

Noninvasive Positive Pressure Ventilation Following Esophagectomy

Safety Demonstrated in a Pig Model

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BACKGROUND: Respiratory complications occur in 20% to 65% of patients who have undergone esophagectomy. While noninvasive positive pressure ventilation (NPPV) is associated with fewer complications than endotracheal intubation (ET), it is relatively contraindicated after esophagectomy due to potential injury to the anastomosis. We created ex vivo and in vivo pig models to determine the pressure tolerance of an esophagectomy anastomosis and compare it to esophageal pressure during NPPV.

METHODS: We created a stapled side-to-side, functional end-to-end esophagogastric anastomosis. With continuous intraluminal pressure monitoring, we progressively insufflated the anastomosis with a syringe until we detected an anastomotic leak, and recorded the maximum pressure before leakage. We performed this experiment in 10 esophageal specimens and 10 live pigs. We then applied a laryngeal mask airway (LMA) to five live pigs and measured the pressure in the proximal esophagus with increasing ventilatory pressures.

RESULTS: The perforation was always at the anastomosis. The ex vivo and in vivo anastomoses tolerated a mean of 101 ± 44 cm H₂O and 84 ± 38 cm H₂O before leak, respectively. There was no significant difference between the pressure thresholds of ex vivo and in vivo anastomoses ($P = .51$). When 20, 30, and 40 cm H₂O of positive pressure via LMA were delivered, the esophagus sensed 5 ± 4 cm H₂O (25%), 11 ± 11 cm H₂O (37%), and 15 ± 9 cm H₂O (38%), respectively.

CONCLUSIONS: Our pig model suggests that an esophagectomy anastomosis can tolerate a considerably higher pressure than is transmitted to the esophagus during NPPV. NPPV may be a safe alternative to ET after esophagectomy.

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ABBREVIATIONS: ARF = acute respiratory failure; LMA = laryngeal mask airway; NPPV = noninvasive positive pressure ventilation

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Esophagectomy for esophageal cancer is a complex operation with a 20% to 60% morbidity rate.¹⁻³ Respiratory complications, commonly including acute respiratory failure (ARF), pneumonia, pleural effusions, and atelectasis, occur frequently and can account for about one-half the total morbidity and mortality of the operation.^{4,5} For the management of ARF, noninvasive positive pressure ventilation (NPPV) has achieved increasing popularity over endotracheal intubation, as it reduces the need for intubation, number of complications, length of stay in the ICU, short-term mortality, and cost.⁶⁻¹⁶ Further, in patients with postoperative respiratory insufficiency short of ARF, NPPV has resulted in lower intubation rates, better gas exchange, and shortened length of stay.¹⁷⁻¹⁹

However, in patients who have undergone esophagectomy, clinicians have hesitated to use NPPV because of concerns that positive pressure would translate into stress on the esophagogastric anastomosis.^{6,10,15,17,19,20} Two European studies have demonstrated safety of NPPV in empirical use in esophagectomy patients.^{6,19} Our aim was to quantify the maximum, safe intraluminal pressures that can be administered to an anastomosis. We then looked to quantify the esophageal pressures experienced with NPPV, thereby establishing a safe range of positive pressure tolerance. This information could be used as a basis for a trial of NPPV in patients who have undergone esophagectomy.

Materials and Methods

Ex Vivo Pig Model for Esophagectomy

An ex vivo model for esophagectomy was developed with porcine, nonpreserved pharyngoesophagogastric specimens ($n = 10$). The esophagus was transected at a midesophageal location, the stomach was transected near the cardia, and a linear stapler (ETHICON ENDO-SURGERY Linear Cutter 75; Ethicon Endosurgery Inc) was used to create a side-to-side, functional end-to-end esophagogastric anastomosis. To create a closed system, the esophagus was ligated with 2-0 silk ties at its most proximal end and the stomach at its most distal end. An 18-gauge angiocatheter was introduced into the esophageal lumen close to the anastomosis, and a pressure probe (FISO FOP 62.5 microns; FISO Technologies Inc) was inserted into the lumen of the esophagus via the angiocatheter. Another 18-gauge angiocatheter was inserted into the esophagus, and a 60-mL syringe was attached to it. With concurrent pressure monitoring, the syringe was used to progressively insufflate the anastomosis until a leak was identified by (1) the failure of the anastomosis to hold pressure, (2) a hissing sound from the anastomosis, or (3) the discharge of air bubbles from the anastomosis when submerged in a water bath. The anastomotic leak was confirmed by the injection into the esophageal lumen and subsequent extravasation of methylene blue from the anastomotic staple lines. The intraluminal pressure at which first evidence of anastomotic leak appeared was recorded. The baseline intraluminal pressure was measured as atmospheric in every experiment and was subtracted from the final maximum esophageal pressure resulting in the applied pressure in cm H₂O.

