Surgical technique and results of tracheal and carinal replacement with aortic allografts for salivary gland–type carcinoma

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Objective: We describe the surgical technique and peroperative management of tracheal and carinal replacement with aortic allografts for large salivary gland–type carcinoma and report the results with a mean 34 months' follow-up.

Methods: We performed tracheal and carinal replacements with aortic allografts in 6 patients with extensive mucoepidermoid (n = 1) or adenoid cystic (n = 5) carcinomas. Tracheal tumor resection was followed by carinal restitution (n = 3) and interposition of the graft, splinted by a silicone stent. The allograft consisted of an aortic segment, either fresh (in the first 2 patients) or cryopreserved (in the last 4). All grafts were wrapped with bulky and well-vascularized flaps (pectoral muscle flap all patients, with an additional ''thymopericardial fat flap'' in the last 2) to promote revascularization and to prevent erosion of adjacent large vessels or fistulas. No immunosuppressive therapy was administered.

Results: Complete resection (R0) was achieved in 5 (83%) of 6 patients. Three of the first 4 patients experienced major morbidity, mainly fistulas between the esophagus and graft. The last 2 patients had an uneventful outcome. All grafts transformed into well-vascularized conduits focally lined with respiratory epithelium. So far, the last 4 patients are disease-free and 3 of them have returned to full-time employment. Stent removal has not been attempted in any patient.

Conclusion: Tracheal replacement with aortic allografts enables resection of extensive tumors with a curative intent. Efficient protective wrap around the graft is mandatory. Further follow-up is required to determine whether cartilage rings are generated within the graft, as in animal models. (J Thorac Cardiovasc Surg 2010;140:387-93)

Supplemental material is available online.

Despite impressive advances in the field of tracheal surgery, extensive resection remains challenging and a suitable tracheal substitute has been sought for decades.[1,2] Experimental studies in sheep showed that replacement of the trachea or carina with fresh[3,4] or cryopreserved[5] aortic allografts (AAs), without additional immunosuppression, produced a neotrachea stiff enough to enable withdrawal of a stent placed across the AA to prevent collapse. We obtained similar results in a pig model by replacing long tracheal segments with fresh[6] and cryopreserved AAs.[7] According to these consistent results, we launched in March 2005 a national tracheal replacement (TR) research program for unresectable tumors. Preliminary results were reported in 2006.[8]

This article aims at describing the surgical technique, perioperative management, recent technical advances, and results of TR.

PATIENTS AND METHODS

Patients

Five men and 1 woman aged 17 to 52 years (mean 34.5 ± 12.8 years) with large mucoepidermoid (n = 1) (MEC) or adenoid cystic (n = 5) carcinomas (ACC) were included in the present study (Table 1). The tumor was revealed by left recurrent palsy in 1 patient and exertional dyspnea in the others. They all underwent thorough preoperative functional and oncologic assessment including pulmonary function tests, chest and upper abdominal computed tomography, brain magnetic resonance imaging, positron emission tomography, and bronchoscopy with a rigid scope with extensive and deep biopsies (rigid forceps) to assess the tracheobronchial mucosal and submucosal extension. Esophageal ultrasonography was performed in case of close contact between the tumor and the esophagus to assess esophageal muscular layer extension. Owing to the severity of their tracheobronchial obstruction, 4 patients underwent 1 or more tumor debulking endoscopic procedures before referral, completed by bifurcated silicone stent insertion in 2 patients. Stents were removed at least 2 weeks before surgery. Diagrams show the gross tumor extension immediately before surgery (Figure 1).

Preoperative Preparation

Patients were hospitalized 2 to 6 days before surgery for respiratory physiotherapy and training with noninvasive positive-pressure ventilation

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Abbreviations and Acronyms

AA = aortic allograft
ACC = adenoid cystic carcinoma
MEC = mucoepidermoid carcinoma
TR = tracheal replacement

(patients 5 and 6). Patient 5 also followed a rehabilitation program for 3 weeks preoperatively.

A percutaneous endoscopic gastrojejunostomy tube was placed preoperatively in the last patient to prevent postoperative aspiration. Antibioprophylaxis included co-amoxiclav (6 g/d) administered 24 hours before surgery and postoperatively for 72 hours. In the last 2 patients, fluconazole (400 mg/d, 72 hours before surgery and until patients' discharge) was added owing to complications experienced by the previous patient.

Fresh and Cryopreserved AAs

For the first 2 patients, 10- to 12-cm long segments of the descending thoracic aorta harvested from brain-dead donors were provided by the Agence de la Biomédecine (Saint-Denis la Plaine, France). Subsequently, we used 10- to 12-cm long cryopreserved segments of the descending thoracic aorta of brain-dead donors provided by the European Homograft Bank (Brussels, Belgium).

Procedures (Table 1)

All patients were positioned supine and conventionally intubated. A median sternotomy combined with an optional collar incision was performed. The trachea was exposed by division of the thyroid isthmus, both lobes of the thymus, and the left innominate vein, followed by a transpericardial approach to the distal third of the trachea with the vena cava retracted to the right and the ascending aorta to the left. The carina and both main bronchi were also exposed, with the right pulmonary artery retracted caudad.

