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Endoscopic Closure of a Tracheal Access Site Using BioGlue after Transtracheal Thoracoscopy in a Nonsurvival Canine Model

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Key Words
Natural orifice transluminal endoscopic surgery · Transtracheal approach

Abstract
Objectives: An ideal wound closure device would repair the wound with minimal complexity. In this report, we describe a simple wound closure method using BioGlue sealant. ***Method:*** Eleven canines underwent transtracheal pericardial window creation under endoscopic guidance for natural orifice transluminal endoscopic surgery (NOTES). The tracheal wound was closed using BioGlue sealant. The integrity of the wound was assessed by determining the amount of air leaking under mechanical ventilation. ***Results:*** Transtracheal thoracic exploration and pericardial window creation was successful for all of the canines, and adequate wound closure was achieved in 10 of the canines. There was 1 case of NOTES-related death arising from misplacement of the endotracheal tube in the left lower lobar bronchus. This caused a collapse of the left upper lobe and ventilatory failure. Minor lung injuries occurred in 3 canines and minor mediastinal bleeding was encountered in 1 canine during the creation of the access site. ***Conclusion:*** BioGlue sealant was found to be effective in sealing the tracheal wound in all but 1 of the canines. This study demonstrates that the use of the sealant is a simple and efficient means of endoscopically closing the tracheal access site in NOTES.

Introduction

The use of natural orifices to access the body cavity is one of the most controversial issues among surgeons and physicians. This method of approach has been used in cholecystectomy, appendectomy, and tubal ligation, among other procedures [1–3]. However, the lack of closure devices for such access sites has delayed the development of natural orifice transluminal endoscopic surgery (NOTES) in humans. Recently, we reported the application of NOTES in a canine model in which the lung was successfully resected via transtracheal incision [4]. The use of a silicone stent after the procedure facilitated complete healing of the tracheal wound 2 weeks after a lung biopsy was obtained. However, complications such as

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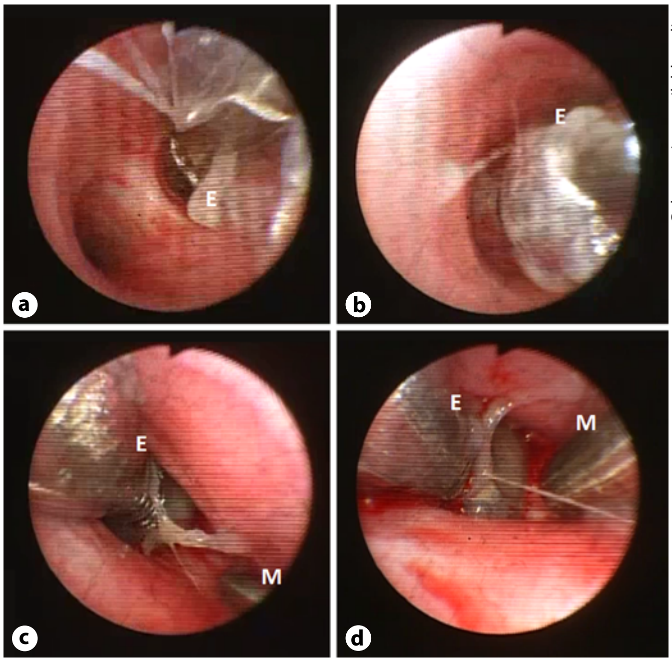

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Fig. 1. a, **b** Endoscopic view of the endotracheal tube and cuff (E) just above the tracheal bifurcation. **c** Endoscopic view of the low tracheal incision (within 4 cm of the carina) which was made using a custom-designed metallic knife (M). **d** The trachea was accessed using the sequential dilation technique.

