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Treatment of Large Tracheal Defects after Resection: Laryngotracheal Release and Tracheal Replacement

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Introduction

Since the 1950s tracheal or laryngotracheal resection developed from an experimental to a routinely performed surgical technique. Although most frequently employed for benign iatrogenic tracheal stenosis, usually from prolonged endotracheal intubation, the spectrum of indications also includes idiopathic stenosis and reconstruction after resection for primary and secondary malignant tracheal tumors[1]. When feasible, the most appropriate treatment of circumferential tracheal stenosis is resection and end-to-end anastomosis. The availability of newer suture materials, jet ventilation, and intensive care medicine has increased the safety and success rate of this procedure. Tracheal resection for stenosis should not be confused with laryngotracheal reconstruction which is employed for subglottic stenosis, usually in children. Resection with anastomosis may include the inferior portion of the cricoid cartilage ("laryngotracheal resection"), but stenotic subglottic lesions extending into the cricoarytenoid or interarytenoid region require a procedure to widen the subglottis, which is known as "laryngotracheal reconstruction," and usually do not require resection and anastomosis. The present review focuses on the importance and the various possibilities of performing laryngotracheal release for reduction of anastomotic tension; and on methods of tracheal replacement for defects too large to bridge by primary anastomosis.

After tracheal or laryngotracheal resection the anastomosis should ideally be entirely free of tension. The tension placed on the tracheal ends depends on the length of the segment resected. This is an important limiting factor in all cases of tracheal resection. With resection lengths of less than 2–3 cm the tracheal ends can usually be brought together without additional measures to reduce tension, but these situations are infrequently encountered. Resection lengths of up to 6.5 cm without such additional measures have been reported in the literature[2]. However, they have usually been unsuccessful.

An isolated canine cadaver trachea can withstand a tensile load of more than 1750 g before rupturing[3]. If an end-to-end anastomosis is created, the load at rupture depends on the suture material used. With Vicryl® 4-0 sutures complete rupture occurs at a load of 179.9 Newton force units (N) and with PDS® 4-0 sutures complete rupture occurred at a load of 161.5 N. These investigations were also carried out on tracheae from human cadavers[4].

In an experimental study in sheep, Behrend et al.[2] showed that increasing the tension on the anastomosis led to progressive stenosis during the course of recovery. Spontaneous rupture of the trachea did not occur in that study. A follow-up period of 6 months was considered sufficient for evaluating the degree of stenosis that had occurred.

Grillo et al.[5] described three types of anastomotic dehiscence: 1. partial dehiscence, 2. partial dehiscence whose space gradually fills with granulation tissue. Healing of a partially dehiscent anastomosis eventually leads to stenosis resulting from scar tissue at the site of the defect, and 3. complete rupture of the anastomosis which often has lethal consequences. The tensile load acting on the anastomosis depends on the length of removed trachea. The local tensile loads exerted on the anastomoses after resection were found to be 7.2 N when a length of 3 cm (equivalent to 13% of the total tracheal length) was removed, 13.6 N by 6 cm (26%), and 21.4 N by 9 cm (39%), respectively[2]. In a large series of 263 patients

undergoing surgery for idiopathic subglottic stenosis 8.7% of patients experienced subsequent recurrence of stenosis[6].

In dogs, Grillo et al.[7] found a mean tension of 675 g on the tracheal ends after tracheal resection of a total length of 7 cm. Under clinical conditions the tension on the anastomosis was found to be 600 g after tracheal resection of 4.5 cm. In another study the same authors investigated fresh cadaveric trachea[5]. They found that, to ensure that the anastomotic tension does not exceed 1100 g, the maximum length of trachea that can be removed is 6.4 cm, 13.4 tracheal rings or 58.7% of the total tracheal length.

Behrend et al.[2] found that the distribution of tension varies with respect to the circumference of the trachea. The ventral part of the trachea is subject to greater tension than the rest. It is recommended that, in long tracheal resections with a tensile load greater than 20 N, traction sutures should always be placed ventrally to reduce the tension on the anastomosis sutures. Rosen et al.[8] systematically investigated the effect of tracheal release after tracheal resection in 10 cadaveric tracheas. By using appropriate release techniques it was possible to remove 6.68 cm, 13.3 tracheal rings or 65.5% of the total length of the trachea without creating tension on the anastomosis of more than 1000 g.

Tracheal Release Procedures

Various tracheal release techniques are effective for reducing tension on the anastomosis and should be considered in complex and long resections.