In patient 1, owing to tumor extension (Figure 1), a left thyroid lobectomy was performed first, followed by mediastinal lymph node dissection. The tracheal tumor was circumferentially dissected (Figure 2, *A*) and complete removal required a left recurrent nerve and anterior esophageal wall resection. After withdrawal of the endotracheal tube, the trachea was sectioned below the second ring and distally until the margin was negative on frozen section analysis (subtotal resection of the main carina) while unilateral ventilation was ensured through cross-field left main bronchus cannulation (Figure 2, *B*).

Carinal restitution was achieved by suturing the right and left main bronchi together with 3-0 absorbable Monosyn (Aesculap, Tutlingen, Germany) glyconate monofilament interrupted sutures. End-to-end anastomosis between the proximal trachea and the fresh AA was then performed with a Monosyn glyconate 3-0 running suture (Figure 2, *C*). With the apneic hyperoxygenation technique,[9] tracheal and bronchial limbs of a Y-shaped silicone stent (Tracheobronxane Dumon; Novatech, Aubagne, France) were checked to fit the length of both main bronchi and trachea to be replaced. Once the left main bronchus was recannulated, the patient was orotracheally intubated with a rigid bronchoscope. Through the operative field, the folded stent was entered into the AA and gently pulled above the proximal anastomosis (Figure 2, *D*). The distal part of the AA and new carina were then approximated with a posterior hemicircumferential running suture. The left main bronchus was extubated and jet ventilation was applied through the bronchoscope. The stent was pushed down and the bronchial limbs entered into both main bronchi (Figure 2, *E*). The distal anastomosis was then completed with interrupted sutures (Figure E1). To avoid postoperative displacement, we secured the stent proximally and distally with transfixiant 2-0 nonabsorbable Dafilon (Aesculap, Tutlingen, Germany) sutures and the patient was then conventionally reintubated (Figure 2, *F*).

To promote revascularization of the graft and prevent erosion of contiguous large vessels, we partially wrapped the graft with a right pectoral muscle flap based on its thoracoacromial blood supply, which was elevated and transferred intrathoracically through a transparietal window performed by resection of the first costal cartilage (Figures 3 and E2). The sternum was closed after pleural and mediastinal tube placement. A double jejunostomy was performed through a left-sided minilaparotomy to prevent postoperative aspiration, allowing placement of a retrograde transpyloric gastric suction tube for gastric emptying and a second anterograde tube enabling enteral feeding.

In patient 2, the procedure started with mediastinal lymph node dissection. Owing to tumor extension (Figures 1 and E3), the trachea was sectioned just below the first cartilage and distally, after a right upper lobectomy, the entire right main bronchus and both first cartilages of the left main bronchus were resected (Figure E3). After a right hilar release, carinal restitution was achieved by suturing the bronchus intermedius and the left main bronchus together. Before reconstruction, since the patient poorly tolerated unilateral cross-field ventilation, the bronchus intermedius also needed to be cannulated to achieve satisfactory ventilation. The rest of the procedure was similar to that of patient 1.

In patient 3, mediastinal lymph node dissection with preservation of the left recurrent nerve was performed first. The tumor was circumferentially dissected from the aortic arch and left pulmonary artery. The left main bronchus was sectioned proximally and cannulated to achieve unilateral cross-field ventilation. A 5.5-cm long tracheal and carinal resection was then performed, according to frozen section (Figure 1). A right U-shaped hilar release and blunt dissection of the pretracheal plane were performed. Since approximation of the trachea to the right main bronchus failed, despite maximal cervical flexion, a cryopreserved AA splinted by a custom-made silicone stent (Tracheobronxane Dumon; Novatech, La Ciotat, France) was interposed with end-to-end proximal and distal anastomoses. After conventional reintubation, the right lung was inflated and ventilated. The left pulmonary artery and veins were then divided with endostapler devices (Endopath; Ethicon Endo-surgery, Cincinnati, Ohio) and the left lung was removed through a transpleural approach. Last, the graft was partially wrapped by means of a left pectoral muscle flap.

In patient 4, tumor-free airway margins required tracheal section below the sixth cartilaginous ring, followed by 10- and 15-mm long resection of the right and left main bronchi, respectively (Figure 1). After bilateral hilar release and restitution of a new carina, an 85-mm long TR was performed with a cryopreserved AA, followed by a wrap as previously described. During resection and reconstruction steps, dual lung ventilation was required to achieve satisfactory gas exchange.

In patient 5, tumor-free margin resection required 10.5-cm long tracheal and left recurrent nerve resections (Figure 1). To improve the graft wrap, we used a novel flap, the ''thymopericardial fat flap'' based on the internal thoracic artery blood supply, including the right internal thoracic pedicle, right thymic lobe, and entire homolateral pericardial fat, which was harvested by freeing up to the thoracic wall, ascending aorta, and pericardium and mobilized to create an interposition between the splinted cryopreserved AA and the esophagus. The wrap was completed by means of a right pectoral muscle flap, as previously described (Figure 4). Finally, a double jejunostomy was performed through a left-sided minilaparotomy.

