel resections. There is still no ideal method for creating these anastomoses. The principles of bowel anastomosis were laid down in the 19th century by several surgeons. Billroth in Vienna performed bowel anastomosis for the first time in 1881 by manually suturing the bowel.[1] In 1892, Murphy [2] introduced a mechanical device for bowel compression anastomosis; it consisted of 2 metal rings that held circular segments of the intestine under continuous pressure, leading to tissue necrosis. The rings were expelled after a few days. Since

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that time, many attempts have been made to develop the concept of compression of the 2 bowel edges by a sutureless device, providing temporary support to the tissue, preventing leakage and facilitating the natural healing process in the compressed region. It was not until 1985 that Hardy *et al.*[3] published the details of a biofragmentable anastomotic ring (BAR) device (Sherwood-Davis & Geck, St. Louis, MO, USA). The BAR was made of 2 identical rings composed of absorbable polyglycolic acid and 12.5% barium sulfate to render it radiopaque. The 2 rings had a scalloped shape, similar to that of the Murphy button, but with a 1.5–2.5-mm gap between the 2 rings in the closed position to prevent tissue ischemia.[3–7] One century after Murphy's work, the use of metal staplers was introduced and gained popularity mainly due to the rapidity of its performance and reproducibility, in spite of the fact that, like sutures, staples act as foreign bodies, causing inflammation and interfering with the healing process.[1,8]

Nickel–titanium alloy has been widely accepted for use in medical implants and devices due to its biocompatibility.[9] Several studies have described the creation of a side-to-side compression anastomosis in colon surgery with a nickel–titanium clip (the compression anastomosis clip, CAC). Over 200 procedures have been successfully performed using this technology.[10–12] The side-to-side CAC anastomosis, however, still requires suture closure of the enterotomies through which the CAC is introduced. The aim of the current study was to evaluate the safety and feasibility of a recently designed gun that applied new technology to old and well-known principles of compression anastomosis. The novel system applies a nickel–titanium compression anastomosis ring (CAR) to create a sutureless end-to-end colorectal anastomosis, and we tested its utility in a porcine model.

MATERIALS AND METHODS

Animal Care

Twenty-four healthy female pigs, *Sus scrofa domestica*, 3.5 months old, weighing 36–42 kg were used in this study, which was conducted in full accordance with the principles and authorization of the local Helsinki IRB for animal studies (Approval No. 010304). A restricted commercially available pig-mix (dry sow mix, Nir Oz Mixture Institute, Israel) diet was given to them 48 hours prior to surgery and 72 hours afterwards, during which solid food was replaced by liquid diet and sweetened water. The gastrointestinal tract of the animals had been prepared and cleansed with soffodex solution and a cleansing enema was administered 2 hours before surgery. Concomitantly with the induction of anesthesia, a single dose of prophylactic antibiotics (cefazolin [30 mg/kg] and Vetrimoxin [3.5 ml]) was given intravenously. Premedication and induction of anesthesia were achieved by intramuscular injection of diazepam (2 mg/kg), xylazine (1.5 mg/kg), and ketamine 10 mg/kg, oro-tracheal intubation, and halothane (5%). Maintenance of anesthesia was by spontaneous breathing of oxygen (2 l/min) enriched by halothane (0.8%–2%). The pigs were infused during the procedure with 10 cc/kg/h of crystalloids.

Compression Anastomosis Device

The compression anastomosis device (NiTi Medical, Netanya, Israel) is a ring made of nickel–titanium alloy that is loaded to the main body of the device after being immersed in icy saline solution (Fig. 1). The initial diameter of the ring is 17.2–17.6 mm and it is expanded to 28.0 mm as the ring is being loaded onto the device. A detachable anvil made of a polyethylene ring is inserted into the proximal bowel lumen and secured by a purse-string suture. The main body of the instrument is inserted transanally up to the stapled end of the rectum. A thin trocar emerges from the instrument's shaft to pierce the distal stapled end of the rectum. This trocar shaft is assembled to the shaft of the detachable head by sliding one into the other. The 2 parts of the device together with both ends of the transected bowel are approximated by rotating an adjusting knob at the extra-anal part of the main body of the device. The anvil pushes the proximal bowel end into the closed distal lumen creating a very short (1 cm) segment of bowel-wall inversion. The final turning of the knob releases the nickel–titanium ring and the ring closes to its predetermined shape while being deployed over the anvil's plastic ring, with the walls of the 2 bowel ends compressed against each other between both rings (Fig. 2). A compression anastomosis is thus created between the plastic anvil ring and the nickel–titanium ring. Squeezing the gun's handle at this stage activates an inner circular knife, which cuts through the line of staples and the inner edges of the 2 bowel ends. This enables the extraction of the instrument, leaving behind the 2 compressing rings joining together the 2 bowel ends by uniform circular pressure over the tissue. The process of pressure necrosis and healing detaches the rings from the lumen of the rectum after a few days, and the device is expelled naturally.

