Role of magnetic compression power in esophageal anastomosis: an experimental study

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Aim

The aim of this study was to asses the role of magnetic power in creation of a complete watertight anastomosis between two created blind esophageal pouches with 3–4-cm distance between them in conditions similar to long-gap esophageal atresia (EA).

Background

Magnetic compression anastomosis (magnamosis) is the practice of using two disc-shaped magnets to form a sutureless anastomosis. It has been proved to be effective in stomach and intestine but has not been tested in esophagus with long-gap EA. To test this notion, a long-gap EA rabbit model was developed.

Materials and methods

A total of 10 New Zealand rabbits of age 8 weeks, weighing between 1.8 and 2 kg, were included. Animals underwent magnetic compression of the esophagus using two disc-shaped magnets after resection of a small segment, creating about 4-cm gap similar to EA. The rabbits survived for 7 days and received nutrition through PEG tube. After 7 days, rabbits were euthanized, and the esophagoesophageal anastomosis was evaluated by radiography, burst pressure test, and histopathology.

Results

Overall, two rabbits died intraoperatively owing to anesthesia adverse effects. Moreover, four rabbits died postoperatively: one rabbit died on the postoperative day 2 owing to esophageal leakage and mediastinitism and three rabbits developed excess oral secretions and respiratory distress and eventually died on postoperative day 4 owing to saliva aspiration and pneumonia. Only four rabbits survived at the end of the experiment. Of the four survived rabbits, three had a well-formed anastomosis. Burst tests showed no leak when injecting saline up to 30 mmHg.

Conclusion

Magnamosis is technically feasible for esophagoesophageal anastomoses. Esophageal gap more than 3–4-cm long requires elongation procedure first before the use of magnamosis.

Keywords:
esophageal atresia, magnamosis, magnetic compression anastomosis

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Introduction

The term congenital atresia of the esophagus describes a large group of variant malformations that share a defect of the esophageal continuity with or without a fistula to the trachea or to the bronchi. The incidence of an esophageal atresia (EA) with or without a fistula is ∼1 in 3000–4500 [1].

EA gross type A (long gap without tracheaesophageal fistula) is a rare and surgical challenging variation in EA that constitutes 7% of the children born with EA [2].

One of the most challenging tasks in pediatric surgery is to create a patent, generous, and watertight esophageal anastomosis in case of EA, especially when the ends come together under tension. The technological difficulty emanating from suturing in the narrow intrathoracic domain of young infants extends operating times and results in complications. For these patients, therefore, a secure and reproducible sutureless alternative would be advantageous for esophageal anastomosis, especially in combination with a minimally invasive approach [3].

A primary esophagoesophagostomy will almost always be impossible, and several surgical techniques to establish the continuity of the gut have been developed with small or large intestinal interposition,

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gastric tube or pull-up, and active elongation of the pouches as the most common [4].

All procedures carry an inherent high risk of postoperative complications and long-term functional problems. The incidence of subclinical musculoskeletal deformities after EA repair with muscle-sparing thoracotomy has recently been reported as high as 25% [5].

Magnetic compression leads to ischemia and devitalization of the interposed tissue, which would ultimately leave a suturefree anastomosis. This method is ideal for digestive tract full-thickness compression and facilitates surgery with impressive success as a quick and straightforward operation. Despite these rewards, magnetic compression anastomosis (MCA) has also been used for regeneration of the biliary tract, bilio-jejunostomy and pancreatico-jejunostomy, and intestinal anastomosis [6].

The work of Harrison and Ponsky resulted in the development of the latest anastomotic system noted in this report, and in the development of two models of EA in pigs [7,8].

The efficacy of magnetic gastrointestinal compression anastomosis in animal models and in the clinical setting has since been proved [9,10].

Case studies using magnetic compression anastomosis for primary esophageal anastomosis [11,12] or recalcitrant strictures [13,14] in children have also been reported.

No formal preclinical assessment of magnetic esophageal compression anastomosis has been published to date, however, and very little is understood about the timeline of magnetic anastomosis development, mechanical stability, subsequent anatomy, or histopathology [3].