Supra-resection release procedures

Anteflexion of the neck

Flexion of the neck helps to remove tension from the anastomosis and should always be continued for 7 days after tracheal resection. In the past the chin was fixed to the chest with heavy sutures or wire. However, such fixation is no longer considered necessary and is not performed at most centers. However, the patient must be prepared to hold his or her chin down continuously after the operation, with the assistance of a pillow or bolster.

Alternatively the patient can be fitted postoperatively with a corset that fixes the head so that it is flexed forward by 30 degrees[9]. This simple routine can achieve a gain in length amounting to around 3–4 cm.

Laryngeal (infrahyoid) release

Dedo and Fishman[10] described what they called the laryngeal release technique in 1969. This requires the cutting of the thyrohyoid muscles and thyrohyoid membrane. The superior horns of the thyroid cartilage are also isolated. This elongates the supraglottis when tension is applied. However, this procedure can lead to aspiration or dysphagia. Grillo et al.[11] reported on a series of 49 patients, each of whom was subjected to a laryngeal release procedure. Postoperative aspiration and swallowing problems occurred in only 1.2% of these patients. Maassen[12] also reported swallowing problems after laryngeal release. These could last for longer periods but most then subsided. Laryngeal release can also performed

in cases of long – segment congenital tracheal stenosis before a slide tracheoplasty with success[13]. Using this procedure affords about 2.5 cm of proximal tracheal mobilization.

Suprahyoid release

In 1974, Montgomery[14] described a technique in which the mylohyoid and geniohyoid muscles were detached from body of the hyoid bone, which was then severed from the greater and lesser cornua, (Figure 1). This releases the laryngotracheal segment from its suprahyoid attachments, permitting downward mobilization. El-Fattah et al.[15] carried out cricotracheal resection in 12 patients, removing 2–4 cm in each case. Suprahyoid release was performed on all patients. None of the patients reported postoperative swallowing problems or aspiration.

In another study tracheal resection of a mean length of 4.2 ± 0.4 cm was carried out in 20 patients with tracheal stenosis[16]. Suprahyoid release was performed in all cases. This procedure led to a mean gain in length of 1.1 ± 0.4 cm. This procedure allows the proximal trachea to be pulled downwards by 2–3 cm and is among the most frequently used mobilization procedures[17].

Infra-resection release procedures

Manual blunt dissection

Ventral blunt digital pretracheal dissection is performed before the trachea is cut below the stenosis. It is important that the pretracheal fascia be opened first in order to prevent a false passage into the mediastinum. The dissection is only done anteriorly so that the circumferential tracheal blood circulation is not interrupted. Mobilization usually extends to just below the brachiocephalic trunk, as limited by the length of a finger. This procedure is technically easy to perform but if bleeding occurs it is difficult to control. Tracheal mobilization results in a gain in length of about 2 cm.

Video assisted mediastinoscopic release

The trachea is exposed by means of an incision in the pretracheal fascia and the video mediastinoscope is inserted into the pretracheal space and dissection conducted in an inferior direction before resection of the tracheal stenosis begins. Mobilization is performed strictly along the front of the trachea using a swab or an isolated aspirator. Adhesions are pushed off by blunt dissection. Minor bleeding can be controlled by targeted electrocoagulation with the isolated aspirator. With this technique, the tracheobronchial tree can be exposed as far as the distal main bronchi and mobilized (Figure 2). Central blood vessels such as the right main pulmonary artery and the vena cava can be identified with certainty and pushed aside[16]. In a previous publication we have confirmed the advantage of video assisted mediastinoscopic release during tracheal resection as a routine procedure[18]. With this technique we are able to avoid a transverse half – sternotomy, such as in a case of tracheal resection reported by Watanabe et al[19]. Using this procedure, which in our view is almost risk-free, the trachea can be mobilized at least 3 cm in a cranial direction. In our opinion this technique is the procedure of choice.

Hilar release

This involves carrying out an anterolateral or posterolateral thoracotomy on the right side. Initially, the inferior pulmonary ligament is divided using electrocautery and the right lung is mobilized in a cranial direction. Then a circular cut is made in the pericardium close to the hilum and in front of the phrenic nerve so that the main trunks of the pulmonary veins and pulmonary artery are also able to move upwards (Figure 3). In addition, the intrapericardial septum connecting the lateral part of the atrium and the lower vena cava is split up to the diaphragm. The azygos vein is divided cranially so that the right hilum can be moved upwards. Around 3 cm in length can be gained with correct right-sided intrapericardial hilar release[20]. This procedure can also be performed using thoracoscopy.