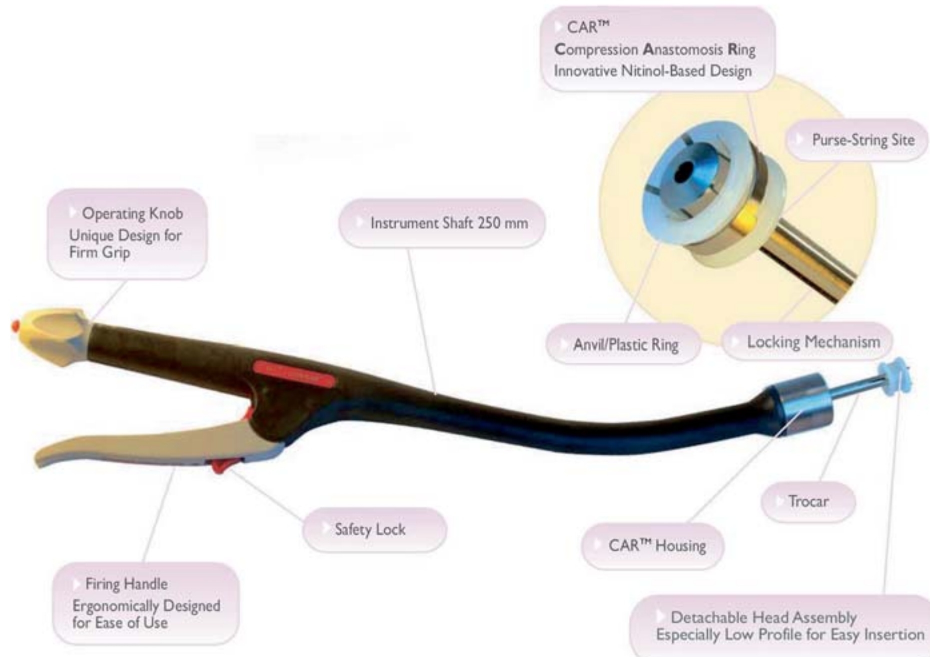

Figure 1. A schematic representation of the compression anastomosis ring (CAR) device for performing end-to-end bowel anastomosis.

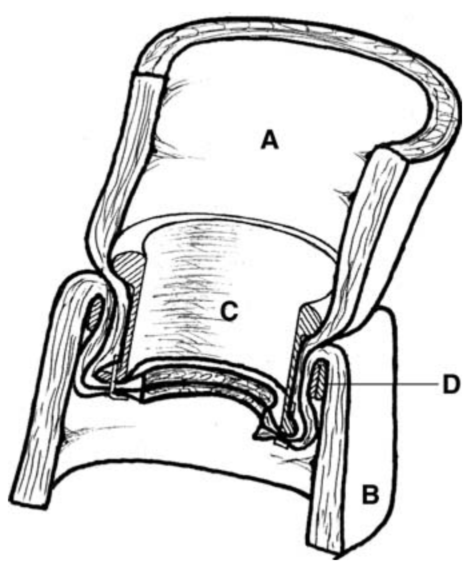

Figure 2. A schematic presentation of the compression anastomosis rings (CARs) compressing both bowel ends to each other in a co-axial fashion: **A.** proximal bowel end, **B.** distal bowel. **C.** inner plastic ring of the anvil, **D.** Nitinol ring.

