Laryngotracheal Reconstruction in Canines

Fixation of Autologous Costochondral Grafts Using Polylactic and Polyglycolic Acid Miniplates

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Objective: To examine the feasibility of a new method of laryngotracheal reconstruction (LTR) that uses a bioabsorbable plating system consisting of polylactic and polyglycolic acid and provides some advantages over currently used methods.

Design and Interventions: Anterior subglottic stenosis was created in 10 beagles that then underwent LTR using an autologous costochondral graft. External laryngotracheal framework and cartilage grafts were secured using a sheet and screws made from a copolymer composed of polylactic and polyglycolic acid. Animals were humanely killed at 40, 60, and 90 days, and specimens were submitted for pathological examination. Histologic analysis included evaluation for inflammatory reaction, polylactic and polyglycolic acid incorporation into cartilage, cartilage necrosis, cartilage remodeling, and graft epithelialization.

Results: All animals underwent LTR after creation of a subglottic stenosis without episodes of airway compromise. After LTR, all airways were returned to prestenosis diameter without significant complication, and all animals were immediately extubated after surgery without difficulty. After the animals were killed, distraction of the stenotic cricoid area was demonstrated in 100% of the cases. Significant necrosis was noted in 2 of 10 grafts grossly; however, histologic analysis demonstrated significant areas of viable cartilage, areas of cartilage remodeling, and good epithelialization despite graft necrosis. Complete epithelialization of grafts was noted in the other 8 specimens.

Conclusions: Using a canine model, we demonstrated a bioabsorbable plating system that offers an effective method for LTR. This model has the advantages of providing external support to the operated laryngeal and tracheal framework, elimination of the difficulties of suture placement, and potential future failure while offering rigid external fixation of a cartilage graft.


The treatment of subglottic stenosis (SGS) continues to challenge those involved in the care of patients with this pathological condition. Treatment options have evolved from the use of tracheostomy and anterior cricoid split to more complex procedures designed to expand the airway, most commonly through the use of autologous cartilage grafts. Attempts at new surgical procedures have been designed to improve the ability to provide a stable and appropriate-sized airway and to reduce postoperative morbidity and mortality. Despite these attempts, many surgical procedures for the resolution of SGS remain technically challenging and present significant opportunity for morbidity and mortality due to factors such as long-term stenting, long-term intubation, and long-term use of narcotics for sedation.

One method to attempt to lessen the technical difficulty and morbidity and mortality in laryngotracheal reconstruction (LTR) for SGS involves the use of external fixation techniques. Initial attempts with external fixation techniques have produced mixed results. The present study examined a plating system composed of a copolymer of polylactic and polyglycolic acid (PLA-PGA) to perform single-stage LTR (SS-LTR) using an autologous costochondral graft in a canine model with SGS with immediate extubation after surgery.

RESULTS

All 10 dogs underwent stenosis-creating procedures. These animals developed mature SGS before LTR, with airway narrowing of 25% to 50%. None of the animals developed stridor at rest, and tracheostomy was never required to rescue an animal with critical airway stenosis.

Laryngotracheal reconstruction was performed on all animals without intra-
MATERIALS AND METHODS

Animals were treated in accordance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals, the National Institutes of Health Guide for the Care and Use of Laboratory Animals, and the Animal Welfare Act; the animal use protocol was approved by the Institutional Animal Care and Use Committee of the Medical College of Wisconsin, Milwaukee. Ten preconditioned female beagles weighing 9.6 to 12.2 kg (average weight, 11.0 kg) were used in this study.

On arrival at the Animal Research Center at the Medical College of Wisconsin, the animals were allowed a 1-week period of adjustment. The initial phase of this experiment involved the creation of an SGS in all 10 animals. Under general anesthesia maintaining spontaneous respiration (2.5% thiopental sodium, 1.0-1.5 mL/kg intravenously), the cricoid cartilage was brought into view using a Killian suspension apparatus and a Zeiss operating microscope. An electric drill and cutting bur were used to surgically remove mucosa and perichondrium in the area of the cri- coid and the first 2 tracheal rings. The animal was then allowed to recover. At 1-week intervals the stenotic site was reinspected using the previously described method to assess for scar formation. Any granulation tissue was excised, and subsequent burr procedures were performed as deemed necessary. Subglottic narrowing of 25% to 50% was desired as measured by sizing the airway with endotracheal tubes. The animals required 2 to 3 procedures in which the subglottic mucosa was denuded with the electric drill and burr to achieve this level of stenosis. All animals achieved acceptable SGS within 6 weeks.