In patient 6, complete tumor removal required a 9-cm long tracheal (Figure 1), left recurrent nerve, and muscular layer esophageal resection. Cryopreserved AA wrap was similar to that of patient 5. Owing to sternal dehiscence experienced by patients 1 and 5, the sternum was closed by using titanium clip devices (ASCO10; Vitalitec, Domalin, France).

Information and Consent

The national TR research program was approved by the French Bioethics Advisory Board, the French Agency for Health Safety (AFSSAPS), and our institutional review board. Informed consent was obtained from all patients. In patients 2, 4, and 5, these requirements significantly delayed the procedure.

TABLE 1. Tracheal replacement with aortic allografts: Procedures and pathology

Patient no. (date)	Age (y)	Sex	Diagnosis delay before procedure (mo)	Length of resection (mm)	Additional procedures	Aortic allografts	Wrap	Duration of procedure (min)	Pathology	No. of stent changes or shortenings
1 (March 31, 2005)	46	M	MEC (1)	90 (CRR)	EMLR GJ	FAA	PMF	710	R1 1N+, 4N–	3
2 (April 22, 2005)	17	M	ACC (28)	110 (CRR)	Right upper lobectomy	FAA	PMF	540	R0 21 N–	4
3 (May 31, 2006)	30	M	ACC (5)	55 (CR)	Left pneumonectomy	CAA	PMF	780	R0 2N+, 15N–	11
4 (July 17, 2006)	27	F	ACC (11)	85 (CRR)	—	CAA	PMF	570	R0 17 N–	3
5 (June 4, 2007)	52	M	ACC (6)	105	GJ	CAA	PMF TPF	615	R0 2N+, 26N–	3
6 (Sept 14, 2007)	35	M	ACC (5)	90	EMLR percutaneous GJ	CAA	PMF TPF	575	R0 12 N–	2

M, Male; *F*, female; *MEC*, mucoepidermoid carcinoma; *ACC*, adenoid cystic carcinoma; *CRR*, carinal resection and restitution; *CR*, carinal resection; *EMLR*, esophagus muscular layer resection; *GJ*, gastrostomy and jejunostomy; *FAA*, fresh aortic allograft; *CAA*, cryopreserved aortic allografts; *PMF*, pectoral muscle flap; *TPF*, thymopericardial fat flap; *R1*, margin positive; *R0*, margin negative; *N+*, lymph node positive; N–, lymph node negative.

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RESULTS

Pathology Findings

Frozen section of the gross tumor showed positive tracheal and/or bronchial margins in all patients. Accordingly, an average of 5.3 (range 4–9) additional tracheal or bronchial sections were required per patient to ensure the absence of tumor on frozen section analysis.

In patient 1 (low-grade MEC), 1 of the 5 resected lymph nodes showed juxtatumoral metastasis (2L). Although frozen sections were negative, final pathologic study of the distal airway margin (left main bronchus) showed microscopic invasion of the peribronchial adventitia (R1 resection).

In all other patients (ACC), proximal and distal airway margins were found to be disease-free (R0 resections). A mean of 19 $\pm$ 6 (range 12–28) lymph nodes were resected. Patients 3 and 5 showed lymphatic spread in 2 nodes (Table 1).

Postoperative Course

All patients were extubated in the operating room. Because of ineffective cough, intensive physiotherapy and daily treatments with a fiberoptic bronchoscope were required in the early postoperative course.

In patient 1, limited dehiscence of the proximal anastomosis required suture on day 13 and sternoplasty for incomplete separation of the sternum on day 15. The patient was discharged on day 40.

In patient 2, acute anterior spinal cord ischemia developed on day 1. Definitive explanation of this severe complication remains elusive. Several factors, including microemboli migrating via the left vertebral artery arising from the aortic arch and/or tumor-related thrombophilia, may have played a role. Severe distortion of the bronchus intermedius, distal to the right limb of the stent, was responsible for purulent retention and required additional bronchial stenting (Ultraflex self-expandable metallic stent; Boston Scientific, Natick, Mass) on day 31. The patient was transferred on day 58 to the regional spinal cord injury rehabilitation center.

In patient 3, pneumonia developed on day 3 and a tracheotomy was done on day 5. He was weaned from the ventilator on day 15 and was discharged on day 30.

Patient 4 showed partial necrosis of the graft related to invasive fungal infection (*Candida albicans*), which required retransplantation on day 18. The wrap was completed by using an omental flap that was transferred intrathoracically through a substernal route. Acute respiratory distress syndrome required tracheostomy and prolonged mechanical ventilation. On day 32, a fistula between the neocarina and the esophagus required emergency placement of gastrostomy and jejunostomy suction tubes. She was discharged on day 90 with a minitracheostomy tube that maintained the stent in a stable position and allowed on-demand tracheobronchial self-suctioning.

Patient 5 required intermittent noninvasive positive-pressure ventilatory support for 10 days. He experienced sternal dehiscence on day 18, treated by sternoplasty with titanium clip devices, and he was discharged on day 30.

Patient 6 had an uneventful postoperative course, and he was discharged on day 29.

Midterm Outcome

In patients, stent maintenance required appropriate humidification (aerosol twice a day) and quarterly follow-up bronchoscopy.

