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# Application of a bioengineered composite neotrachea in a dog model

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ABSTRACT

*Background:* Surgical treatment of extensive tracheal lesions remains a major challenge because of lack of an ideal airway substitute that is well vascularized, rigid, and autologous. We describe a novel surgical technique of tracheal reconstruction using a combination of a polypropylene mesh material and anterior cervical myocutaneous flap in a dog model.

*Materials and methods:* A 3.5–4 cm length of cervical trachea was resected in 16 dogs and replaced with a myocutaneous cervical neck flap wrapped around the plain polypropylene tube (group 1, $n = 7$) or wrapped around a composite of polypropylene tube with an implanted Z-type metallic-covered stent (group 2, $n = 9$). The cervical tracheal defect was repaired with the previously mentioned substitute that was directly sutured to the remaining tracheal ends. Dogs were followed up using bronchoscopy and x-rays and euthanized at predetermined times for histologic examination.

*Results:* In group 1, four dogs died within 2 wk from respiratory failure with varying degrees of airway collapse and difficulties in expectoration. In group 2, eight dogs survived, whereas one died of anastomotic dehiscence 1 wk after surgery. Necropsy and histologic examination of the anastomotic sites revealed good healing tissue. Pathologic examination also revealed excellent healing of the squamous epithelium of the neotrachea and the columnar epithelium of the native tracheal mucosa.

*Conclusions:* The tissue compatibility of the polypropylene mesh material and anterior cervical myocutaneous skin flap makes this a promising therapeutic substitute for treatment of patients with extensive tracheal lesions.



## 1. Introduction

Most of the short segment benign and low-grade malignant tracheal lesions can be safely resected and a primary reconstruction undertaken. The general limits for safe resection are approximately half the tracheal length in adults, and probably a third in small children. When the length of the tracheal resection exceeds 5–6 cm, a direct end-to-end anastomosis of the remaining trachea is not possible due to the excessive tension [1,2], and therefore a tracheal transplantation or

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replacement is required. Tracheal transplantation and replacement is challenging because of a number of anatomic features unique to the trachea. A variety of graft materials and transplantation approaches have been used in an attempt to generate a tracheal biologic substitute with clinical applicability [3,4]. At present, there is a lack of availability of a viable biologic autogenous substitute in tracheal reconstruction. The reported surgical success, complications, and survival rate vary widely. There are rare reports of limited clinical success with the use of various biologic substitutes.

The goal of our experimental study was to evaluate the clinical applicability and efficacy of a bioengineered autologous neotrachea using a combination of cervical skin flap along with composite mesh and metallic stents in a dog model. The long neck of the dog is conducive to the surgical procedure because of the ease of use of a pedicle myocutaneous flap. Our findings indicate that the polypropylene mesh was able to stimulate the subcutaneous tissue to form granulation tissue within 2 wk. This in turn played an important role in the support of the airway and provided an autologous tissue, which had full healing potential with no concerns for immunologic rejection. We believe that a composite bioengineered neotrachea using tubular polypropylene mesh material along with autologous cervical skin flap fulfills most of the requirements necessary for successful tracheal replacement.

## 2. Materials and methods

### 2.1. Animals

A total of sixteen healthy dogs, ranging in weight from 12.5–15.1 kg, were obtained from the Experimental Center of The Second Hospital of Shandong University, China. All dogs received care in compliance with the "Principles of Laboratory Animal Care" of the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" formulated by the National Academy of Sciences. The study was approved by our institutional ethics committee. The dogs were randomly assigned to different groups.

A dog has a typical tracheal length of >20 cm, with a tracheal diameter that is similar to that of humans. Five days before the surgical treatment, the dogs were depilated in a 10 × 10 cm cervical region, using 8% sodium sulfide. At 5 d, the acute inflammatory reaction resulting from the depilatory stimulus had subsided, and the skin had returned to its normal status.

### 2.2. Harvest of the cervical flap

The dogs were anesthetized with 3% pentobarbital (1 mL/kg). Throughout the procedure, the pulse was monitored, and crystalloid solution was used for resuscitation. Longitudinal incision approximately 3.5–4 cm in length (this length made the surgical procedure easier) was made in the anterior cervical skin approximately 3.5 cm from the midline. The skin and myocutaneous tissue was freed up toward the midline and to the right to make a 7.0 × 4.0 cm pedicled skin flap (as shown in the diagram).

### 2.3. Tracheal reconstruction

The anterior neck dissection was undertaken and the trachea exposed. Five to seven tracheal rings were removed distal to the third ring. The distal trachea was intubated to maintain spontaneous respiration. The dogs were divided into two groups. In group 1, airway continuity was reestablished with an interposition of a composite of cervical flap in a tube wrapped on the outside by the polypropylene mesh material. This neotrachea was sutured to the tracheal ends with 3-0 polypropylene sutures ensuring that the skin surface was facing the tube cavity. The flap used was a few millimeters larger than the defect to ensure adequate coverage of the border of the defect without tension. A piece of monofilament-knitted polypropylene mesh of the same size, as the skin flap was fixed to the soft tissue of the skin flap ensuring that the average distance between fixation points, was approximately 0.8 cm (Figs. 1–3). In dogs from group 2, we implanted a metallic-covered Z-type tracheal stent into the skin flap tube to avoid collapse of the neotrachea. The stent and the graft were secured with absorbable sutures to avoid stent dislodgement. Finally, the skin incision on the left side was closed.

### 2.4. Postoperative care

Postoperatively, animals were extubated at the end of the procedure. The cervical drains were removed on day 1. All dogs received intramuscular injections of mezlocillin sodium plus sulbactam sodium (2.5 gm) for 3 d and penicillin (16 million U) for 4 d after the procedure. The surgical incisions were disinfected with povidone iodine solution.

### 2.5. Postoperative monitoring and assessment

The dogs were monitored in an animal facility with approved safety measures. Wound healing, respiratory distress, and quality of life were observed daily.

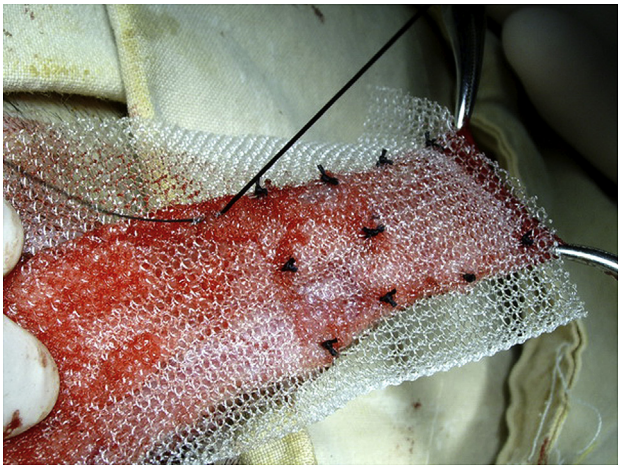

**Fig. 1 – A piece of monofilament-knitted polypropylene mesh was fixed to the soft tissue of the skin flap. (Color version of figure is available online.)**