To fill this vacuum, we performed an experimental analysis to build and test esophageal anastomoses in rabbits using specially built custom-made neodymium magnets.

Materials and methods

Animal welfare and ethics

The procedure was accepted by the Committee on the Ethics of Animal Studies at Menoufia University. The animals used in our experiment received humane treatment in strict accordance with the University of Menoufia's Animal Care and Use Committee. Both procedures were conducted under the anesthesia of xylazine and ketamine, and an attempt was made to alleviate animals' suffering.

Experimental animals

A total of 10 New Zealand white rabbits at the age of 8 weeks, weighing 1.8–2 kg, were obtained from a local seller and housed under controlled conditions, including a 12-h light–dark cycle and a temperature of 25±2°C, with free access to standard chow and water. Before the experiment, all rabbits were adaptively fed for 1 week.

Magnets characteristic and design

A disc-shaped neodymium N52 magnet, with an external magnet diameter of 8 mm and a thickness of 1 mm, has a vertical pull power of 0.39 kg.

The neodymium magnet is the most widely used type of magnets. It is a permanent magnet made from an alloy of neodymium, iron, and boron to form the $Nd_2Fe_{14}B$ tetragonal crystalline structure (Fig. 1) [15].

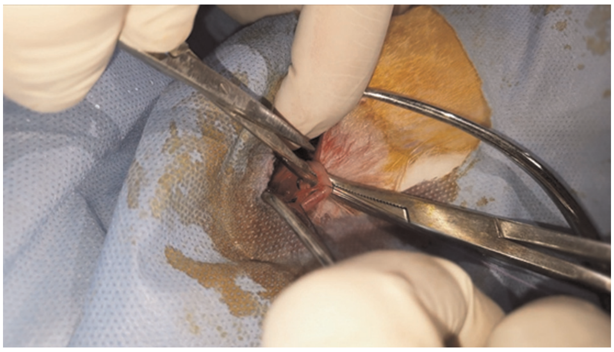
Surgical technique

Animals were anesthetized with xylazine (3–5 mg/kg, intramuscular administration) and ketamine (10–40 mg/kg intramuscular administration). Pulse oximetry, end-tidal CO_2, respiratory rate, temperature, and airway pressure were monitored intraoperatively. Fluids were administered (through an aural intravenous catheter normal saline, 10 ml/kg/h). The animals were fixed on an operating table after confirmation of the absence of the corneal reflex, and the right thoracotomy was performed with the animal in the left lateral decubitus position. The

Figure 1

Disc-shape neodymium N52 magnet with an external diameter of 8 mm and a thickness of 1 mm.

Figure 2



Esophagus was identified and hanged by two stay sutures and the esophagus was generously dissected both superiorly and inferiorly, and then excision of ~3–4-cm segment was done to create a gap.