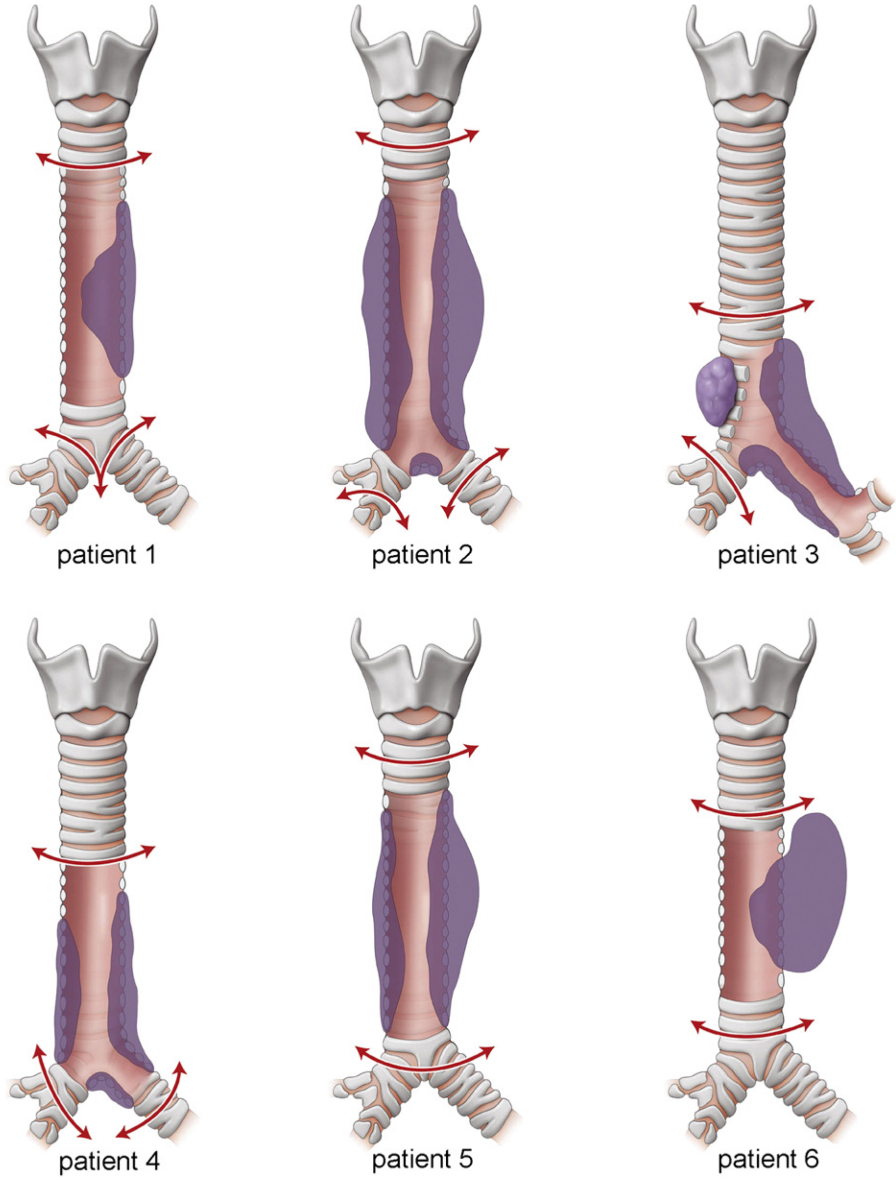

FIGURE 1. Gross tumor extension, proximal and distal sections of the airway, in patients 1 to 6 *(double arrows)*.

Stent removal was attempted at 21 and 24 months in patients 1 and 2, respectively. Both patients were found to have a 0.5 cm large esophageal fistula, which was asymptomatic so long as the tracheobronchial stent was present. Additionally, the graft was not stiff enough to maintain a patent airway, so that after several days, both patients had a new bifurcated stent inserted to splint the central airway. In patient 2, a surgical attempt to close the fistula failed and the patient died of massive hemoptysis 26 months after TR.

In patient 3, instability of the stent led to several stent changes: straight silicone stents (n = 3) changed to self-expandable covered metallic stents (n = 7) and then to a straight silicone stent placed across the right upper lobe orifice with a lateral window to facilitate ventilation and clearance of secretions, which currently has been in place for 15 months (Table 1). At 6 months, partial disruption of the lower anastomosis required surgical closure, buttressed by a contralateral pectoral muscle flap. Last, a straight back syndrome developed at 27 months, treated successfully by partial manubrium sterni resection.[10]

In patient 4, closure of the carinal fistula and colonic esophagoplasty were performed 1 year after retransplantation. The postoperative course was complicated by acute respiratory distress syndrome and clinically unapparent anterior wall graft disruption. The patient was discharged on day 81, and subsequent chest computed tomographic follow-up demonstrated closure of the graft disruption.

The midterm course was uneventful in patients 5 and 6.

