GENERAL THORACIC SURGERY

ADENOID CYSTIC CARCINOMA OF THE AIRWAY: THIRTY-TWO–YEAR EXPERIENCE

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Methods: **We have reviewed our experience in 38 patients with adenoid cystic carcinoma of the upper airway seen between 1963 and 1995. The mean age was 44.8 years (15 to 80 years) with a male/female ratio of 1:1.1. Thirty-two of the 38 patients were treated by resection and reconstruction (primary anastomosis 28; Marlex mesh prosthesis 4). Twenty-six of the 32 patients undergoing resection received adjuvant radiotherapy. Six patients with unresectable tumors were treated primarily with radiotherapy only.** ***Results:*** **Pathologic examination revealed local invasion beyond the wall of the trachea in all patients. In a majority, microscopic extension was found in submucosal and perineural lymphatics, well beyond the grossly visible or palpable limits of the tumor. Lymphatic metastases were relatively uncommon, occurring in only five of 32 (19%) patients undergoing resection. Metachronous hematogenous metastases occurred in 17 of 38 patients (44%). Thirteen of these 38 patients (33%) had pulmonary metastases. Sixteen of 32 resections were complete and potentially curative. There were two deaths within 30 days of operation. The mean survival in the 14 patients undergoing complete resection was 9.8 years (12 months to 29 years). Sixteen of 32 resections were incomplete (residual tumor at the airway margin on final pathologic examination), with one operative death occurring in this group. The mean survival in the 15 surviving patients was 7.5 years (4 months to 21 years). Six patients were treated with primary radiation only and had a mean survival of 6.2 years (2 months to 14.3 years). In the patients with pulmonary metastases, mean survival was 37 months (4 months to 7 years) from the time of diagnosis of the pulmonary metastasis until their death.** ***Conclusion:*** **Adenoid cystic carcinoma of the upper airway is a rare tumor, which is locally invasive and frequently amenable to resection. Although late local recurrence after resection is a feature of this tumor (up to 29 years), excellent long-term palliation is commonly achieved after both complete and incomplete resection. There was a small difference in survival between patients having complete and incomplete resection. Long periods of control can be obtained with radiotherapy alone. The best results, in this series of patients, were obtained by resection. Adjuvant radiotherapy is assumed to favorably influence survival. (J Thorac Cardiovasc Surg 1996;112:1522-32)**

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The incidence of primary tracheal tumors is less than 0.2 per 100,000 persons per year, with a prevalence of 1 per 15,000 autopsies. Tracheal cancer causes less than 0.1% of cancer deaths.[1] Squamous cell carcinoma and adenoid cystic carcinoma are the most frequent histologic types, accounting for approximately two-thirds of primary neoplasms of the air-

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Table I. *Treatment of 38 patients with adenoid cystic carcinoma of the upper airway*

	No. of patients
Primary resection and reconstruction	32
Primary anastomosis	29
Prosthetic reconstruction (Marlex mesh)	3
Subsequent local recurrence resected	3
Primary radiotherapy only	6
Subsequent local recurrence resected	2

way.[2-7] The clinical and pathologic features of adenoid cystic carcinoma of the trachea were first reported in 1859 by Billroth.[8] Few centers throughout the world have accumulated significant patient numbers to report results of management of this tumor.[2-9]

During a 32-year period from 1963 to 1995, 38 consecutive patients were seen by our service with a diagnosis of primary adenoid cystic carcinoma of the airway. Their management and follow-up are reported.

Patients and methods

We retrospectively reviewed the charts of 38 consecutive patients with adenoid cystic carcinoma of the airway who were referred to the Toronto Hospital. Follow-up data were complete in all 38 patients. Survival was calculated by the Kaplan-Meier actuarial method. Survival curves were compared by means of the log-rank test. Continuous data were analyzed by two-tailed t tests and expressed as the mean ± standard deviation. Statistically significant difference is defined as a p value ≤ 0.05.

Clinical presentation. Of the 38 patients, 18 were male and 20 female. The mean age at presentation was 45 years (15 to 80 years). There was frequently a long interval between the onset of symptoms and diagnosis. This delay is understandable because the plain chest radiograph in these patients often shows no abnormalities (Fig. 1). The mean duration of symptoms before diagnosis was 15 months (1 to 72 months). The most common symptoms were shortness of breath (n = 28; 72%), wheeze (n = 15; 39%), cough (n = 9; 23%), stridor (n = 8; 21%), and hemoptysis (n = 7; 18%). Many patients had two or more symptoms. In many instances, symptoms of upper airway obstruction (dyspnea and wheeze) resulted in an incorrect diagnosis of asthma or bronchitis.