Surgery

Through a midline laparotomy, the proximal rectum was transected by a linear cutter after ligation of the appropriate mesentery. A short segment (2–5 cm long) of the proximal rectum was resected. Anastomosis was carried out by transanal application of a co-axial CAR device (Fig. 3). In 9 animals, this newly created anastomosis was resected along with a 20-cm segment of distal colon and proximal rectum for immediate visual evaluation of the anastomosis and for carrying out burst pressure studies at time 0. The 2 bowel ends were anastomosed again by using the same method with a new device. A colorectal end-to-end anastomosis was performed. No additional sutures were used to reinforce the anastomosis.

Follow-up

The pigs were allowed to recover and were followed daily by an experienced veterinarian. The clinical follow-up evaluation included the general health status and extent of weight gain. During the 72 hours following the procedure, the animals received tap water and a liquid diet. Regular chow dissolved in water was started on the 4th postoperative day. The subsequent follow-up included behavioral evaluation, gastrointestinal tract function, blood samples on days 3 and 6 and an abdominal X-ray 4 days postoperatively. The rings were retrieved and evaluated after expulsion. The pigs were sacrificed after different time points, between 0 and 8 weeks postoperatively. According to the study protocol, 10 pigs were sacrificed after 12–14 days, 7 pigs after 3 weeks and 6 pigs after 2 months. During the second operation, just before sacrificing the animal, the abdominal cavity was

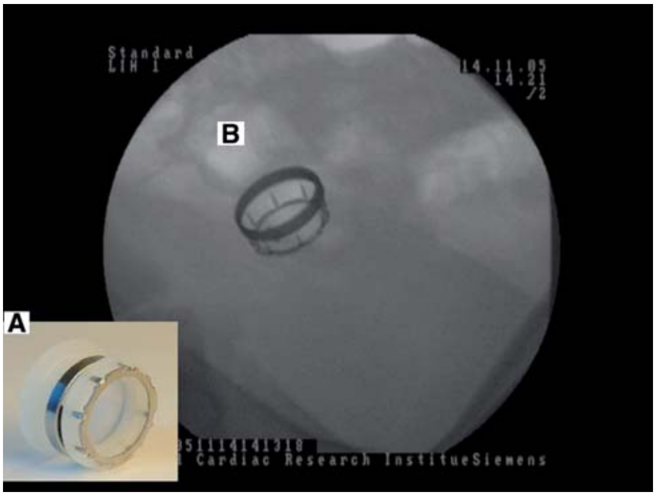

Figure 3. Plane lower abdomen X-ray showing the compression anastomosis rings (CARs) in the rectum on the 4th postoperative day following rectal resection and anastomosis in a pig. *Left lower corner*: the CAR rings after firing the instrument (without bowel).

evaluated for signs of possible infection, leaks or bowel obstruction. The anastomotic segment was resected and the anastomotic burst pressure was measured as previously described.[13] The anastomotic index was calculated in 5 pigs that were autopsied 2 months after the creation of the anastomosis.[14] All the segments were histopathologically examined.

RESULTS

All the animals but 1 fully recovered from the operation. One pig died from severe septic shock 9 days after the surgical procedure and was operated on post-mortem: its abdominal cavity was carefully evaluated and the rectal segment with the anastomosis was resected and examined extra-corporeally. The autopsy findings revealed an iatrogenic thermal injury to the spiral colon, 30 cm proximal to the anastomosis, not noted during the operation, which had resulted in perforation and severe fecal peritonitis. The anastomosis was clean and intact, and the compression rings were still present in the anastomotic site. There was no evidence of morbidity in the other 24 animals. They all exhibited normal behavior and normal gastrointestinal tract function during the recovery period and gained weight as expected. Postoperative blood counts were within normal limits. Abdominal X-rays from the 4th postoperative day demonstrated normal gas distribution, and the CAR was detected in the proximal rectum until its expulsion with the feces. The rings were found in the stool after 6–11 days (mean: 8.54 days):

Table 1.
Measurements

Time	Number of tests (performed in 23 animals)	Burst pressure range, mmHg (mean)	Anastomotic index
0	9[a]	160–300 (247.7)	
2 weeks	10	270–300 (295.7)	
3 weeks	7	210–300 (264.0)	
2 months	6	Over 300 (<300)	0.60–0.92 (0.81)

[a]Time 0 burst pressure measurements were performed in resected bowel segments of pigs that were immediately re-anastomosed and further followed for different periods.