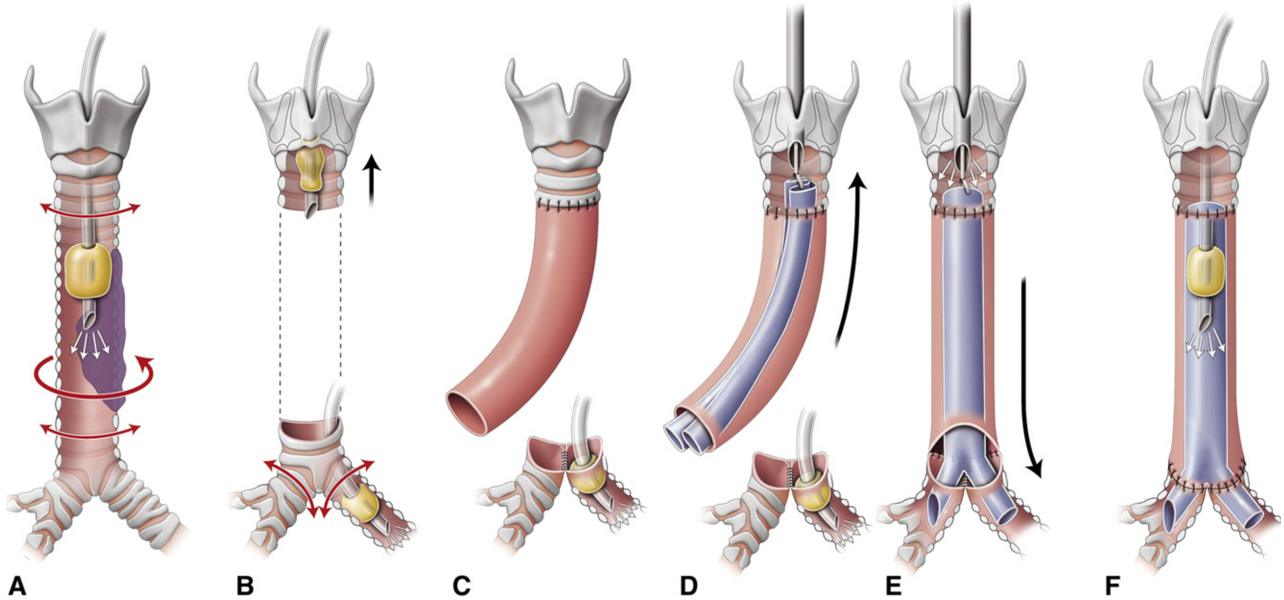

FIGURE 2. Main steps of the procedure, in patient 1. A, Orotracheal intubation and ventilation; circumferential tumor dissection *(large arrow);* removal of the gross tumor extension *(double arrows).* B, Withdrawal of the endotracheal tube and cross-field left main bronchus cannulation; distal sections after frozen section analysis *(double arrows).* C, Carinal restitution by suturing the right and left main bronchi together; end-to-end anastomosis between the proximal trachea and aortic allograft. D, Orotracheal intubation with a rigid bronchoscope; the folded stent was pulled with a forceps introduced through the bronchoscope. E, Jet ventilation was applied through the bronchoscope; the bifurcated stent was gently pushed caudally with a forceps. F, The anterior distal anastomosis was completed and the patient was conventionally reintubated.

Long-Term Outcome

Twenty months after TR, slowly progressive metastatic disease refractory to chemotherapy developed in patient 1, who died 45 months after TR without evidence of local relapse. Patient 2 was disease-free before death, 26 months after TR. No postmortem examination could be performed in either patient.

Four patients are alive and disease-free so far, with a mean follow-up of 34 months (range 26–42 months). Three of them returned to full-time employment (patients 3, 5, and 6).

Graft Transformation

Within the first weeks of TR, bronchoscopic examinations through the translucent stents showed a progressive transformation of the whitish internal face of aortic grafts into a pink, highly vascularized conduit. In 3 patients, a fistula developed between the graft and the esophagus. One of these (in patient 4) was large enough to be seen through the stent at day 32 after retranplantation; the others were discovered in patients 1 and 2 once the stent had been removed (at 21 and 24 months, respectively). As seen in experimental studies,[3-7] 4 patients showed sparse calcifications suggestive of osseous metaplasia within the graft (follow-up computed tomography). Six months after TR, follow-up also showed progressive contraction of the graft (mean 28% ± 10%; range 15%–40%). This required serial endoscopic procedures for tracheal limb shortening or stent replacements (Table 1), which provided the opportunity to appreciate the stiffness of the graft. None of the patients experienced acute airway collapse when their stent was removed, thereby attesting to some degree of graft stiffness. At the end of ''free-of-stent periods,'' which ranged from 12 to 21 days, the graft consistently showed centripetal shrinking as seen in experimental studies.[3-7] At this time, no patient has a graft stiff enough to allow definitive stent withdrawal.

Superficial biopsies of the middle part of the graft performed 1 year after TR in patients 1 and 2 showed an internal surface focally lined with respiratory epithelium and residual islets of elastic fibers of aortic implant with dense inflammatory infiltrate within the graft (Figure E4). In patient 1, these microscopic features were persistent 43 months after TR. In patients 5 and 6, the biopsy specimens were more superficial and showed conjunctive tissue with dense inflammatory infiltrate, without evidence of residual elastic tissue, and focally lined by squamous metaplasia (patient 5) or without surface epithelium (patient 6).