The second phase of the study consisted of performing LTR in the area of the SGS through the use of a costochondral graft fixed in place with a bioabsorbable plate and screw system to expand the stenotic area.

All animals were treated with 500 mg of cefazolin intravenously before surgery. Anesthesia was induced with 2.5% thiopental sodium intravenously (1.0-1.5 mL/kg) and atropine, 0.1 mg/kg, intravenously. Animals were intubated endotracheally and maintained under general anesthesia with 0.5% to 1.0% inhalational halothane. Animals were mechanically ventilated (2 L/min oxygen, tidal volume of 230 mL, 15 breaths/min) throughout the procedure and had continuous cardiac and pulse oximetry monitoring.

The neck and right anterior chest were shaved and steriley prepared with povidone-iodine solution. The area overlying the first “floating rib” was infiltrated with 1% lidocaine with 1:100,000 epinephrine. The strap muscles were divided along the median raphe to allow exposure of the larynx, cricoid, and superior trachea. A midline incision was then made through the inferior half of the thyroid cartilage and extended through the cricoid cartilage and the first 2 tracheal rings. The costochondral graft was shaped in an elliptical fashion to allow placement and expansion of the larynx, cricoid, and tracheal incision. The perichon- drium was left intact along the graft surface that was to face the airway lumen. Costochondral graft dimensions ranged from 0.3 to 0.6 cm wide and 2.4 to 4.0 cm long (mean area, 2.8 cm²). The graft was then attached to a PL A-PGA copolymer plate cut from a 30 × 50 × 0.75-mm sheet (LactoSorb part 915-2832; W. Lorenz Company, Jacksonville, Fla) with 1.5 × 4.0-mm PL A-PGA screws (LactoSorb part 915-2313). The graft was fixed to the plate with 2 screws, 1 superior and 1 inferior (Figure 1). The screw hole was drilled through the plate and graft as a single unit using a pneumatic drill and a 1.2-mm drill bit. Saline irrigation was used throughout drilling. The drill hole was manually tapped with a 1.3-mm tap, and the screw was advanced until tension caused the screw head to break off, as designed by the manufacturer. The bioabsorbable plate, now attached to the costochondral graft, was heated to allow for molding of the plate to conform to the external structure of the larynx and trachea, with the graft positioned to expand the incision made through the area of airway stenosis. The heating source used for the plate molding is an enclosed saline bath provided by the manufacturer (W. Lorenz Company). The bioabsorbable plate–costochondral graft unit was secured into place using four 1.5 × 5.0-mm PL A-PGA screws (LactoSorb part 915-2326). Screws were placed through 2 holes drilled and tapped as above in the thyroid and cricoid cartilage (Figure 2). The wound was irrigated and closed in layers over a 5-mm Penrose drain using absorbable sutures. Bacitracin ointment was placed over the wounds. All animals were extubated when breathing spontaneously.

Drains were removed and regular diets were started on postoperative day 1. Treatment with oral cephalaxin (20 mg/kg per dose, 4 times per day) was continued until postoperative day 3. All animals were closely monitored for wound infections and airway integrity.

Humane killing was undertaken 40 days (3 animals), 60 days (3 animals), and 90 days (4 animals) after surgery using euthanasia solution consisting of highly concentrated pentobarbital and phenytoin as approved by the Panel on Euthanasia of the American Veterinary Medical Association. The laryngotracheal complex was removed. Gross observations were made and sections were sent for histologic examination. Slides were analyzed for graft viability, presence of inflammatory reaction, and presence of graft mucosalization.

operative complications. After completion of the LTR, extubation was successfully performed once the dog was breathing spontaneously in all cases. There were no instances of respiratory distress or stridor during the immediate or prolonged postoperative period. No animal required reintubation, and there were no incidences of graft dislocation or migration causing airway compromise.

After LTR, all airways were returned to prestenosis diameter, as measured by endotracheal tube, without significant complication. Minor complications occurred in 4 of 10 animals. Two dogs developed small chest wound...
hematomas that resolved without surgical or medical management. Two different dogs developed a small amount of serous drainage from their neck wounds on postoperative days 7 and 9. Both subsided with administration of oral cephalixin (20 mg/kg per dose, 4 times per day) for 5 days.

After humane killing, gross examination of the laryngotracheal complex demonstrated distraction of the cricoid cartilage in 100% of the cases. Two animals killed at 40 days had evidence of graft necrosis on gross inspection. These grafts were not associated with the animals that developed wound infections. Histologic analysis demonstrated cartilaginous resorption but also significant areas of viable cartilage, areas of cartilage remodeling, and good epithelialization despite graft necrosis (Figure 3).