Intrapericardial release on the left side leads to a smaller gain in length than on the right side. The upward movement of the left main bronchus is hindered by the aortic arch. In addition, on the left side, Botalli's ligament must always be divided.[20].

In special cases a bilateral anterior thoracotomy may be employed for initial access. Once both thoracic cavities have been opened, this complicated access method makes it possible to perform intrapericardial hilar release on both sides in a single session.

Reinsertion of the left main bronchus

In very rare cases the distal trachea and the right main bronchus can be transposed upwards. The left main bronchus must first be severed at the tracheal bifurcation. After upward mobilization of the right main bronchus, the left main bronchus is then reinserted without tension on the right bronchus intermedius. The operation is performed via right thoracotomy. It brings an upward gain in length of the distal trachea of about 3 cm[20].

The table[20] summarizes the different release procedures and the gain in length that can be achieved with each procedure.

Swallowing dysfunction following laryngotracheal resections

Late complications of tracheal resection include the potential for swallowing dysfunction. Unfortunately remarks about this issue in the literature are rare. The extent of aspiration and dysphagia are extremely variable and dependent on multiple factors including the impact of presenting disease, the extent of surgical resection and the need for adjuvant therapy.

In patients with benign strictures, local structures including the recurrent laryngeal nerve and oesophageal lumen are not involved. Tracheal resection in this group is associated with low rates of post-operative dysfunction, which is often related to injury to the recurrent laryngeal nerve [21], [22]. Even in a group of pediatric patients (n = 30), the performance of a laryngotracheal reconstruction did not influence the swallowing function. The growth and the feeding status of the children were normal during the late postoperative period (10–14 months) [23] In case of a suprahyoid release, the resection of the hyoid bone has no influence on the swallowing function[15].

Patients with thyroid carcinoma invading the trachea swallowing also have good swallowing outcomes with around 15% showing evidence of aspiration at 1 month post op[24], and less than 10% of patients reporting aspiration or dysphagia in the long term[25].

In patients with more aggressive disease, the degree of dysfunction is more difficult to predict. Pre-operative swallow assessment should be considered routine and realistic expectations based upon the extent of disease and the expected morbidity associated with resection. In patients with locally advanced malignancy who are still considered candidates for surgery, long-term enteral feeding tubes may be required in the pre and postoperative period.

Choice of Release Maneuvers Depending on the Location of Stenosis

The type of tracheal release employed depends mainly on the length and location of the resection. In most cases, resection of more than 3 cm cannot be repaired by direct anastomosis without a tracheal release procedure. During the operation the surgeon tests the amount of tension that is likely by attempting to approximate the tracheal ends. Release procedures are carried out until the tension is as low as possible. If the resection zone is too long, a replacement graft or prosthesis may be the only way to achieve tracheal continuity. Release procedures are performed depending on the location of resection. We distinguish three tracheal regions:

1. Upper third: below the cricoid cartilage to the sternal notch (may include the inferior half of the cricoid arch and lamina).
2. Middle third: reaches from the sternal notch to 2 cm above the intrathoracic entry of the azygos vein into the vena cava.
3. Lower third: reaches from 2 cm above the entry point of the azygos vein to the tracheal bifurcation.

Upper third

Merati et al.[26] reported on 17 tracheal resections in the upper third with a maximum resection length of 4 cm; none with tracheal release. Only one patient developed re-stenosis and no cases of anastomotic dehiscence occurred. In comparison, Cordos et al.[27] carried out 60 tracheal resections of the same length (up to 4 cm) in the upper third and always performed blunt pretracheal dissection and neck flexion after the operation. Only one patient developed re-stenosis. Anastomotic dehiscence did not occur in any of the patients reported. Zannini et al.[28] performed resections with a maximum length of 5 cm in 83 patients. Suprahyoid release was carried out in 4 patients. At the time of follow-up examination none of the patients had developed stenosis or wound dehiscence. Weidenbecher and Gentsch[9] reported similar results in 16 patients with tracheal stenosis who underwent resection of lengths of up to 5 cm. With suprahyoid release and postoperative flexion of the neck they reported no postoperative complications.