All patients were evaluated with chest roentgenography and bronchoscopy, including use of a rigid bronchoscope and measurement of the extent of tumor involvement. In 13 patients seen before 1980, tomograms and contrast tracheograms were used. After 1980, patients were examined with computed tomograms. No patient had evidence of distant metastasis at the time of initial diagnosis or treatment.

In 36 of 38 patients the tumor arose in the trachea with extension into the cricoid level or subglottic region and within the cricoid ring (n = 6), larynx (n = 4), or carina (n = 13). Two patients had isolated involvement of the main bronchus when first examined.

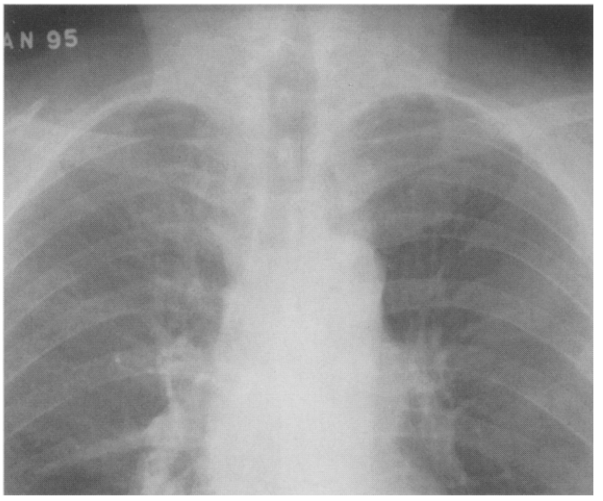

Fig. 1. Chest radiograph of patient with 5 cm tracheal lesion extending into the carina and left main bronchus. This x-ray film was interpreted as showing no abnormalities.

Methods of treatment for these 38 patients are summarized in Table I.

Primary resection. Thirty-four patients underwent 37 resections. Thirty-two patients were treated by primary resection with the expectation of complete resection of the primary tumor as initial therapy. In 29 of these patients the trachea was reconstructed with a primary anastomosis and in three patients a Marlex mesh prosthesis (Bard Implants, Billerica, Mass.) was used.

Three of the 32 patients undergoing resection had a local recurrence and were reoperated on for recurrent disease at 2, 6, and 16 years; a primary anastomosis was done in two and a Marlex mesh prosthesis was used in one.

Marlex mesh prosthesis. A cylinder of Marlex mesh was used for reconstruction in a total of five patients.[10] Four of these five patients were operated on between 1963 and 1967, before the techniques of extended resection were known. Before 1968, it was generally believed that no more than 3 cm of trachea could be resected and still safely reconstructed by primary anastomosis.[10] In retrospect, three of the five patients (tumor involving an extensive length of trachea only) could now undergo primary anastomosis; a fourth patient required resection of a long segment of the trachea, the carina, and right main bronchus including the right upper lobe. The fifth patient in whom a Marlex prosthesis was used had an extensive local recurrence in the trachea and larynx after primary resection and adjuvant postoperative radiotherapy. A second operation in this patient consisted of laryngectomy and resection of the entire trachea, esophagectomy with gastric replacement, and reconstruction of the airway with a cylinder of Marlex mesh. This prosthesis was secured to the main carina inferiorly and sutured to skin as an end-tracheostomy above.

Preoperative management. Before resection, 12 patients required airway stabilization with debridement of the airway by use of a biopsy forceps through a rigid bronchoscope ($n = 7$), laser coagulation ($n = 3$), or both ($n = 2$). One patient required a temporary tracheostomy.

Anesthesia. All 37 resections were managed by intubation and intermittent ventilation of the distal transected airway. No patient required cardiopulmonary bypass. Although jet ventilation was an option, it was not used in our patients. If the position of the tumor permitted, the distal trachea was intubated, and both lungs were ventilated simultaneously after transection of the trachea below the tumor. In patients with low tracheal or carinal tumors, it was necessary to intubate each side of the distal bronchial tree separately and independently. (A detailed description of the techniques of anesthesia for carinal resection was reported in an earlier publication.[11]) The principles of anesthetic management for carinal resection are summarized as follows: Once the airway was divided below the lesion, each lung could be independently ventilated through the distal bronchial stumps.[11] With this technique, it is possible to achieve good ventilation, even through a short stump of relatively small diameter, such as the bronchus intermedius. In most cases, anesthesia was maintained through cuffed armored endotracheal tubes attached with sterile connections across the operative field. All patients were extubated as soon as possible after completion of the operation to minimize impairment of the circulation at the level of the anastomosis by the inflated cuff of the orotracheal tube. Early extubation in the operating room or recovery room was achieved in 32 of 37 resections. Five patients required assisted ventilation for 2 to 14 days after the operation.