The other 8 dogs demonstrated graft survival and essentially complete epithelialization of the luminal surface of the graft (Figure 4). The only exceptions to complete epithelialization were small areas of granulation tissue noted on the luminal surface of 4 of 10 grafts. These grafts were from animals killed at 40 days (n=2), 60 days (n=1), and 90 days (n=1). This granulation tissue seemed to be associated with a PLA-PGA screw protruding into the lumen and contacting the newly formed graft mucosa (Figure 5). The amount of granulation tissue was small in all cases and did not clinically compromise the airway in any of the animals. Acute inflammatory reactions were noted in the vicinity of the plate. No granulation tissue was noted, however.

The PLA-PGA copolymer plating material was present in all specimens. At 40 and 60 days after implantation, the plates and screws appeared intact and rigid. Figure 6 demonstrates a screw tract incorporated within
viable cartilage. At 90 days, the plating material had lost structural integrity and crumbled easily during specimen preparation.

**COMMENT**

The evolution of surgical management of SGS in children has greatly improved the morbidity and mortality of this patient population. In 1980, Cotton and Seid introduced the anterior cricoid split. After modifications and specific guidelines were created, Cotton et al reported that 70% of patients were successfully extubated without the need for tracheotomy.

Further advances involved the use of more extensive airway incisions to alleviate subglottic and tracheal stenosis and the use of cartilaginous grafts to assist with maintaining the patency of the airway and its increased intraluminal diameter. In most cases, mild to moderate SGS can now be managed as a single-stage procedure (SS-LTR), with reconstruction of the laryngotracheal framework performed over an endotracheal tube stent removed several days to a week after surgery, thus avoiding the need for a tracheotomy.

Despite these advances in the treatment of subglottic and tracheal stenosis, several aspects of the surgical procedures used in resolving this pathological condition remain problematic. Laryngotracheal reconstruction can be technically challenging, especially in a young child, requiring precise placement of sutures. Misplaced sutures or sutures that pull away from a graft or the site at which the suture is anchored can lead to graft displacement, airway compromise, and surgical failure to correct the area of stenosis. Postoperative care after SS-LTR can also be problematic because most surgeons maintain an endotracheal tube in place as an internal airway stent for several days. Use of this stent is meant to reduce the chance of a dislodged graft and subsequent airway compromise. Methods to reduce the difficulty from using a stent have included reducing the time intubated and using an indwelling nasotracheal tube without mechanical ventilation. However, especially in younger children, an SS-LTR still generally requires several days of intubation with mechanical ventilation and subsequent airway compromise as well as difficulties from medication withdrawal. The risk of complications during this postoperative phase continues to elicit debate within the literature regarding optimal management.

Zeitouni and Manoukian reported 4 complications in a series of SS-LTRs, including 2 cases of severe narcotic withdrawal requiring medical treatment. Rothschchild et al recommend refraining from the use of paralytic agents during the stenting phase of recovery, instead titrating analgesics and sedatives for comfort. They demonstrate success rates similar to those in studies in which paralysis is used. Still, some would argue that this increases the risk of self-extubation or accidental extubation and jeopardizes healing because of graft motion.

The purpose of this study was to examine a new method of LTR that would provide some advantages over currently used methods. The goals of this method of LTR were to develop a technique using a well-established model of SGS\(^5-10\) to (1) increase the diameter of a stenotic subglottic airway; (2) provide a means of external fixation that would immediately and rigidly maintain the increased diameter created in the incised airway; (3) provide the rigid external fixation without interfering with laryngeal and tracheal growth and development; and (4) provide a faster, technically less challenging and potentially more rigid and secure method of fixating a tissue graft in the incised airway.

The advantages of providing rigid external support through an external fixation system in LTR were initially identified by Zalzal and Deutch, who used a metallic alloy plating system to successfully perform LTR in dogs. Weisberger and Nguyen reported use of an external fixation system using a Vitalium alloy in adults, with 77% success. However, Mitskavich et al performed anterior cricoid split in a porcine model with SGS and noted intraluminal migration of the plates in 50% of the subjects, which raised concerns regarding using such external fixation systems in a developing larynx. The permanence of the metallic plating systems also produced concerns regarding long-term laryngeal and tracheal growth and development.

Use of bioabsorbable plating materials has become well accepted in the treatment of osseous craniofacial diseases in children. The resorbable quality of such materials is ideal for use in children because although it provides initial rigid support, it is resorbed over time and...
has minimal long-term impact on structures that are still growing and developing. The resorbable quality of these materials also limits concerns regarding migration of the rigid fixation material or the need for eventual removal of the material. Polylactic and polyglycolic acid, a copolymer currently used extensively in pediatric craniofacial surgery, demonstrates initial strength similar to titanium. Degradation seems to occur over a 12-month period. At 2 months, there is no change in the size of this type of implant; by 6 months, implant material has significant loss in size; and by 9 months, greater than 95% of the implant is resorbed.