In Vivo Pig Model for Esophagectomy

The ex vivo model was then applied to live, nonsurvival pigs to determine any difference in pressure tolerance between both types of tissue. A pig weighing 30 to 40 kg ($n = 10$) was anesthetized, prepared, and draped in the usual sterile fashion. A xiphoid-umbilical incision was performed for the creation of the gastric conduit. The stomach with its gastroepiploic blood supply was passed through the diaphragmatic hiatus. The pig was then placed in the right lateral decubitus position, prepared, and draped in sterile fashion and a thoracotomy was performed to visualize the tho-

racic esophagus (Fig 1A). The stomach conduit was then delivered into the thorax via the diaphragmatic hiatus. We proceeded with removal of the distal esophagus and performed a side-to-side, functional end-to-end stapled anastomosis identical to the ex vivo model. Once again, 18-gauge angiocatheters were used to introduce pressure probes and insufflate the anastomosis with a syringe (Fig 1B) until an anastomotic leak was identified and confirmed with methylene blue (Fig 1C). The intraluminal pressure at which an anastomotic leak occurred was recorded.

Application of NPPV in Live Pigs

To measure the amount of pressure transmitted to the esophagus in NPPV, pressure probes were inserted via an angiocatheter into the normal, proximal esophagus in five live, anesthetized pigs that had undergone a thoracotomy and had a patent GI tract. Because NPPV via a face mask was not feasible with the size and shape of the pig's mouth and nose, we opted for a size 4 laryngeal mask airway (LMA) device placed proximal to the glottis above the esophageal and laryngeal inlets.^{21,22} The LMA placed in this location exerted a positive pressure to both the airway and the esophagus. Positive pressure, at 20, 30, and 40 cm H₂O, was delivered in a pressure-controlled manner as the esophageal pressures were measured. Consistent pressures > 40 cm H₂O could not be applied due to extensive leakage around the LMA into the proximal pharynx and mouth. The baseline intraluminal pressure was measured as atmospheric in every experiment and was subtracted from the pressure transmitted to esophagus from NPPV, resulting in the net exerted pressure in cm H₂O. Our project was approved by the Institutional Animal Care and Use Committee of Dartmouth College (protocol erkm.cp.1).

Statistical Analysis

All data are reported as a mean with 95% CI and error bars as SEM, unless otherwise stated. Continuous data comparison between the in vivo and ex vivo groups was performed with the two-tailed Student *t* test. We obtained 95% CIs with nine degrees of freedom and a *t* value of 2.262 for anastomotic pressure tolerance ($n = 10$) and four degrees of freedom and a *t* value of 2.776 for pressure transmitted to the esophagus in NPPV ($n = 5$). Statistical analysis was performed with GraphPad Prism version 6.00 (GraphPad Software Inc).

Results

Pressure Tolerance of Esophagectomy Anastomosis

Ex vivo anastomoses tolerated a mean of 101 ± 44 cm H₂O of pressure (95% CI, 57-145), while in vivo anastomoses withstood 84 ± 38 cm H₂O of pressure (95% CI, 46-122)

before leakage was demonstrated (Fig 2A). The range of pressures tolerated by ex vivo and in vivo anastomoses before leakage was 21 to 232 cm H₂O (median, 92 cm H₂O) and 54 to 225 cm H₂O (median, 57 cm H₂O), respectively. There was no significant difference in maximum tolerated pressure between ex vivo and in vivo

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