Operative exposure. The 32 patients undergoing resection were operated on by means of a variety of exposures, depending on the location of the primary tumor. A cervical collar incision was used in 11 patients and had to be extended to obtain adequate exposure in four of the 11 (median sternotomy, $n = 3$; left thoracotomy, $n = 1$). Fourteen patients were operated on by means of only a median sternotomy, and 11 patients were treated by a high posterolateral thoracotomy (right, $n = 9$; left, $n = 2$). One patient had an esophagectomy with a gastric replacement in addition to the tracheal resection.

Types of resection. Primary resection of the airway was performed with the objective to remove all gross and microscopic tumor. The segment resected varied considerably in length, from 3 to 8 cm. There were 12 carinal resections, nine of which required the additional resection of some lung: sleeve resection of the right upper lobe in five, left pneumonectomy in two, sleeve lobectomy of the right upper and middle lobes in one, and right pneumonectomy in one. In the two patients requiring a left pneumonectomy, a normal left lung was sacrificed because the extent of trachea and left main bronchus resected made it impossible to perform a primary anastomosis between the stump of the remaining left main bronchus and either the trachea above or the bronchus intermedius on the right side.

In four cases the tumor extended superiorly to involve the airway within the cricoid ring. In these four patients, subglottic resections were done with partial cricoid resection and thyrotracheal anastomosis, with preservation of the larynx and recurrent laryngeal nerves. In three patients laryngeal extension required laryngectomy and end-tracheostomy in addition to resection of the tracheal segment. In two patients the tumor was confined to a main stem bronchus and was resected by left pneumonectomy in one and a right middle and lower sleeve lobectomy in the other.

Release procedures were performed in 20 patients to reduce tension at the anastomosis. Intrapericardial release of the pulmonary hilum was done in 15 patients: right hila in eight and both left and right hila in seven. A hilar release is performed by dividing the inferior pulmonary ligament and then mobilizing the pulmonary hilum by incision of the pericardium and its reflections around the pulmonary veins and the main pulmonary artery. On the right side, hilar release requires the additional division of an intrapericardial septum that joins the lateral aspect of the atrium and inferior vena cava to the pericardium. On the left side, the ductus arteriosus must be divided to allow the hilum to shift upward. Superior laryngeal releases were used in seven patients: thryrohyoid release as described by Dedo and Fishman[12] in three, and suprahyoid release as described by Montgomery[13] in four.

Pathology of resected tumors. A wide resection of the tumor margins is almost always limited on the lateral surfaces of the tumor because of the proximity of vital structures such as the esophagus, superior vena cava, and great vessels. However, margins could always be evaluated microscopically at the transected ends of the airway. A complete resection is defined as a case in which all grossly visible and palpable tumor was removed and the airway margins were reported to be histologically free of tumor at final pathologic examination. An incomplete resection is one in which any of the airway margins were reported to show residual tumor in the final pathologic examination. Intraoperative frozen section was used in every case to evaluate lines of transection of the airway. Microscopic tumor always extended beyond the gross limits of visible or palpable tumor, and such spread continued for 1 cm or more in many cases (see Figs. 2 and 3).

Primary radiotherapy. Six patients were judged to have unresectable lesions because of the extent of the airway involved. They were treated with primary radiotherapy. The dosage given varied between 5000 and 7500 cGy. One of the six patients was unable to complete the recommended course because of symptomatic bifrontal meningiomas that ultimately necessitated resection. Two of these six patients were subsequently operated on for local recurrence of the tumor 7 and 8 years after irradiation. One of these two patients had airway obstruction and underwent an 8 cm tracheal resection and reconstruction with a Marlex mesh prosthesis. A second patient with local recurrence had a tracheoesophageal fistula and underwent an esophagectomy with gastric replacement and tracheostomy. This operation closed the fistula, but 2 years later a total laryngectomy was done for control of disabling aspiration.