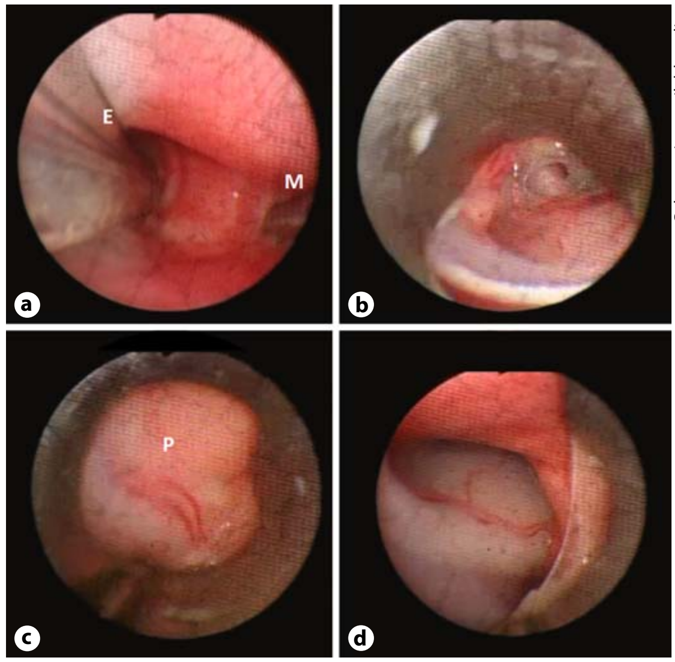

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Fig. 2. a Endoscopic view of the endotracheal tube (E) and high tracheal incision (>4 cm above the carina) using a metallic knife (M). **b–d** Endoscopic view of the intramediastinal location of the working metallic tube after sequential dilation. The blunt metallic tube was used to gently separate the walls of the pleura (P) for thoracic exploration.

stent migration and granulation were observed at the edge of the stent [4, 5].

BioGlue surgical sealant (CryoLife Inc., Kennesaw, Ga., USA) is a synthetic sealing agent that adheres firmly to tissues. It has been used successfully in numerous patients for reinforcing anastomotic suture lines after aortic root replacement, reduction of alveolar air leaks after pulmonary resection, and sealing of bronchial anastomoses after tracheobronchial reconstruction [6–8].

We evaluated the feasibility and effectiveness of using BioGlue sealant to seal tracheal wounds after transtracheal thoracoscopy in a nonsurvival canine model. We believe that identifying a simple, convenient, and effective wound closure method will facilitate the development of intrathoracic surgery via natural orifices.

Materials and Methods

The study was approved by the Ethics Committee on Animal Research of Chang Gung Memorial Hospital. The aim of the study was to evaluate the use of a sealant to close a tracheal wound after transtracheal pericardial window creation in a nonsurvival canine model. The thoracic cavity was accessed at 2 different sites: a low tracheal incision in which the tracheal wound was performed over the right lateral wall of the lower trachea (within 4 cm above the carina), and a high tracheal incision (4–8 cm above the carina). The amount of air leaking from the chest tube was determined to assess the integrity of the tracheal access site.

Preanesthesia sedation was performed on each canine in the supine position with an intramuscular injection of ketamine (5 mg/kg) and xylazine HCl (10 mg/kg). A custom-designed endotracheal tube was inserted into the trachea until it reached the endotracheal cuff just above the tracheal bifurcation. Anesthesia was maintained throughout the procedure with isoflurane (3%) and oxygen (3.0 l/min) with a bolus infusion of xylazine HCl (5 mg/kg; i.v.), if required.

A 2-mm tracheal incision was performed according to a previously described technique over the right lateral wall of the trachea using a custom-designed metallic knife (fig. 1, 2; online suppl. video 1; for all online suppl. material, see www.karger.com/doi/10.1159/000334281). The tracheal incision was sequentially dilated to 9 mm with a homemade metallic tube and used as a working channel for thoracic exploration. A flexible bronchoscope (outer diameter, 4.9 mm; Olympus Optical Co. Ltd., Tokyo, Japan) was then inserted through the metallic tube into the thoracic cavity. A small pericardial window (1 cm) was made anterior to the phrenic nerve through the working channel