they were evaluated visually and appeared to be intact and undamaged, and contained remnants of necrotic tissue compressed between both the plastic anvil and the nickel–titanium rings. The post-procedure laparotomies, prior to sacrifice, revealed a clean and normal peritoneal cavity, with a relatively mild degree of adhesion in the pelvic area. The anastomotic site could barely be recognized visually or by palpation. A 20-cm-long segment of the large bowel and rectum, from both sides of the anastomosis and including the anastomotic site within it, was resected for evaluation. At that stage, the animals were compassionately euthanized. The burst pressure of the anastomosis was measured in all animals (Table 1). The anastomotic index was calculated as the ratio of the mean bowel diameter 5 cm proximal and distal to the anastomosis, and the mean anastomotic diameter was measured on the anterior–posterior and lateral views of standard barium images of the resected bowel segment. Standard pressure of the barium solution within the resected segment was achieved by raising the barium reservoir 100 cm above the bowel segment. Measurements (Fig. 4) were carried out only in the long-term group of animals (Table 1). The histopathological examination revealed normal bowel patterns of all rectal layers, both proximally and distally to the anastomotic site itself. Histopathological examination of the anastomotic site after 2 weeks revealed evidence of good and uniform healing processes with minimal inflammation. The anastomotic line was represented by a very thin transmural circular band of fibrosis and granulation tissue with moderate leukocyte infiltrate in the muscularis. There was good alignment of the respective rectal layers (Fig. 5). Re-epithelialization could be detected after 3 and 4 weeks, and the mucosa appeared to be continuous in parts of the circumference, with mild lymphocyte infiltrate. Minimal focal fibrosis was present, with no evidence of inflammation, 2 months after the procedure. A thin scar was almost invisible 3 weeks after the procedure (Fig. 6).

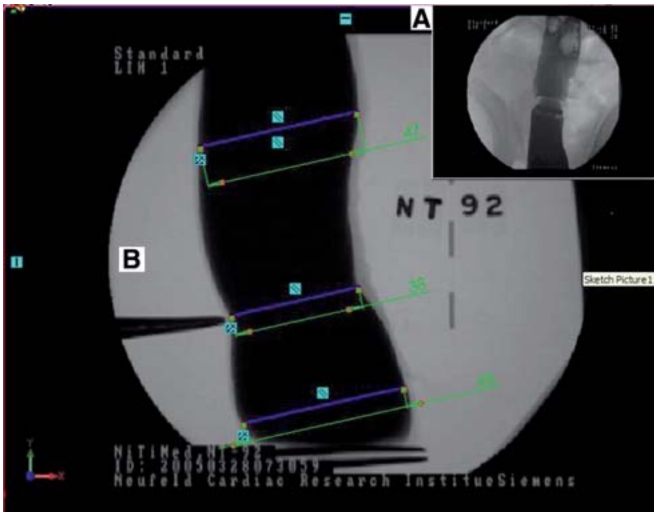

Figure 4. **A.** *Right upper corner* Lower abdominal X-ray with intraluminal contrast demonstrating a patent anastomosis with the compression anastomosis rings (CARs) in the anastomotic site. **B.** Anastomotic index measurements 8 weeks after rectal resection and anastomosis using a CAR.

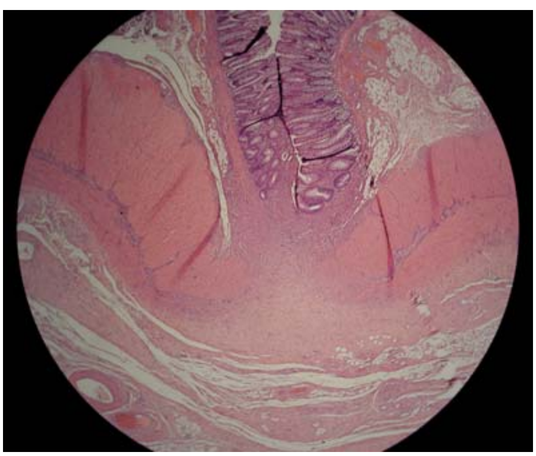

Figure 5. Histopathology of the compression anastomotic line 8 weeks after its creation, showing a delicate submucosal fibrotic area.