DISCUSSION

ACCs and low-grade MECs of the trachea are rare, slow-growing tumors usually associated with prolonged survival. ACCs spread by direct extension, perineural invasion, and to the tracheal mucosa without altering the overall architecture. Thus, endoscopic and peroperative examination may underestimate the tumor spread. Nodal metastases are relatively

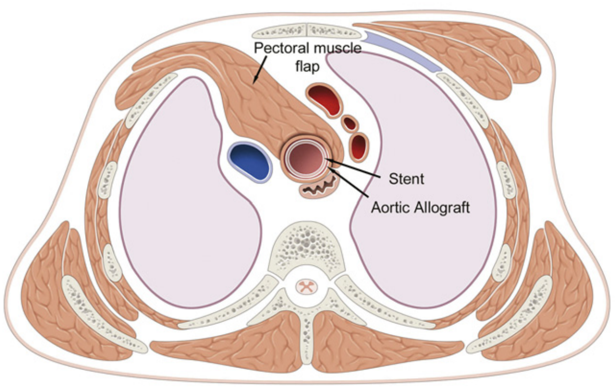

FIGURE 3. Partial wrap. Pectoral muscle flap interposed between the splinted aortic allograft and the large vessels (patients 1 to 4).

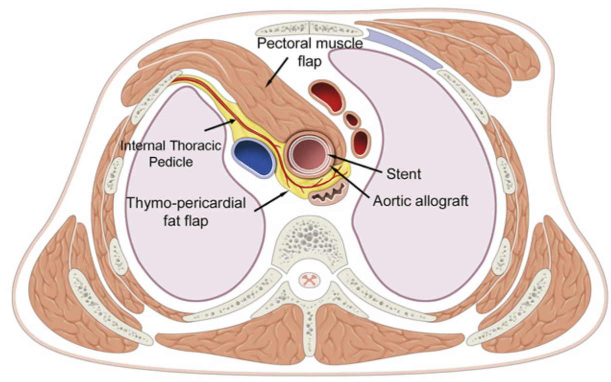

FIGURE 4. Complete wrap. ''Thymopericardial fat flap'' with its right internal thoracic pedicle, on the right and posterior face of graft, and the right pectoral muscle flap interposed between the graft and large vessels (patients 5 and 6).

uncommon, occurring in 13% to 19% of patients.[11,12] Distant metastases tend to occur, mainly to the lung, and may remain silent for many years. Low-grade MECs are mainly endoluminal, polypoid, and noninvasive tumors. Lymphatic spread and distant metastases are unusual and their prognosis after complete resection is excellent.[13,14]

Treatment options include resection reconstructed by primary anastomosis, whenever possible, radiotherapy, or a combination of these. In ACC, the extent of resection remains controversial. Maziak and associates[12] demonstrated excellent long-term palliation after both complete and incomplete (tracheal margin positive) resection followed by postoperative radiotherapy. In contrast, Gaissert and colleagues[11] demonstrated that complete resection with a negative air margin resulted in higher survival than did incomplete resection or unresectable tumors. There was no survivor beyond 13 years in the unresectable group, whereas survival after incomplete resection at 15 years was 14.5%. In patients with unresectable tumors, radiotherapy with or without intraluminal brachytherapy can lead to long-term survival and occasionally to cure.[15] Last, a recent case report suggests that some primary tracheal ACCs may respond to a combination of carboplatin/paclitaxel and 3-dimensional conformal radiation therapy.[16]

In both resectable and unresectable groups, tumor debulking endoscopic procedures can be effective in relieving airway obstruction before surgery, radiation therapy, or palliative stent placement.

In the present study, in which surgery with a curative intent was the treatment option, the extent of the airway defect after resection of the gross tumor precluded reconstruction by primary anastomosis and TR was mandatory. Microscopic examination of the resection lines was essential to ensure tumor clearance, and an average of 5.3 tracheal or bronchial sections was required to obtain safe margins on frozen section analysis. However, despite 9 tracheal sections, the patient with MEC was found to have a positive distal margin on final pathologic study. TR allowed us to perform such large resections reconstructed by interposition of either fresh or cryopreserved AAs, the latter being readily available in tissue banks and bacteriologically safe.[7] On the other hand, the additional mediastinal lymph node dissection led to skeletonization of the mediastinum and weakened the vascularization of surrounding stuctures. Therefore, wrapping of the graft was mandatory to prevent life-threatening complications such as arterial erosion[4,12] and to promote angiogenesis within the AA. The first 4 patients received a partial wrap, by using a pectoral muscle flap, according to our previous experience[17] and experimental study in a canine model, demonstrating satisfactory viability in either fresh or cryopreserved tracheal autografts implanted in abdominal wall muscle.[18] Despite this precaution, esophageal fistula was observed in 3 of 4 patients, a complication that had never been described in animal models.[3-7] The fistula was most likely the consequence of a focal graft necrosis and lack of posterior wrap interposed between the graft and the esophagus. Subsequently, we devised the ''thymopericardial fat flap'' to complete the wrap and protect from fistula of the esophagus. Outcome was noticeably uneventful in both patients with such a double flap. Despite the absence of immunosuppressive therapy, none of the patients had acute or chronic graft rejection phenomenon. This was consistent with prior results of orthotopic transplantation of AAs in humans and heterotopic transplantation in animal models.[3-7] In the patient with MEC and a positive distal margin, no radiotherapy was administered, according to the low-grade status of the tumor[14] and to the absence of knowledge regarding potential harmful consequences of AA irradiation. The remaining patients did not undergo radiotherapy either, because their resection was complete[19] and the benefit of radiation therapy in patients' survival has never been demonstrated by randomized trials.[12] In agreement with previous experience in animal models, significant graft shrinking[3-7,20] and likely osseous metaplasia[3-7] were observed in our patients. Although the heterotopic AA transformed into a well-vascularized conduit focally lined with respiratory epithelium, it is so far unclear whether cartilage rings are generated within the graft, as in animal models, and whether the stent can be definitively removed without adverse effect.