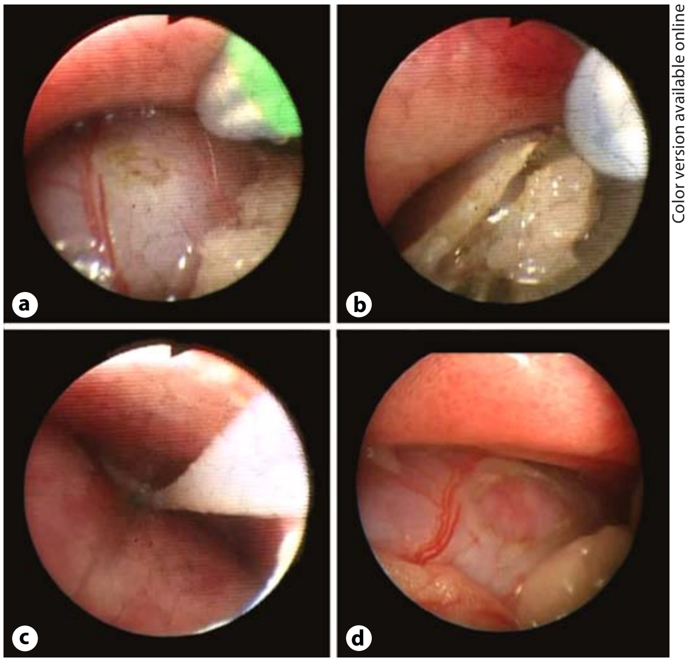

Fig. 3. a, **b** Endoscopic view of the creation of the pericardial window with a needle knife. **c**, **d** The pericardial cavity was explored through the pericardial window.

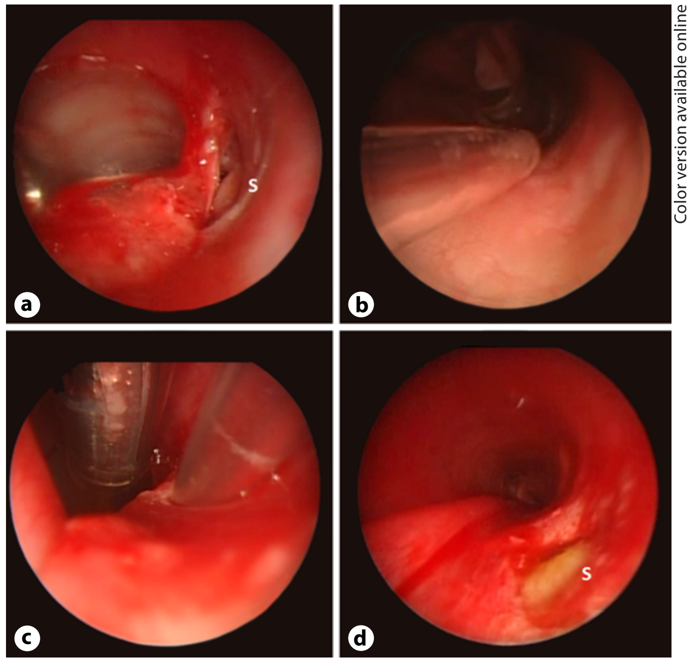

Fig. 4. a Tracheal access site (S) after transtracheal exploration and creation of the pericardial window. **b**, **c** Endoscopic view of the application of sealant to secure the tracheal access site. **d** Bronchoscopy revealed a sealed tracheal access site (S) after application of the BioGlue sealant.

of the bronchoscope using a needle knife (KD-31 C-1; Olympus, Tokyo, Japan) (fig. 3; online suppl. video 1). The tracheal wound was repaired by applying the sealant using a custom-designed rubber catheter under endoscopic guidance (fig. 4; online suppl. video 2). Because the sealant would adhere to the target lesion immediately after application, the rubber catheter was removed after application of the sealant to improve the treatment outcome and decrease the risk of adhesion of the catheter to the mediastinal structure and tracheal wound.

After the sealant was applied, a thoracotomy tube was inserted into the right pleural cavity to evaluate the adequacy of wound closure. The animals were mechanically ventilated using a high-volume ventilator (>25 ml/kg). The integrity of the tracheal wound was assessed by the amount of air leaking from the chest tube. A complete wound closure was defined by the absence of air leakage from the drainage tube under 30 min of mechanical ventilation.

The canines were sacrificed after the procedure by intravenous administration of Xylocaine (200 mg). Sternotomies were performed to assess the effectiveness of the creation of the pericardial window, the effectiveness of the wound closure, and the existence of any complications (e.g. organ injury or major bleeding). The region of the tracheal incision was subsequently explanted for gross and pathologic examination (fig. 5; online suppl. video 2).

Results

Transtracheal exploration of the thoracic cavity and pericardial window creation was achieved successfully for all of the canines (n = 11). The mean operating time, including tracheal incision, thoracic approach, pericardial window creation, and tracheal closure, was 77.90 min (range, 45–94 min) (table 1).

The low tracheal incision approach (within 4 cm above the carina) was used initially on 4 of the canines. Minor bleeding due to lung injury was noted in 3 canines, possibly as a result of excessive probing of the metallic tube within the pleural cavity. The bleeding was not significant, and there were no air leaks. The animals required no further management. One of the canines was found to have slight mediastinal bleeding during the creation of the tracheal wound but required no further treatment. One animal suffered hemodynamic compromise accompanied by respiratory distress after the endotracheal tube entered the lobar bronchus. The animal was sacrificed prior to the closure of the tracheal wound after an unsuccessful attempt at intraoperative cardiopulmonary resuscitation.

