Endoscopic balloon dilation is commonly performed in children with airway stenosis, but guidelines are needed for selecting safe and effective balloon inflation parameters. Several recent case series have demonstrated promising outcomes for pediatric patients undergoing balloon dilation, either as primary therapy for subglottic stenosis or in conjunction with other approaches. However, the mechanism by which balloon dilation produces long-term resolution of airway stenosis is not known. One prevailing theory is that dilation mechanically disrupts scar maturation during the early development of subglottic stenosis. Another possibility is that balloon dilation actually produces full- or partial-thickness fractures of the cricoid cartilage, ultimately decompressing the cartilaginous framework of the subglottis.

There are currently no evidence-based guidelines for selecting the balloon diameter and inflation pressure in children undergoing endoscopic airway dilation. An excessively large balloon may rupture the airway or damage the underlying tissue, potentially leading to acute obstruction or long-term scarring. However, inadequate balloon size or pressure may diminish the likelihood of maintaining long-term airway patency.

An animal model provides the opportunity to systematically examine the safety of airway balloon dilation in vivo and to correlate these observations with different balloon sizes and pressures. For over 25 years, the New Zealand white rabbit has been used as a model to investigate wound healing in the lar-
yinx and evaluate novel airway procedures.10-22 The animal’s weight and size approximate those of a human neonate, and its larynx resembles that of a 3- to 9-month-old human infant.9,16 This study examines the feasibility and safety of laryngotracheal balloon dilation in live rabbits and lays the groundwork for future histological analysis of the postprocedure rabbit airway.

Methods

All procedures were conducted under a protocol approved by the Institutional Animal Care and Use Committee at Weill Cornell Medical College.

Thirty-two male New Zealand white rabbits (Covance) were acquired at age 8 months and allowed 5 days to acclimate to the animal facility. On the day of procedure, general anesthesia was induced using intramuscular (IM) ketamine, 50 mg/kg; xylazine, 7.5 mg/kg; and acepromazine, 0.75 mg/kg. Subcutaneous dexamethasone, 0.1 mg/kg, was also administered, but the rabbit never regained spontaneous breathing or circulation. Postoperatively the rabbits were evaluated 3 times daily, making note of their vital signs, activity level, urine output, and fecal output. On postoperative day 1 half the rabbits were euthanized via administration of IM ketamine, 50 mg/kg; IM xylazine, 10 mg/kg; and intravenous pentobarbital, 120 mg/kg. The remaining animals were euthanized on postoperative day 7. The laryngotracheal complex of each animal was harvested and preserved in formalin for future histological examination.

The airway was visualized using a Miller laryngoscope and a 0° 4-mm telescope.

Results

Rabbits weighed an average of 3.27 kg (range, 2.53-3.75 kg), and the airway diameter of all rabbits was sized to a 4-0 endotracheal tube (outer diameter, 5.4 mm). Balloon dilation was performed safely with no intraoperative complications in 25 of 30 cases. Endoscopy performed immediately after balloon removal demonstrated no gross evidence of mucosal trauma, airway edema, hemorrhage, or other injury.

One rabbit developed cyanosis during balloon inflation (8 mm/10 atm), which resolved after 30 seconds with the administration of oxygen. No endoscopic evidence of airway trauma was seen.

Three rabbits died intraoperatively while undergoing dilation with 10-mm balloons at 3 different pressures. These rabbits became cyanotic and stiff soon after the balloon was inflated and were found to be in cardiopulmonary arrest. One of the 3 rabbits was being monitored with continuous electrocardiography at the time of death—a late modification to the protocol motivated by earlier rabbit mortalities. Balloon dilation did not directly trigger any cardiac arrhythmias; the initial waveform during cardiopulmonary arrest was pulseless electrical activity, followed later by ventricular fibrillation that persisted despite the administration of intravenous antiarrhythmic drugs and positive pressure ventilation.

One additional rabbit underwent balloon dilation uneventfully (7 mm/5 atm) but became cyanotic and apneic in the recovery area 10 minutes after the procedure. Chest compressions, bag ventilation, and intramuscular epinephrine were administered, but the rabbit never regained spontaneous breathing or circulation.

All rabbits that died perioperatively received postmortem laryngoscopy and bronchoscopy to evaluate for airway abnormalities; none was noted to have any significant trauma, obstruction, or hemorrhage. Full necropsy also failed to reveal cardiovascular or pulmonary disease that could explain the cause of death.

All surviving rabbits recovered from the procedure with no evidence of respiratory difficulty. Four animals, however, developed poor oral intake as evidenced by scant urine and fecal production 24 hours following balloon dilation. At the request of the study veterinarian these rabbits were euthanized with the postoperative day 1 group to prevent further dehydration and discomfort. There was no clear relationship between postoperative feeding, balloon size, and inflation pressure. Rabbits in the postoperative day 7 group returned to their normalcy; none was noted to have any significant trauma, and no evidence of respiratory difficulty.
normal feeding and activity levels with no clinically evident sequelae from balloon dilation.

Discussion

The management of subglottic stenosis in infants and children has evolved rapidly over the past 3 decades. Recent technological advances have facilitated endoscopic approaches that promise fewer wound complications, decreased postoperative pain, shortened hospital stays, and no external scarring.23 One common endoscopic device is the balloon catheter, which was initially developed for endovascular interventions and later adapted for use in tracheobronchial stenosis by interventional radiologists and pediatric surgeons.24-26 Modern balloon catheters possess low profiles, allowing them to be passedatraumatically through small stenotic areas and subsequently inflated. Balloon catheters apply force radially and allow the surgeon to control both pressure and diameter, allowing the surgeon to apply pressure to a focused area and theoretically minimizing collateral mucosal trauma.1,23,27 Modern catheters are also oblong in shape, leading to higher stability and resistance to motion when inflated.5 For these reasons, balloon dilation has gained increasing popularity in recent years.