According to Har-El et al.[29], all the tracheal release procedures that were performed in a comparable group of 19 patients only affected the neck. Right hilar release was not

necessary in any of their patients. In rare cases, if resection of a long laryngotracheal stenosis is to be carried out in a child, additional right hilar release may also be necessary[30]. Interestingly, Donahue et al.[31] operated on 75 patients with recurrence of tracheal stenosis. Once again, up to 5 cm of trachea were resected. Suprahyoid release was performed in 25% of those cases.

As mentioned above, if the resection length is less than 2 cm it is usually not necessary to perform a release procedure. We recommend postoperative flexion of the neck. With resection lengths of up to 5 cm, suprahyoid and video assisted mediastinoscopic release of the trachea in a caudal direction is recommended. Flexion of the neck should be maintained for 7 days postoperatively.

Middle third

Neck access is often combined with sternotomy to reveal the middle section of the trachea[32]. In our opinion, video assisted mediastinoscopic mobilization of the trachea in a distal direction should always be performed. Using this technique the trachea can be mobilized distally as far as the bifurcation. If the patient has undergone sternotomy the pleura on the right side can be opened and right hilar release can be performed. With maximal release, resection of 4 cm of trachea can be achieved in this area with tension free anastomosis.

Lower third

As a rule, posterolateral thoracotomy is performed on the right side for resection of the lower third of the trachea. Right hilar release is almost always performed. In addition, the anterior wall of the trachea is bluntly mobilized in a cranial direction with a finger. After the operation we recommend flexion of the neck for 7 days.

Tracheal Grafting and Replacement

Even with its limitations, direct anastomosis is currently the “gold standard” of therapy for patients with tracheal disease. Nevertheless, in adults only half the tracheal length can be reliably treated by tracheal resection and anastomosis, while in pediatric patients the limit drops to about one third. This issue becomes challenging because several diseases lead to defects greater than those amenable to direct resection and anastomotic repair. In the past a number of experimental treatments have been tried to overcome these limitations. This includes the shaping of a tracheal conduit from a variety of tissues and materials, such as autografts, allografts, prosthetic materials or a combination of different methods. These techniques have not proven to be practical because of restrictions inherent to them, such as inability to mimic the properties of native tissues, as well as the occurrence of extrusion, incomplete host-tissue integration and infection.

A tracheal transplant is another option, but donor tissue is difficult to obtain. Additional problems include vascularization of the transplanted segment and immunogenicity. Thus, results of direct tracheal transplantation have been disappointing due to ischemia and rejection. Since the blood supply to the trachea makes it unsuitable for direct revascularization, most attempts at tracheal transplantation have been performed with staged

indirect revascularization. This type of revascularization can be achieved by wrapping the tracheal allograft in heterotopic tissue from the recipient that is well vascularized and perfused by an identifiable vascular pedicle, such as forearm tissue pedicled on the radial artery.

Multistaged tracheal transplant is a months long process that requires initial immunosuppressive therapy. The posterior tracheal wall becomes necrotic one month after implantation into the forearm and must be removed and replaced by buccal mucosa from the recipient. The epithelial lining consists of squamous epithelium and respiratory epithelium that originates from the recipient's buccal mucosa and the donor's tracheal epithelium, respectively. Chimerism occurs after the withdrawal of all immunosuppressive therapy 4–5 months after the provisional implant, and the recipient buccal mucosa grows progressively over the lumen of the cartilaginous tracheal transplant. The endothelial and respiratory cells that originated from the donor disappear shortly. Because of the presence of recipient cells in the allograft, immunosuppressive therapy may be discontinued. The revascularized allograft is dissected with its radial artery and two radial veins and the vascular pedicle is sutured to appropriate neck vessels. Immunosuppressive therapy during revascularization of the tracheal transplant is necessary for establishing connections between the donor's capillary network around the trachea and the recipient's fascial blood vessels. Conversely, the cartilaginous framework is not recognized by the immune system due to the lack of blood vessels in the adult cartilage. Nevertheless, tracheal transplantation presents some unsolved problems. Repopulation of the mucosal lining by recipient cells, to compensate for necrosis of the donor mucosa, is usually incomplete, and this results in partial loss of the allotransplant in some patients. Measures to maximize recipient cell repopulation may be important in maintaining the viability of the transplant after cessation of immunosuppression[33,34].

