Airway Transplantation

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KEYWORDS

• Trachea replacement • Tissue engineering • Allogenic transplantation
• Immunosuppressive medication • Rejection

KEY POINTS

- Replacing long segments or the entire trachea in humans.
- Allotransplantation.
- Surgical challenges.
- Organ rejection.
- Tissue engineering.

A variety of benign or malignant disorders affecting the trachea can theoretically be treated by simple resection and subsequent end-to-end anastomosis of the remaining trachea.[1] This primary reconstruction is, so far, the only curative treatment in patients with tracheal diseases but, unfortunately, it is feasible only when the affected tracheal length does not exceed 6 cm in adults and about 30% of the entire length in children. Besides this technical restriction, local anatomy, previous treatments, and type of pathologic condition can further restrict the already few therapeutic options.

Longer segments cannot be treated surgically because it is impossible to perform safely a direct reconstruction of the airway that, under these circumstances, would ultimately fail because of the excessive tension at the anastomotic site. Benign diseases have been approached with various endoluminal solutions.[1,2] Because most of primary tracheal malignancies are diagnosed in an advanced local stage, only palliative options remain available, such as stenting, tumor debulking or radiotherapy.[1,3] Consequently, tracheal transplantation could be a valid alternative for many patients (**Table 1**). To this end, different replacement strategies have been investigated in experimental settings and some of them translated to the clinic. However, so far, none of them has turned into a routine clinical procedure. The requirements of an ideal tracheal substitute are multifaceted but crucial for a successful clinical application (**Table 2**).

TYPES OF TRANSPLANTATIONS

In 1963, Fonkalsrud and Sumida,[4] and, in 1971, Fonkalsrud and colleagues,[5] reported two initial clinical cases of tracheal replacement using the patients' own esophagus in congenital agenesis and long-segment stenosis. Initially, the patients recovered remarkably but then died within the first 6 weeks postoperatively. Both neotrachea required permanent stenting and did not provide normal

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Table 1
Indications for potential tracheal transplantation and eligibility criteria

Indications	Benign Diseases	Malignant Diseases
—	• Trauma • Benign stenosis • Relapsing polychondritis • Osteochondroplastica • Amyloidosis • Tuberculosis	• Unresectable tumors • Postlaryngectomy recurrences or diseases
	Eligibility Criteria	
	• Extended (>60% total length) benign & malignant diseases • Already maximally pretreated • Age between 10 and 75 y • No absolute surgical contraindications • No regional and/or micrometastasis (bone-marrow biopsy proven) • Normal psychological or psychiatric habitus • Independent review board, ethics and national transplant clearance • Written informed consent	

function. No similar transplants have been made since. Instead, a variety of approaches have been attempted clinically that use either allotransplantation or tissue engineering (TE) approaches.

TRACHEAL ALLOTRANSPLANTATION

Fresh Cadaveric Trachea

In 1979, Rose and colleagues[6] described the first case of allogenic tracheal replacement using a fresh cadaveric tracheal graft in a 21-year-old male patient with extensive benign tracheal stenosis. In a two-stage procedure, the graft was initially implanted into the sternocleidomastoid muscle region to provide indirect vascularization and subsequently transferred to the orthotopic site. The patient was discharged 9 weeks after the transplantation without immunosuppressive medication and no signs for organ rejection or health status impairment. At that time, it was assumed that the tracheal immunogenicity was not relevant and graft failure was only provoked by graft ischemia and infection.[6] In contrast, Levashov and colleagues[7] transplanted on a donated trachea but with different findings. They used the omentopexy to obtain indirect blood supply of the cadaveric trachea and reported signs of organ rejection at day 10 postoperatively. The investigators affirmed the promising overall outcome 4 months after the transplantation but emphasized the essential need of adequate donor-recipient selection and modern immunosuppressive medication. Similar

Table 2
Requirements of ideal tracheal substitute

Scaffold for Tissue Replacement	Characteristics
General properties	• Nonimmunogenic • Nontoxic • Nontumorigenic • Allows for cell adhesion, migration, proliferation, and differentiation
Tracheal-specific properties	• Airtight and liquid-tight seals • Mechanical properties to react on both lateral and • Longitudinal forces • Support airway patency and respiratory function
Required mechanical properties based on native trachea	± 75° (right/left axial rotation at 0° maximum flexion) ± 75° (right/left axial rotation at 0° flexion) Flexion/extension 70°/60° and 40% of strain limit (flexion-extension bending) 40%:20% for tension/compression (axial/tension/compression) Lateral (right/left) bending: 48° and expected strain limit of 40%