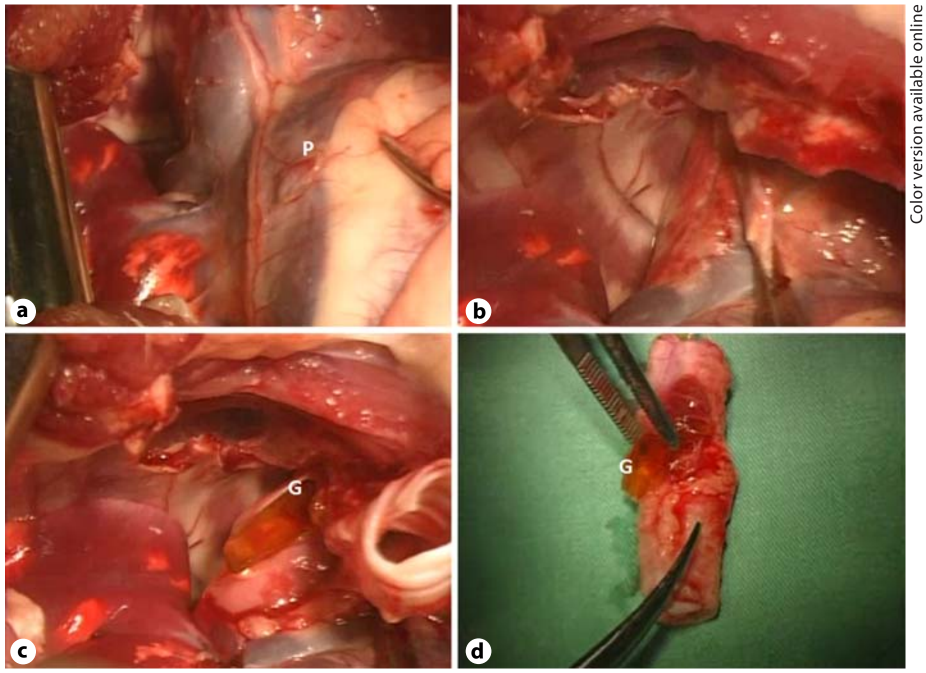

Fig. 5. a, **b** Autopsy revealed a pericardial window (P) anterior to the phrenic nerve and no evidence of intrathoracic injury. **b–d** Closure of the tracheal incision with BioGlue (G).

Later, we discovered that the high tracheal incision approach (4–8 cm above the carina) allowed for more extensive exploration of the upper lung region, decreased the risk of mediastinal and lung injury, and provided adequate working space to create the pericardial window. Thus, the high tracheal incision approach was used on the remaining 7 canines, and the pericardial cavity was successfully explored with a flexible bronchoscope without difficulty or injury to the organs.

For tracheal wound closure, the sealant was applied via a catheter inserted into the wound and positioned 0.5 cm distal to the edge of the tracheal incision. Complete sealing of the tracheal wound was achieved in 10 cases with 13 applications of the sealant (range, 1–2). No complications were encountered during the endoscopic closure of the wounds. No air leaks were identified in any of the 10 animals after 30 min of ventilation. This indicated that complete sealing of the wounds was attained in these 10 cases.

Autopsies of the 11 animals confirmed the successful creation of the pericardial window anterior to the phrenic nerve. Necropsy revealed that there was no mediastinal vital structure or hilar injury except for a minor upper lobe pulmonary contusion caused by the metallic tube during the creation of the tracheal access site. A necropsy also demonstrated that the tracheal wounds were sealed inside the mediastinum.

Discussion

NOTES has the potential to reduce the discomfort experienced after laparoscopic or thoracoscopic surgery [9, 10]. In the case of thoracic disease, several NOTES approaches (transvesical, transesophageal, and transgastric) have been reported which describe technical limitations involved in accessing the thoracic cavity. Such approaches have also been associated with perioperative complications, including thoracic infection, pneumothorax, massive bleeding, and mortality [11–15]. Our team also has successfully performed multiple transtracheal thoracic procedures (i.e. thoracic explorations, surgical lung biopsies, and creation of pericardial windows) and has found that one of the most critical issues preventing the advancement of NOTES is the ability to ensure secure closure of visceral incisions [16, 17] (table 2).