As yet, with a mean follow-up time of 34 months, this clinical study might be considered as an intermediate result in terms of patient survival, with regard to the low-grade status of the tumor. Although the 4 patients still alive are disease-free so far, longer follow-up is needed to evaluate the benefits of this novel procedure in terms of survival, in comparison with incomplete resection followed by radiotherapy[11,12] or most recent chemoradiotherapy.[16]

In the field of central airway replacement, tissue engineering is a promising technique as well. Although Walles and associates[21] elegantly demonstrated that a bioartificial trachea could be engineered on a vascularized scaffold, the engineered trachea still lacked the 3-dimensional aspect and the biomedical profile of a functioning trachea. These difficulties might be resolved by using in situ tissue engineering with a collagen-conjugated airway prosthesis and omental wrap[22,23] or by using bioengineered human airways.[24] Thus, biologic and synthetic scaffold for host tissue regeneration are in competition in the field of central airway replacement and we await the clinical application of these techniques, mainly in the challenging procedures of intrathoracic tracheal and carinal replacement. From a practical point of view, we emphasize the importance of effective graft wrap with bulky and well-vascularized flaps, whichever tracheal substitute might be used.

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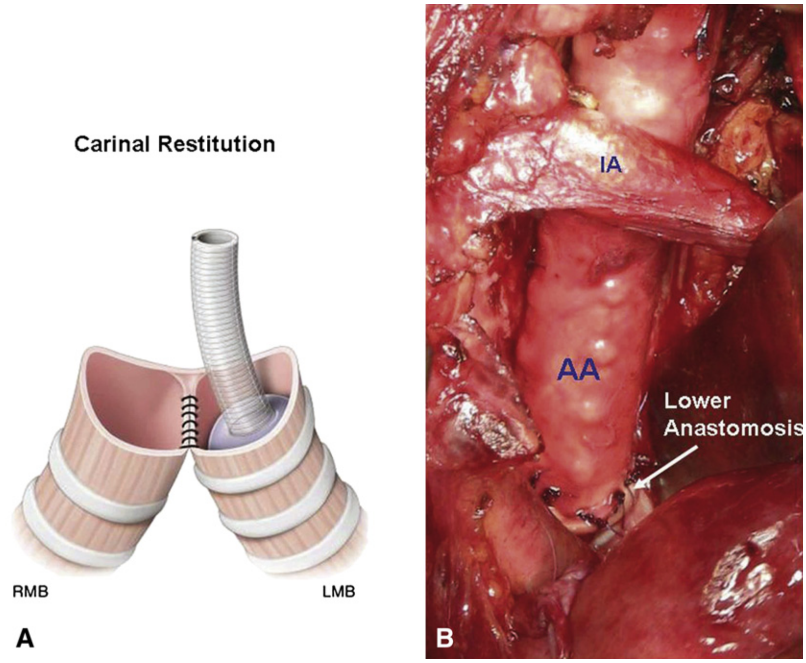

FIGURE E1. A, Carinal restitution in patient 1. *RMB,* Right main bronchus; *LMB,* left main bronchus. B, Operative view of the tracheal reconstruction with the fresh aortic allograft in place, in patient 1. *IA,* Innominate artery; *AA,* aortic allograft.