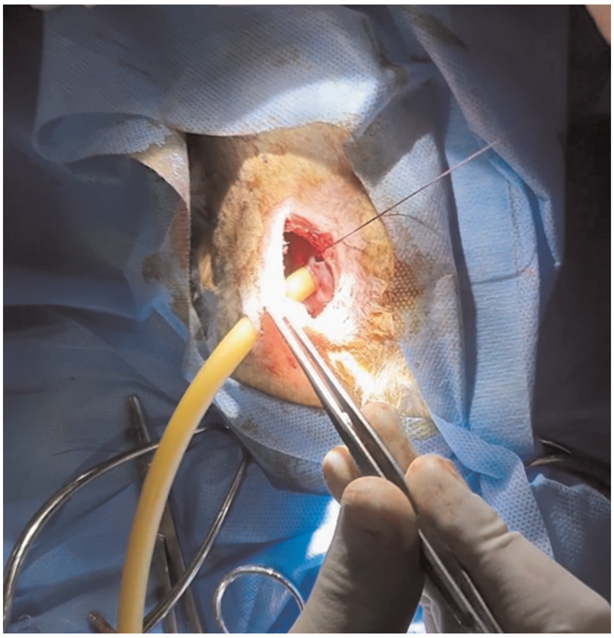
incision site was two rib spaces above the tip of the scapula. Dissection of subcutaneous tissue and splitting the intercostal muscles were done, and then esophagus was identified and hanged by two stay sutures. Thereafter, the esophagus was generously dissected both superiorly and inferiorly using blunt dissection, and care was taken to avoid injury to the anterior and posterior vagus nerve branches. Excision of about 3–4 cm segment was done to create a gap (Fig. 2), then two disc-shaped magnets were placed, one in the proximal end and the other in the distal end (Fig. 3). This was followed by closure of the proximal and distal esophageal ends, and a 24-Fr chest tube was placed through a separate stab incision in the right posterolateral chest. The ribs were approximated, muscle and fascia were closed, and the skin was closed with 4/0 vicryl simple sutures. After closing the thoracotomy wound, we placed the gastrostomy tube by opening a midline small incision, then dissected the subcutaneous tissues until the peritoneum, opened the peritoneum, hanged the stomach by burse sutures, incised the stomach wall, placed a 24-Fr gastrostomy tube, inflated the tube balloon by 5 cm normal saline, and fixed the tube to the stomach by the burse sutures and the inner abdominal wall by 2 vicryl 4/0 simple sutures, and then closed the wound by mass closure (Fig. 4).

From previous experiments, we predict the anastomosis to occur within 6–7 days. Therefore, rabbits were expected to be slaughtered after 7 days of surgery. Chest radiograph were conducted on the day of killing to record the magnet status and position in the esophagus. The esophagus was exposed to a burst pressure test after esophageal extirpation. Lastly, for histopathologic analysis, the anastomotic portion was fixed in formalin.

Figure 3

Placing two disc-shaped magnets, one in the proximal end and the other in the distal end.

Figure 4



Gastrostomy tube insertion and fixation.

Postoperative care

Rabbits were returned to their cages after recovery from anesthesia and fed manually by steadily administering the grinded water-soluble and liquid diet (protein 18%, raw fat 2.4%, and raw fibers 13.6%) three to four normal feedings to the target of feeding 100 ml/kg/day through the gastrostomy tube, and antibiotic (oxytetracycline 50 mg/kg body weight) was used in postoperative medicine. Painkillers (diclofenac sodium 1.5 mg/kg body weight) and famotidine (0.2 mg/kg) were given every 12 h during the experiment via the gastrostomy tube. On postoperative day 3, the chest tube was cut out.

Specimen collection

As the pairs of magnets fell off the anastomoses on day 7, the rabbits were euthanized by administering an anesthetic dosage of xylazine and ketamine again, then administering ~20 ml of air directly into the heart, then redoing the right thoracotomy and excising ~10 cm of the esophagus of the rabbits, including the anastomotic section, to assess the burst pressure and conduct histological examination.

Measuring the burst pressure

A catheter was placed at one end of the excised section of the esophagus and the other end was closed with silk. After a particular pressure gauge was attached, the pressure was assessed by saline injection until a bubble or blasting sound occurred. The burst pressure was deemed to be the measured pressure and registered.

Histological examination

The specimen was immediately fixed in formalin (10%). After fixation, tissue was embedded in paraffin and cut into 4-mm-thick sections at the site of the anastomosis. These sections were stained with hematoxylin–eosin and Masson's trichrome stain and examined under a light microscope.

Statistical analysis

Results were collected, tabulated, and statistically analyzed by an IBM compatible personal computer with SPSS statistical package version 23 (SPSS Inc. released 2015. IBM SPSS statistics for Windows, version 23.0; IBM Corp., Armonk, New York, USA). Descriptive statistics was expressed in number, percentage, mean, and range.