Airway stents are effective for relieving airway stenosis and sealing airway fistulae [18]. Recently, we demonstrated that a silicone stent placed over the tracheal access site in the thoracic cavity facilitates complete wound healing [4, 5, 16]. However, it is difficult to determine the accurate size of the stent to be used. If the wrong size stent is used, the ensuing migration and granulation may require a second operation to remove the stent. Therefore, the availability of a simple and effective modality for wound closure would facilitate the development of

Table 1. Procedure characteristics and animal outcomes

Animal	Body weight kg	Duration min	Tracheal access site	Success of pericardial window creation	Success of tracheal wound closure	Air leaks under mechanical ventilation	Complication	Survived >30 min after surgery	Necropsy, finding of chest and mediastinum	Necropsy, finding of tracheal incision region
Dog 1	9.5	94	low tracheal incision	yes	yes (1)	no	lung injury	yes	right upper lobe contusion	BioGlue over mediastinum and tracheal incision region
Dog 2	10.6	67	low tracheal incision	yes	yes (2)	no	lung injury and minor mediastinal bleeding	yes	right upper lobe contusion and mediastinal hematoma	BioGlue over mediastinum and tracheal incision region
Dog 3	7.8	45	low tracheal incision	yes	not performed	not performed	respiratory distress/mortality	no	no injury of vital structures	no tracheal repair
Dog 4	10.2	84	low tracheal incision	yes	yes (2)	no	lung injury	yes	right upper lobe contusion	BioGlue over pulmonary hilum, mediastinum, and tracheal incision region
Dog 5	9	92	high tracheal incision	yes	yes (1)	no	none	yes	no injury of vital structures	BioGlue over mediastinum and tracheal incision region
Dog 6	8.9	80	high tracheal incision	yes	yes (2)	no	none	yes	no injury of vital structures	BioGlue over mediastinum, tracheal lumen, and tracheal incision region
Dog 7	11	58	high tracheal incision	yes	yes (1)	no	none	yes	no injury of vital structures	BioGlue over mediastinum and tracheal incision region
Dog 8	8.1	76	high tracheal incision	yes	yes (1)	no	none	yes	no injury of vital structures	BioGlue over mediastinum and tracheal incision region
Dog 9	9.2	81	high tracheal incision	yes	yes (1)	no	none	yes	no injury of vital structures	BioGlue over mediastinum and tracheal incision region
Dog 10	8.8	86	high tracheal incision	yes	yes (1)	no	none	yes	no injury of vital structures	BioGlue over mediastinum and tracheal incision region
Dog 11	8.4	94	high tracheal incision	yes	yes (1)	no	none	yes	no injury of vital structures	BioGlue over mediastinum and tracheal incision region

Table 2. Previous studies of various approaches (transvesical, transgastric, transtracheal, and transesophageal with pneumothorax complications) and limitations in natural orifice transluminal endoscopic approach for thoracic cavity

NOTES approaches	Reference	Animal model	Animals n	Intrathoracic procedures	Wound closure method	Pneumothorax rate, %	Mortality rate %	Limitations of technique
Trans-vesical	Lima et al. [11]	pigs	6	lung biopsy	none	0	0	(1) difficult to approach the apical region of the pleural cavity (2) difficult to approach the right thoracic cavity (liver is located just below the diaphragm)
Trans-esophageal	Sumiyama et al. [12]	pigs	4	mediastinal exploration	clips	25	25 (respiratory distress)	difficult to determine the side of the thoracic cavity, difficult to approach and perform interventional procedures over apical lung region
	Willingham et al. [13]	pigs	5	thorax and mediastinal exploration	clips	20	0	
	Delius et al. [14]	pigs	8	mediastinal exploration	none	37.5	12.5 (tension pneumothorax)	
Trans-gastric	De Palma et al. [15]	pigs	4	lung biopsy	clips	0	0	(1) difficult to approach the apical region of the pleural cavity by retroflexion of a regular gastroscope via a gastric incision (2) difficult to approach the right thoracic cavity (liver is located just below the diaphragm)
Trans-tracheal	Liu et al. [16]	dogs and pigs	12	pericardial window creation	silicone stent, glues	58.3	25 (tension pneumothorax)	difficult to approach the basal region of the lower lobe of the lung
	Chen et al. [present study]	dogs	11	pericardial window creation	glues	0	9 (endotracheal tube malposition)	

NOTES involving the thoracic cavity. Our study shows that the use of BioGlue produced air-tight wound closures in all except 1 of the animals investigated.