Tracheal transplantation can be useful for tracheal stenosis but is not suitable for extensive malignant tumors of the trachea because it requires a long interval of time between stages, and in addition, involves immunosuppression. To overcome these difficulties, the use of cryopreserved aortic allografts to replace long tracheal segments has been experimentally evaluated in minipigs[35]. Intense inflammation and progressive disappearance of typical histologic structures of the aorta were seen within the first 3 months. After that period all animals showed transformation of the graft into a chimeric conduit sharing aortic and tracheal histologic patterns, including respiratory ciliated epithelium, respiratory glands, and islets of cartilage. Wurtz et al.[36] have reported the results of tracheal replacement with aortic allografts in 6 patients with extensive malignant tumors. Tracheal tumor resection was followed by interposition of the graft, splinted permanently by a silicone stent. The allograft consisted of an aortic segment, either fresh or cryopreserved. All grafts were wrapped with bulky and well-vascularized flaps such as the pectoral muscle flap to promote revascularization and to prevent erosion of adjacent large vessels or fistulas. No immunosuppressive therapy was administered. Three of the patients experienced major morbidity, mainly fistulas between the esophagus and graft. All grafts transformed into well-vascularized conduits focally lined with respiratory epithelium. As prosthetic replacements, autologous tissue transfer and allografts have failed in offering functional solutions for the treatment of long circumferential tracheal defects, The use of tissue-engineering techniques

utilizing autologous stem cells to create new tissues opens new perspectives. Tissue engineering merges biology, engineering, and materials science to generate new tissues in vitro for later use in vivo. A variety of approaches have been proposed for airway replacement, ranging from collagen scaffolds supported by silicone stents to cartilaginous tubes created by in vitro culture methods[37], or resorbable nanocomposite polymers[38]. The potential clinical advantages of autologous stem-cell-derived transplants are that patients who receive them would not need immunosuppression and that the transplants are hypothesized to be remodeled by local stroma to simulate native tissue[39]. Until now, four human cases have been reported, two of them with short follow-up periods, and the others ranging from 2–4 years. In three patients a tissue-engineered trachea was transplanted using a decellularized deceased donor trachea repopulated with the recipient's respiratory epithelium and mesenchymal stromal cells[39–41], whereas in the remaining patient the airway was replaced with a tailored bioartificial nanocomposite previously seeded with autologous bone-marrow mononuclear cells via a bioreactor[42].

The donor trachea is first decellularized using a detergent (without denaturing the collagenous matrix), because it is of vital importance that MHC class I and II antigens disappear from the matrix. Bone marrow mesenchymal stem cells are retrieved preoperatively and seeded onto the scaffold, with patches of autologous epithelium. Topical human recombinant erythropoietin is applied to encourage angiogenesis, and transform growth factor β to support chondrogenesis. In this way the graft becomes revascularized within 1 week after surgery, but cytological evidence of restoration of the epithelium is not evident until 1 year. Finally, a specifically designed bioreactor enhances the reseeded of the pre-expanded and pre-differentiated autologous cells in vitro on the desired surfaces of the decellularized matrix^{35,39}. However, there are many questions that need to be addressed to make this technology universally available, such as the flexibility, stiffness, and compliance of the engineered tissue, to create an airtight structure, and to assure the growth of the implant in the patient, which is particularly important in the pediatric population[43].

Further research is required to develop bioengineered tracheal replacements with lower morbidity, better biomechanics and at an acceptable cost. Future clinical trials of such constructs should include comprehensive assessments of airway physiology, biology, and quality of life[40].

Conclusions

In cases of tracheal resection of more than 2–3 cm a tracheal release procedure should be additionally performed to reduce tension on the anastomosis. The release procure employed depends on the location of the resection. Occasionally a combination of different release techniques should be used. Despite application of the described techniques there is still a risk for wound healing disturbances in cases of large resections. In this context, the latest developments in stem cell tracheal bioengineering and allogenic tracheal transplantation could be of interest in the future[37]. Prefabricated composite free flaps are also an attractive option for certain challenging cases of airway reconstruction[44]. Interdisciplinary cooperation between head and neck surgeons and thoracic surgeons as well as those with

experience in advanced bio-engineering Is necessary for solution of the most difficult problems.

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Figure 1.
The principle of suprahyoid release with cutting of the hyoid bone and mobilization of the trachea in a caudal direction (↓)

Figure 2.
Mobilization of the distal trachea (→) and both main bronchi using video assisted mediastinoscopy

Figure 3. Mobilization (↔) of the right hilar vessels in a cranial direction by cutting the pericardium (right hilar release)