Results

Magnet localization, oral nutrition, and survival

(1) Magnets were found at their original location in three of four survived rabbits at the end of the experiment by day 7, but in the fourth survived rabbit, the distal magnet fell down to the stomach and lost in the rabbit's bowel.
(2) The survived rabbits tolerated the liquid gastrostomy feeds on postoperative day 1 and were noted to have gained weight. Mean weight gain for these rabbits was 50 g/day (range, 40–60 g/day) during the observation time (Table 1).
(3) Unfortunately, six (60%) of the 10 rabbits used in this study died either intraoperatively or in the early or late postoperative period.
(4) Overall, two rabbits died intraoperatively (20%) owing to dehydration and other adverse effects of the anesthesia, such as hypothermia, hypoglycemia, bradycardia, and respiratory depression.
(5) Moreover, four (40%) rabbits died postoperatively: one rabbit died postoperatively on day 2 owing to esophageal leakage leading to mediastinitis, and three rabbits developed excess oral secretions shortly after surgery and died owing to saliva aspiration and pneumonia on postoperative day 4.
(6) Only four (40%) rabbits survived to the end of the experiment and gave enough time for anastomosis to occur (Table 2).
(7) Upon initial placement of the magnets, there was an obvious gap between the magnets, and 5 min later, the gap had decreased significantly to 1 mm intraoperative in three rabbits, but with moderate tension on esophagus, indicating compression of the tissues and demonstrating the attractive forces of the magnets.
(8) Unfortunately, in the other seven rabbits, the magnets did not attract each other

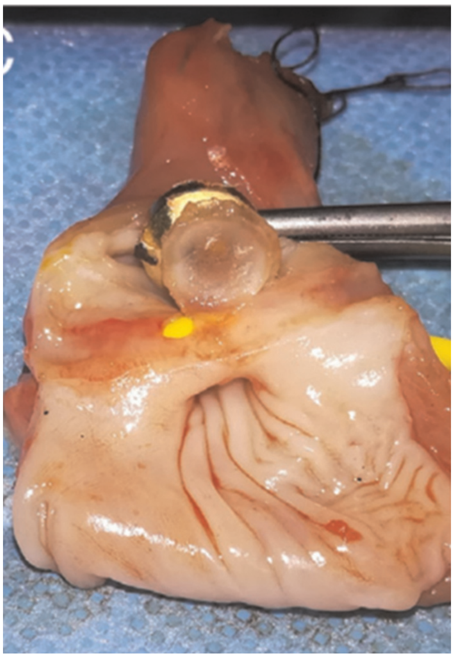
Table 1 Rabbits' observation interval and weight

Rabbit numbers	Observation interval (days)	Weight start (kg)	Weight end (kg)	Mean weight gain (g/day)
1	0	1.827	–	–
2	7	1.965	2.280	45
3	0	1.854	–	–
4	7	1.981	2.324	49
5	7	1.993	2.364	53
6	4	1.865	–	–
7	4	2	–	–
8	2	1.853	–	–
9	7	1.979	2.378	57
10	4	1.995	–	–
Mean	4.20	1.98	2.34	51
Minimum	0	1.97	2	45
Maximum	7	1.99	2	57

Table 2 Rabbits' survival and complication percent

Rabbit numbers	Complications (intraoperatively and postoperatively)	Survival
1	Yes (intraoperative)	No
2	No	Yes
3	Yes (intraoperative)	No
4	No	Yes
5	No	Yes
6	Yes (aspiration and pneumonia)	No
7	Yes (aspiration and pneumonia)	No
8	Yes (leakage and mediastinitis)	No
9	No	Yes
10	Yes (aspiration and pneumonia)	No
Percentage	60	Survival 40 Death 60

Figure 5



Careful dissection of one of the specimens harvested on postoperative day 7 with the magnet not yet detached and still *in situ*. The magnets are firmly embedded in the tissue. Between the firmly mated magnets is the necrotic tissue disk with the developing anastomotic lumen in the center.

intraoperatively and finally, at the end of the experiment, the magnets did not fulfill the anastomosis in one of the survived rabbits.