We used the air leak test to evaluate the adequacy of the closure of the tracheal incision. Air leaking from the tracheal wound under a high-volume ventilator for 30 min was examined via a chest tube from the right pleural cavity. Results showed that the use of the sealant achieved leak-proof closure without evidence of wound dehiscence immediately after surgery. Attaching the tube over the telescope with a peri-strip may improve the therapeutic outcome. This maneuver allows for simultaneous visualization and application of a sealant over the tracheal wound while moving the telescope [19]. We did not encounter any difficulties during the endoscopic sealing of the tracheal incision in any of the 10 animals.

One concern with the NOTES approach to the peritoneal or thoracic cavity is the risk of injuring a vital organ during wound creation [16, 20]. To minimize the risk of mediastinal and lung injury, we marked the custom-designed metallic knife and tube before use, and ensured that the puncture entry of this knife did not exceed a predetermined safe length (approx. 1 cm) into the mediastinum and thoracic cavity via the tracheal incision during surgery. This knife was then exchanged for a 2-mm blunt-tip metallic rod, which was used to guide the creation of a working tract for thoracic exploration as previously described [4, 5, 16]. The tip of the metallic tube was not inserted in the thoracic cavity following the sequential dilation maneuver. Instead, it was advanced in the direction of the right thoracic cavity, and the blunt tip of the tube was used to gently separate and puncture the walls of the parietal pleura for thoracic exploration.

We previously reported that the transtracheal approaches have the advantage of enabling the surgeon to approach the target lesion head-on without the need for retroflexion, which is needed in the transesophageal approach using a gastroscope [16–20]. In the present study, we explored the thoracic cavity using both low and high tracheal incision methods. When the low tracheal incision method is used, the sequential dilation maneuver via the metallic rod placed inside the incision produces a direct working port for thoracic exploration. However, the disadvantages are the short working distance between the pulmonary surface and the mediastinum and the possibility of organ injury. In contrast, the high tracheal incision technique, in which the working tube is located high in the mediastinum (4–8 cm above the carina – in the region of the thoracic inlet), carries little risk of lung injury but requires a meticulous dissection of the adjacent mediastinal structure and mediastinotomy (separate and puncture the walls of the pleura) with the metallic tube under the endoscope.

Our previous study reported the complications of tension pneumothorax during NOTES thoracoscopy and advocated for the prophylactic use of a chest drainage tube to improve animal safety [5, 16]. However, increased surgical experience and improved anesthesia techniques have led to improved experimental outcomes even without the use of a chest tube during surgery. In the present study, 1 animal suffered hemodynamic collapse during surgery after the endotracheal tube entered the lobar bronchus, causing collapse of the left upper lobe and ventilatory failure. This animal had to be sacrificed before the experiment was complete. Serious respiratory complications related to endotracheal tube placement did not occur after we marked the optimal insertion length of the endotracheal tube (endotracheal cuff just above the tracheal bifurcation). With regard to minor complications, the transtracheal puncture maneuver resulted in inadvertent minor lung and mediastinal injury in 3 cases. To overcome these complications, we approached the thoracic cavity using the high tracheal incision technique and stopped mechanical ventilation to collapse the lung during tracheal puncture to decrease the risk of lung injury. This maneuver allowed for the creation of the working tract without injury to adjacent vital structures and lung in the remaining 7 animals. In this aspect, avoidance of a transtracheal thoracoscopy via low tracheal incision is a reasonable approach. Additional randomized data from larger studies of animals will be needed to determine the optimal location of the tracheal incision.

This study has some limitations. First, it was performed on only 11 animals. Second, complications such as delayed wound infection and mediastinitis could not be evaluated. Third, only the right thoracic cavity approach via tracheal incision was evaluated. The left thoracic cavity approach via left tracheal incision might be more challenging due to the presence of the aorta on the left lateral walls of the trachea, and thus further animal studies are required to evaluate the efficacy of this approach. Despite these limitations, the study outcomes demonstrate that transtracheal thoracic exploration and pericardial window creation can be performed in a non-survival canine model without making incisions in the skin. Moreover, the sealant method is a reliable means for closing the tracheal incision immediately after the procedure.

In conclusion, this study demonstrates that 9-mm tracheal wounds can be adequately sealed using BioGlue surgical sealant. A survival study comparing silicone stents and BioGlue is necessary to determine the safety and efficacy of using BioGlue sealant in NOTES wound closure.

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