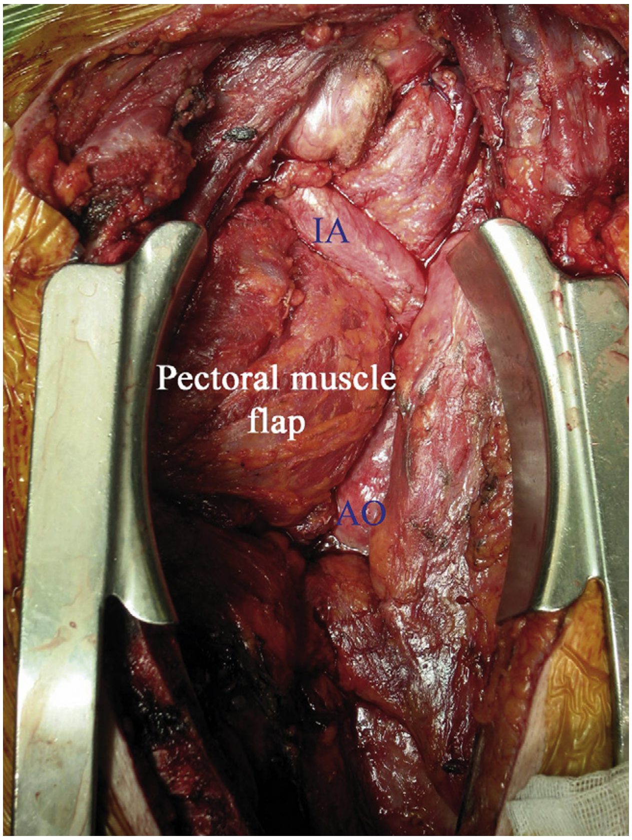

FIGURE E2. Operative view of interposition of the pectoral muscle flap between the graft and large vessels, in patient 1. *IA,* Innominate artery; *AO,* aorta.

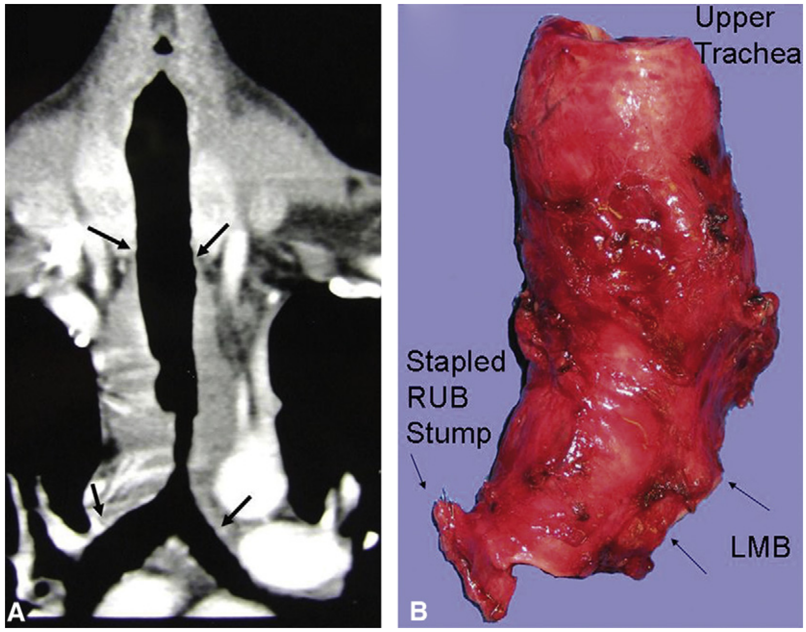

FIGURE E3. A, Chest computed tomographic scan in patient 2. The *arrows* show the upper and lower limits of the tumor. B, Tracheal and carinal resection specimen including the stapled bronchial stump of the right upper lobe. *RUB,* Right upper lobe bronchus, *LMB,* left main bronchus.

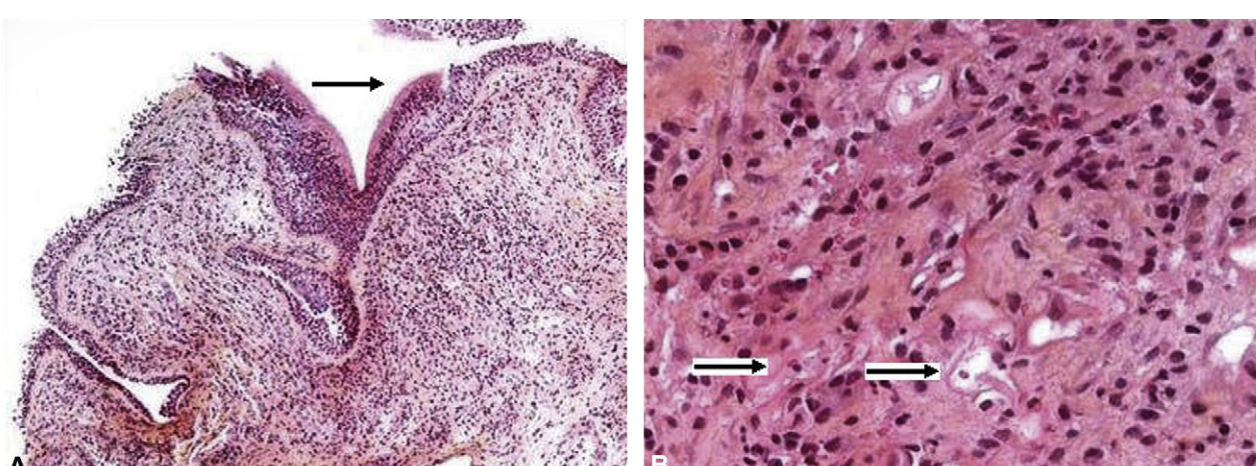

FIGURE E4. A, Normal respiratory epithelium and basement membrane lining the graft (arrow), in patient 1 (hematoxylin–eosin stain ×100). B, Persistence of islet of elastic fibers *(arrows)* within a dense inflammatory infiltrate in patient 1 (hematoxylin–eosin stain ×400).