Postmortem macroscopic findings

Just three of the four remaining rabbits (30% of the total) had developed a patent anastomosis. In the anastomosis, the magnets in these three rabbits were located at the anastomosis level without full magnet detachment (Fig. 5), but in the other survived rabbit, the magnet in the distal pouch fell down distally to the stomach and was lost in rabbit's bowel. No esophageal necrosis was observed, and the anastomotic bridges were intact, with no leakage or inflammation (Table 3).

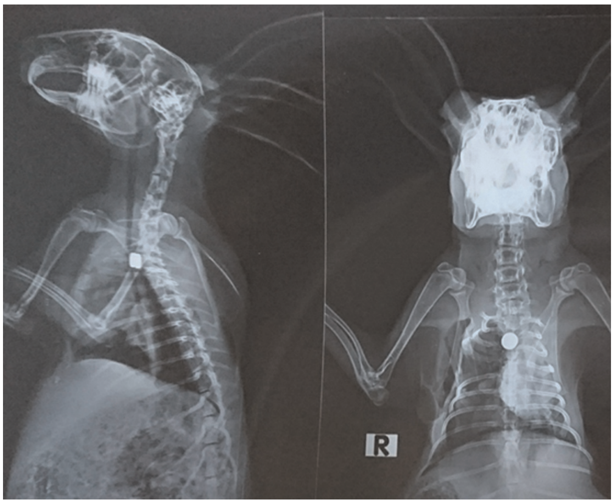
Radiographic evaluation

(1) At day 7, after euthanization of the four survived rabbits, chest radiograph was done to show the state and position of the magnets.
(2) In three rabbits on postoperative day 7, as seen in Fig. 6, the magnets were strongly attracted to each other without unintended separation at the site of the anastomosis, but in the other survived rabbit, the magnets were not attached to each other, where the proximal magnet was at the end of proximal pouch and the distal magnet was lost in the rabbits bowel.

Table 3 The experiment study outcome

Rabbits numbers	Formed anastomosis	Burst pressure (mmHg)	Patency by contrast radiograph
1	No	–	–
2	Yes	<30	Yes
3	No	–	–
4	No	–	No
5	Yes	<30	Yes
6	No	–	–
7	No	–	–
8	No	–	–
9	Yes	<30	Yes
10	No	–	–
Percentage	Formed anastomosis in 30	Burst pressure < 30 in 30	Patency in 30

Figure 6



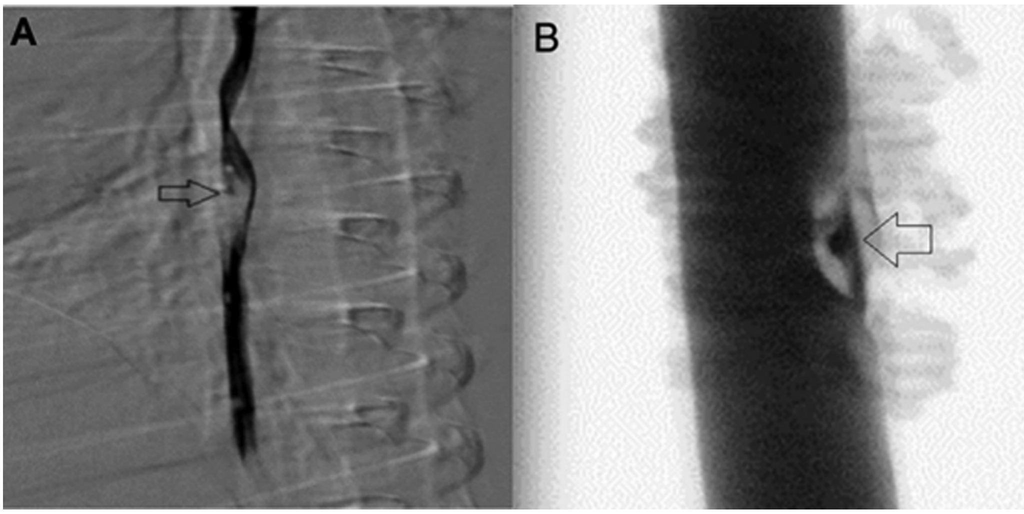
On postoperative day 7, the magnets were firmly attracted to each other with no accidental separation at the site of the anastomosis.