Figure 6. Macroscopic view of the compression anastomotic line 3 weeks after surgery.

There was no sign of micro-abscesses, necrosis or giant cell reaction to foreign material in any of the specimens.

DISCUSSION

This animal study was designed to evaluate the feasibility, safety, and preliminary efficacy of a memory shape alloy device for achieving transanal end-to-end compression anastomosis. We conducted the investigation on healthy animals who had no gastrointestinal illness or evidence of tumoral, obstructive, inflammatory or ischemic pathologies of the kind that could lead to surgical interventions in humans. One pig died due to severe postoperative intra-abdominal sepsis. The post-mortem autopsy revealed a perforation in its spiral colon, 30 cm proximal to the rectal anastomosis. The anastomosis itself was intact and uninvolved in the septic process, with no visible signs of a stricture. We concluded that this complication was due to accidental damage to the spiral colon, which was not noted during the procedure. We had considered that the perforation might have been related to the device itself and to the creation of the anastomosis, but concluded that this would be highly unlikely because the application of the CAR device involves only the insertion of the anvil to the proximal bowel end, with the rest being performed mostly transanally.

The only potential source of pressure within the alimentary tract is due to peristaltic activity, which exerts an average sustained intraluminal pressure of 22 mmHg.[15] Following gastrointestinal surgery, peristaltic activity, if present, is minimal. Burst pressure measurements indicated the creation of airtight anastomoses at time 0, at the time of clip expulsion, 2–3 weeks after the procedure, and 1–2 months after the procedure. It is noteworthy that the burst pressures recorded in this animal study exceed the pressures typically associated with peristalsis by a factor > 6, indicating that the CAR device creates a safe anastomosis. The mean expulsion time of the compression rings was 8.5 days (range 5–11 days). This value represents the length of mechanical support exerted on the anastomotic site during the post-procedural period. It appears highly likely that the most vulnerable period of compression anastomosis would be immediately after the mechanical support of the device is no longer present. The burst pressure measurements taken in 5 pigs very close to that time, however, revealed relatively high pressures, similar to those measured after longer periods of time. There was neither incidence of anastomotic leakage after the first procedure nor clinical or visual evidence of leakage during the re-laparotomy. The number of operated animals and the lack of comparative groups in the present study does not permit any conclusions to be drawn about leakage rates in CAR anastomoses. Nevertheless, the fact that CAR comprehensively supports the entire circumference of the anastomosis, with no inter-suture or inter-clip gaps, may prove to be an important advantage of the system.

The results of the histopathological evaluation, performed by an independent laboratory, were impressive. No tissue damage or abnormal reactions to the host intestinal tissues that could be related to the plastic anvil or to the nitinol rings, was observed. Moreover, there was a normal inflammation process typical of postoperative tissue reaction and an active healing process. As expected, there was evidence of granulation tissue formation (active scarring) in the submucosa and the muscularis. Both the macroscopic and the microscopic evaluations of the anastomosis exposed a very thin and delicate fibrotic line, with a slight inflammatory reaction in its region. Between 12 and 14 days following the procedure, it became difficult to visually identify the site of the anastomosis. In our opinion, these features should be attributed to the lack of any foreign material—neither suture material nor metal staples—within the anastomotic site, and to the gradual compression applied to the tissue of both sides of the anastomosed bowel. This is not the case with the various stapling technologies that crush the tissue and reinforce the crushed tissue with metal foreign bodies. We intend to challenge 2 other technologies, and are about to embark on a comparative, 2-armed prospective animal study. The anastomotic index that was calculated for our current long-term subgroup revealed patent anastomoses, often at a diameter close to the original dimensions of the bowel. The diameter of the compression rings themselves was less than 18 mm, but the compression anastomosis became dilated due to internal forces and minimal fibrosis, and the measured diameter of all the anastomoses after 2 months was more than double the initial diameter of the rings.

We conclude that the old and very well-known principles of compression anastomosis are better executed with the use of memory shape alloys. This device for end-to-end transanal anastomosis has several advantages over devices described previously: it exerts continuous equal pressure on the bowel wall until the healing process detaches the supporting rings and it is entirely sutureless. The results of this preliminary feasibility and safety animal study should encourage further exploration of this promising technology.

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