The possibility of using bioabsorbable materials in airway surgery was introduced by Willner and Modlin, and only one other study has been published investigating the use of this material in airway reconstruction. In these investigations, the resorbable material was not used to fixate a cartilaginous graft. Also, in both of these studies, the bioabsorbable plate was sutured into place and not held with screw fixation, making true rigid fixation less likely. Our study is the first to incorporate PLA-PGA plates and screws to perform SS-LTR. Use of a plating and screw system provides the opportunity for a more rigid external fixation system that can add immediate stability to the expanded airway and maintain its increased diameter. In addition, our model relies on screw integrity, rather than sutures, to maintain its rigidity and to hold a costochondral graft in place.

Although the efficacy and ability of bioabsorbable materials to achieve rigid fixation is well documented when used in an osseous environment, transferring these materials and the principles of rigid fixation with plates and screws has not been attempted in a cartilaginous environment. The advantages of this technique to provide immediate rigid external support to an enlarged airway are self-evident. The airway would be immediately maintained at its increased luminal diameter without the need for an interposed material such as a cartilage graft to keep this increased diameter. The rigid fixation of the airway would also potentially provide for more rapid extubation and preclude the need for endotracheal tube stent. The potential new difficulties include the costochondral graft being without the plate and screw system, although this did not occur in our study. The results of our study demonstrated overall success. The procedure did not present any technical challenges and could be completed in a timely manner. All animals were extubated immediately without any airway complications during this study.

The costochondral graft was viable in 8 of 10 cases. In the remaining 2 cases, where significant necrosis was identified, distraction of the subglottic airway was maintained by the fixed plates, and good epithelialization occurred over most of the grafted site. There is a possibility that graft survivability was affected by heating the plate-graft unit to allow for molding of the plate to the laryngeal and tracheal framework. Future studies are planned in which the plate would be heated and molded before fixing the costochondral graft, thus avoiding the high level of heat to, and possible damage of, the cartilage graft. Another possibility is that a certain amount of graft necrosis, with neochondrification or cartilage remodeling subsequently taking place, is the natural course of this procedure. This possibility was demonstrated by Jacobs et al, who presented similar necrosis and neochondrification in their histopathologic analysis of cartilage grafts used in LTR in a rabbit model. Similarly, in our study, all grafts without significant necrosis demonstrated essentially complete epithelialization. Several of these grafts also demonstrated some areas of cartilage necrosis, with areas of cartilage remodeling on histologic examination. Intraluminal granulation tissue appeared to occur over areas of the graft where the screw came into approximation with mucosa, but no airway compromise was noted in these cases clinically. An additional means of dealing with the potential reactivity of the bioabsorbable material within the airway would be to use a system with a shorter screw or a technique of “welding” down the excess screw length using a heating unit. This technique is frequently used in craniofacial surgery to prevent any distal portion of the screw from penetrating into the intracranial cavity.

This study has some shortcomings that deserve discussion. This is a small study that does not completely account for the predicted life span of the PLA-PGA material (12 months). Also, these animals did not have severe SGS, which might place increased stress on the plate-graft complex. We also cannot take into account possible long-term effects on voice production or laryngeal development. Examining these areas would be worthwhile in future investigations. In addition, this study only examined one possible bioabsorbable material. Several different products exist, each of which has its own properties, including rate of resorption, initial strength, and tissue reactivity. The material used in this study has the quickest rate of resorption and loss of structural integrity of products currently available. This might be the most favorable scenario given the desire to limit effects on growth and development of laryngeal and tracheal framework and the desire to minimize chances for the migration of materials. However, a material with a somewhat
longer period of resorption might be more advantageous because these materials generally provide for a lesser degree of tissue reaction during resorption. Alternatively, potential exists for a manufacturer to design a material specifically for use in a cartilaginous environment, with applications designed for procedures such as LTR. This material would likely be superior to those that have been primarily designed for specific applications within an osseous environment.

CONCLUSIONS

This study presents a new technique for LTR that has the potential advantage of providing external airway support within a system of rigid fixation of a graft with a plate and screw system. The bioabsorbability of this system within a developing and growing larynx is particularly attractive, as is the speed and relative technical ease with which the procedure is performed. Future investigations using this or similar models would be worthwhile to further determine the utility of these techniques.

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