(3) Contrast esophagrams were performed and showed no leakage and free contrast passage in three rabbits with formed anastomoses (Fig. 7).
(4) However, in the other survived rabbit, there was blind-ended proximal esophageal pouch, no anastomosis was founded, and no passage of the contrast distally (Table 3).

Burst pressure test

Anastomosis was able to tolerate pressures above 30 mmHg without leakage. The pressure at which the anastomosis was disturbed was estimated at above 50 mmHg during the full burst pressure measurements. The disturbance was confined to the cranial part of the anastomotic zone in the burst pressure test (Table 3).

Figure 7



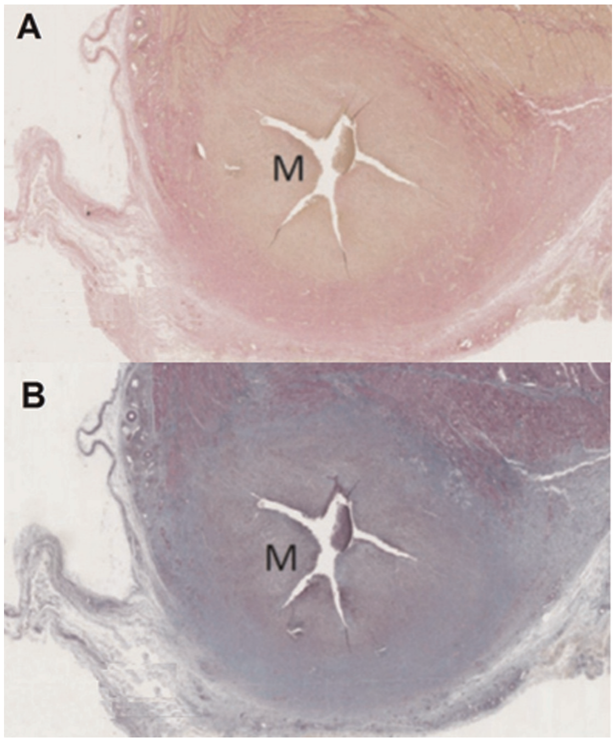
Digital subtraction radiograph (a) of the esophagus at 7 days after magnet placement and high-resolution contrast image of the same explanted esophagus (b). The arrows indicated the site of magnetic anastomosis.

Histopathology

As the pairs of magnets dropped off, the inner wall of the anastomosis was eventually covered by endothelium. Sealed anastomoses are seen in histological examination with evidence of moderate mucosal inflammation and submucosal and muscular layer fibrosis. In addition, as in Fig. 8, the inner wall of the anastomosis was coated with mucosa.

Histopathology also revealed the site of compression surrounded by granulation tissue, with epithelium development starting on day 6 within the new lumen (Fig. 8) and maturing on day 7 to a well-defined anastomosis consisting of circular scar tissue covered by epithelium.

Figure 8



Van Gieson (a) and Goldner (b) stains of the esophageal segment at the level of the magnetic anastomosis (M) at 7 days; beginning epithelialization of the anastomosis is noted.

Discussion

In five adult pigs, magnetic compression anastomosis was first tested using a bifurcated esophagus model to permit postoperative feeding of the animals through a gastrostomy tube. Of the five pigs, three died in this sample owing to problems related to the model itself rather than the internal method of magnetic compression. However, this research found that an esophagoesophageal magnetic compression anastomosis was possible in the two remaining pigs, and that the anastomosis endured intraluminal pressures of up to 30 mmHg [14,16].