At the present time, there are no studies addressing the safety of airway balloon dilation in the pediatric population. A wide range of diameters and pressures are reported in the clinical literature, reflecting the fact that little is known about the underlying biomechanical effects of balloon dilation. An animal model provides the opportunity to systematically examine how the airway responds to dilation forces and identify balloon parameters that influence perioperative morbidity. Two studies have successfully documented endoscopic airway balloon dilation in live animals. Tubbs et al28 induced subglottic injury in 10 ferrets and performed dilation 48 to 72 hours following the injury. The subglottic airway measured 5.3 mm in diameter. Dilation was performed with either balloon catheters (5 mm diameter, 12 atm pressure, 30 seconds) or sequence...
The balloon catheter was centered on the subglottis and inflated for 30 seconds.

tially larger endotracheal tubes (to a maximum of 5.3 mm outer diameter). The animals were euthanized immediately after dilation and examined histologically. Subglottic narrowing was notably improved in all specimens, and ferrets that underwent balloon dilation exhibited thinning of the submucosa and lamina propria.

Wycherly et al29 induced tracheal stenosis in 6 adult New Zealand white rabbits and subsequently performed dilation using 8-mm balloons. Three of the animals underwent dilation with subfreezing cryoballoons, while the other 3 underwent dilation with room-temperature catheters. One animal with predilation stenosis of 80% was unable to tolerate balloon inflation and was euthanized intraoperatively. The remaining 5 rabbits survived until they were euthanized 2 to 4 weeks after balloon dilation and demonstrated varying degrees of relief from tracheal stenosis. Histological analysis demonstrated decreased tracheal collagen deposition in 1 rabbit undergoing cryodilation in comparison with a room-temperature counterpart.

Our current study represents the largest series of balloon dilation procedures in a live animal model and the only study, to our knowledge, that addresses the key variables of balloon dilation procedures in a live animal model and the only study, to our knowledge, that addresses the key variables of balloon dilation and pressure. Balloon dilation was performed without intraoperative complications in most rabbits (25 of 30). Airway visualization and catheter insertion were straightforward and performed under spontaneous ventilation in all cases.

The perioperative death of 4 rabbits was an unexpected finding. Mortality during balloon dilation may occur for several reasons, including hypoxic arrest, laryngospasm, airway rupture, obstructive edema, airway hemorrhage, and vasovagal-induced cardiac arrhythmia. In all 4 rabbits, endoscopic examination excluded airway edema and hemorrhage as the cause of death. Electrocardiographic monitoring failed to identify any cardiac rhythm abnormalities occurring during balloon inflation. Pulse oximetry demonstrated that 30 seconds of airway occlusion generally would not cause significant hypoxia, although 1 rabbit briefly developed cyanosis requiring blow-by oxygen. Laryngospasm was unlikely because each animal’s larynx was topically anesthetized prior to instrumentation, and laryngospasm was not observed in any of the postprocedural endoscopic examinations.

Dilation with the largest balloon size (10 mm) was responsible for 3 of the 4 rabbit deaths, representing a 50% mortality rate with the 10-mm catheters. While this observation suggests that airway rupture contributed to the death of these rabbits, the animals developed cardiopulmonary arrest shortly after balloon inflation with no preceding stridor or dyspnea. Endoscopic examination failed to demonstrate gross laryngeal trauma, and ultimately the exact cause of death remains unclear. A fourth mortality occurred approximately 10 minutes after uncomplicated dilation with a 7-mm balloon. The rabbit was again found to have a patent airway at the time of respiratory arrest with no evidence of gross laryngeal trauma. Rabbit deaths occurred at all inflation pressures (2 deaths at 5 atm, 1 at 10 atm, and 1 at 15 atm), suggesting that balloon diameter plays a greater role than pressure in determining intraoperative mortality.

Four rabbits failed to resume a normal oral diet postoperatively and were euthanized to prevent complications of dehydration. None of them exhibited stridor, dyspnea, or other evidence of airway compromise. The underlying reason for these feeding difficulties was unknown, and there was no obvious relationship between postoperative feeding, balloon size, and pressure.

Ultimately, New Zealand white rabbits provide a reliable model for studying the effects of endoscopic balloon dilation in vivo. Our observations suggest that balloons exceeding the airway diameter by 4.6 mm carry a high risk of intraoperative death and should be avoided. Oxygen saturation should be monitored throughout the procedure owing to the risk of transient hypoxia. Oral intake should be monitored postoperatively, as feeding difficulties can occur regardless of balloon diameter. Inflation pressure does not seem to have a significant impact on perioperative morbidity.

Although this study provides some insight into selecting safe balloon inflation parameters, its clinical relevance is somewhat limited. Slight differences in proportion between the rabbit larynx and the infant larynx require caution when generalizing animal findings to the human population.22 Furthermore, each rabbit in the study had a nonpathological airway; balloon dilation is typically used in areas of subglottic or tracheal stenosis, where scarring may alter the biomechanical properties of the tissue.

Future studies should examine the effects of different balloon diameters and pressures on animals with subglottic stenosis. Histological analysis should also be performed to examine how the balloon parameters relate to microscopic evidence of mucosal injury, fibrosis, and cricoid fractures. Studies extending beyond the 7-day postoperative period will also be necessary to determine the long-term sequelae of balloon dilation in an animal model.

Conclusions
Endoscopic airway balloon dilation is feasible and generally well tolerated in New Zealand white rabbits. Intraoperative
Airway Balloon Dilation in a Rabbit Model

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