The challenges of a chronic animal model of EA are largely owing to the inability of the animal to clear saliva, leading to aspiration and subsequent death. Unless the institution's animal facility is equipped with an ICU and 24-h care to suction the saliva, an alternative method of clearing secretions must be used, and as we did not have animal ICU for close monitoring of rabbits or suction facilities, so we had to manually aspirate the saliva every 6 h by orogastric tube and 50 ml syringe at the first 4–5 days of the experiment till the anastomosis is formed and open the way to allow passage of the saliva from rabbits esophagus to their stomach. However, after complete ligation of the esophagus, three rabbits expectorated all oral secretions, which led to aspiration, pneumonia, and finally, death at the postoperative day 4. So, in the future, it would be helpful if there is a well-equipped animal institution with equipped animal operation room, specialized animals anesthesiologist, and postoperative ICU for postoperative close monitoring of the animals to deal with postoperative complications, as well as decrease the number of postoperative animal loss. Moreover, an additional procedure for drainage of the saliva is advisable in such future experiments to decrease the risk of aspiration and pneumonia in the experimental animals. All these problems and difficulties explain the relative high animal mortality rate (60%) in our study and should be avoided in future studies.

A significant challenge encountered was initial placement of the distal pouch magnet. The magnets situated in the proximal and distal esophageal pouches are able to attract one another owing to their opposite polarity. Once the magnets have connected, the tissue between them becomes ischemic and sloughs while the outer rim heals establishing the anastomosis. Patients with esophageal gaps of more than 4 cm are not candidates for placement of a catheter-based magnet device owing to the fact that this length surpasses the strength of the magnetic field and will fail to achieve attraction and connection [17].

In our experiment, initial attempts to place the distal magnet without going distally to the stomach was very difficult, especially with presence of long gap between the two created esophageal pouches. The attracting power of the magnets was very helpful in about three rabbits, and immediate magnets attachment happened intraoperative, but in other rabbits, the gap was relatively long and affected the traction power of magnets, resulting in failure of compression anastomosis. So, we believe that esophageal elongation procedure in such cases of long-gap EA would be very helpful before use of magnetic compression procedures, as using more powerful magnets will cause significant traction on esophagus and compromise the esophageal blood supply.

In the remaining rabbits with a succession of anastomosis, the magnets were not removed from the anastomotic site at the end of the trial. The apparent drawback of this argument being that the rabbits were killed before the magnets could disperse or the presence of a stricture at the anastomosis site stopping the magnets from traveling distally.

In patients with EA, magnetic anastomosis was first reported in five infants in Argentina. Anastomosis was achieved in all of the patients on an average of 4.8 days [17].

The results in our 7-day research on surviving rabbits with active anastomoses revealed that our specially planned experiment with progressive luminal epithelization produced a patent, leak-proof anastomosis. This anastomosis was immune to intraluminal supraphysiologic pressurization. Esophageal pressure *in vivo* rarely exceeds 50 mmHg, especially in children. For our burst pressure measure, we thus selected 75 mmHg, which hence comfortably covers the entire physiological spectrum. Unfortunately, the leakage occurred about 40 mmHg (36–43 mmHg) in the anastomoses. We assume this existed for two reasons: first, the difference in thickness between the rabbit and the esophagus of human children. Second, the relative short experiment duration (7 days), as if the anastomoses had more duration, and this may have led to further maturation of the anastomoses.

Long-gap EA, defined as cases in which a primary anastomosis of both ends of the esophagus cannot be performed without significant tension, is a technically challenging condition to treat [18].

Five kids with EA without a fistula were treated in one 2009 study by putting neodymium-iron-boron magnets in both pouches and enabling them to mate. Early symptoms of sepsis occurred in one patient, and stenosis occurred in four of the five cases, with one patient ultimately needing an operative revision. Nevertheless, this analysis shows that, in theory, magnetic esophageal compression anastomosis is possible [19].

A case study on the therapeutic use of magnets to produce esophagoesophagostomy following a Foker-type lengthening operation was recently reported in the case of a 4-month-old born at 28 weeks of gestation with a previously ligated upper fistula. The anastomosis was established, but for a year after the operation, the patient required serial balloon dilatations approximately every 2 weeks [20].

Latest experimental experiment on magnetic compression anastomosis was performed on one dog in Egypt, by creating two blind-ended pouches in dog cervical esophagus and inserting two disc-shaped magnets, one in proximal pouch and the other in the distal pouch, and the animal was fed by insertion of feeding tube into the distal esophagus. The study shows presence of well-formed esophageal anastomosis after 7 days, and the anastomosis was confirmed patent by contrast dye study [21].

For a variety of factors, we concluded that a rabbit model was optimum in our research. Rabbits are available, easy to reach, and simple to handle. The anatomy in humans is identical. Probably more importantly, there is a reduced chance of aspiration, and the rabbits are unlikely to vomit as their guts do not have an antiperistaltic reflex.

This thesis reveals the possibility of using transient magnetic attraction to conduct sutureless compression anastomoses. In general, to form a transluminal compression anastomosis, there must be adequate compression to affect central necrosis ischemia in such a way that a new channel is created rather than an ulcer or fistula. Pressure, however, must be managed so that the noncompressed tissue surrounding has time to remodel and shape a competent ring around the new anastomotic tube. This is consistent with Senn's theory that proper anastomosis of compression does not require necrosis at the real anastomosis site [22].

As an alternative to traditional surgeries, including stitches in hand-sewn esophagoesophagostomy, the availability of a convenient and reproducible way to produce esophageal anastomosis using magnetic compression has the potential to revolutionize the surgical diagnosis and treatment of babies born with EA. Not only can it greatly decrease operation times and risks in these patients that frequently experience tenuous physiology and potential associated congenital defects, but it may also pave the way for a minimally invasive procedure to be used more commonly.

Although open EA repair has been the norm for decades, a recent multicenter study found that after open thoracotomy for EA repair, most children experience thoracic wall morbidity and deformity [16].

Therefore, minimally invasive approaches are more likely to be increasingly favored in the future. The most technically complicated and exhausting section of the technique, which is manual suturing in a very small space, will be replaced by magnetic compression anastomosis. Hypothetically, as it needs less dissection and manipulation than a hand-sewn anastomosis, it is possible that magnetic compression anastomosis is advantageous and may also induce less compromising of the delicate intramural blood flow. The potential advantages of esophageal magnetic compression anastomosis are not limited to technological convenience and shorter operating time but also include avoidance of airway-related or nerve-related problems during complicated redo-case dissections and avoidance of esophageal devascularization during dissection.

Repair of EA can have significant associated morbidity. As such, it represents an area of pediatric surgery that is positioned for significant improvement in both technique and technology. However, without an animal model, such innovation may not be possible. It is expected that further validation of this model may help to facilitate creation and testing of a variety of different devices and techniques. More significantly, the existence of an animal model provides a safe experimental platform that avoids unnecessary or premature human experimentation. The use of magnets in patients with EA may be particularly beneficial for patients with cardiac or other congenital anomalies and those who have undergone previous operations or complications in which preoperative surgery is not optimal. In these select patients, the use of the magnets may avoid operation and potentially an anesthetic as well. In addition, the magnets may also be used in combination with surgery such as for postoperative esophageal strictures not amenable to dilation or in a staged manner for esophageal gaps more than 4 cm after initial operative stretching procedures [14,20].

There are so many variables that play a role in magnetic compression anastomosis that before implementing such devices in infants, extensive laboratory research in animals is mandatory. These variables include magnet form, intensity, distribution of the gradient force on the compressed tissue, as well as configuration.

Conclusion

The significant advance of this study is the creation of a complete watertight anastomosis in three of 10 rabbits in spite of the presence of about 3–4 cm gap between the two created blind pouches of the esophagus, simulating long-gap EA.

Using our technique, magnetic compression anastomoses of the esophagus developed in 7 days, were patent and eventually coated with epithelium, and in rabbit models, are mechanically resistant to supraphysiological intraluminal pressures. In patients born with EA, these results form the basis for a possible therapeutic application.

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Conflicts of interest

There are no conflicts of interest.

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