Results

Mortality. Three patients died within 30 days of the operation (9%) (see Table II). One patient,

treated by prosthetic reconstruction, died 2 weeks after the operation of a trachea–innominate artery fistula caused by erosion of the artery by the Marlex mesh prosthesis. A second death followed resection of the trachea and carina, including a right upper sleeve lobectomy, again reconstructed with a Marlex mesh prosthesis. This patient died on postoperative day 10 after dehiscence at the lower end of the prosthesis, bronchopneumonia, and cardiac arrest. A third patient had a cardiac arrest caused by presumed pulmonary embolism after resection of the trachea, carina, and left lung. This young man never regained consciousness and died 5 days later with bronchopneumonia and hypoxia. The embolus was thought to have originated in the left innominate vein, which was stretched and traumatized during the operation.

Morbidity. Complications are summarized in Table II. Recurrent nerve palsy occurred in nine patients, transient in five and permanent in four. In the four patients who had a permanent unilateral recurrent nerve palsy, the nerve was deliberately divided at the time of the resection because of tumor involvement. Granulation tissue at the anastomosis complicated the course of eight patients but was easily managed with bronchoscopy and local debridement. No patient required reintubation because of obstruction owing to granulation tissue.

There were five wound infections. Two of the five occurred in collar incisions and one in a median sternotomy. These three patients were treated locally and with antibiotics. The remaining two infections occurred after dehiscence of a right thoracotomy and of a sternotomy. Both patients required operative closure of the dehiscence.

Dysphagia occurred in four patients. All four had superior release procedures added to the reconstruction. In all but one of these four patients, the dysphagia was temporary. The patient with permanent dysphagia received radical postoperative radiotherapy (6200 cGy), which resulted in a radiation-induced esophageal stricture and permanent obstruction to swallowing.

Although stenosis occurred in three patients, only one of them required reoperation and revision of the tracheal anastomosis. The other two patients had a benign anastomotic stricture after carinal resection and were satisfactorily treated by dilatation. Miscellaneous complications include bronchopneumonia ($n = 2$), temporary tracheostomy ($n = 2$), wound dehiscence ($n = 1$), and an esophageal fistula after esophagectomy ($n = 1$).

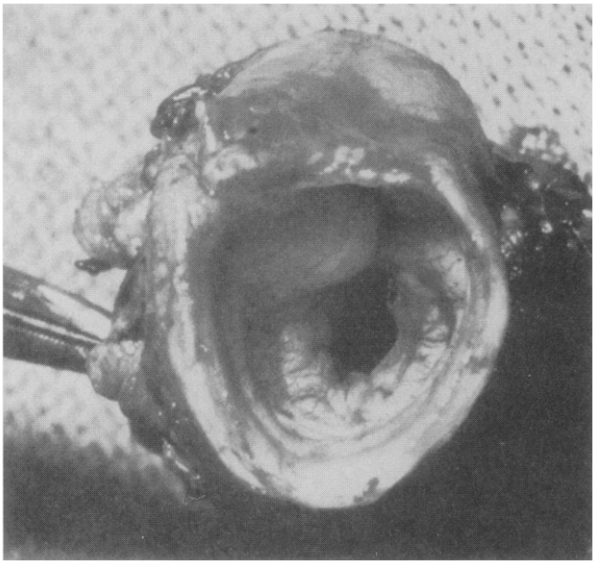

Fig. 2. Gross appearance of a resected specimen of adenoid cystic carcinoma. The overlying mucosa is intact and the gross margins of the tumor appear circumscribed.

Survival data. Follow-up data were complete in all 38 patients. Survival was calculated by the Kaplan-Meier actuarial method. Survival curves were compared by means of the log-rank test. Continuous data were analyzed by two-tailed t tests and expressed as the mean ± standard deviation. Statistically significant difference is defined as a p value ≤ 0.05.

Survival data are summarized in Table III. Mean survival for the entire group of 38 patients was 85 months (5 days to 29 years). Twenty-five of these 38 patients are dead. There were three operative deaths. Thirteen deaths were due to adenoid cystic carcinoma, from either hematogenous metastasis ($n = 5$) or local recurrence ($n = 8$). An additional two deaths were due to unrelated disease in patients who had known clinical recurrence of the primary tumor. Seven patients died of unrelated disease and appeared to be clinically free of tumor at the time of death.

Primary resection. Thirty-two patients were treated by primary resection with a mean survival of 85 ± 89 months (5 days to 352 months). These data are expressed as actuarial survival in Fig. 4: 79% at 5 years and 51% at 10 years. According to the log-rank test, these survival curves showed no statistically significant difference.

The 32 patients undergoing resection were divided into two groups: 16 patients undergoing pre-

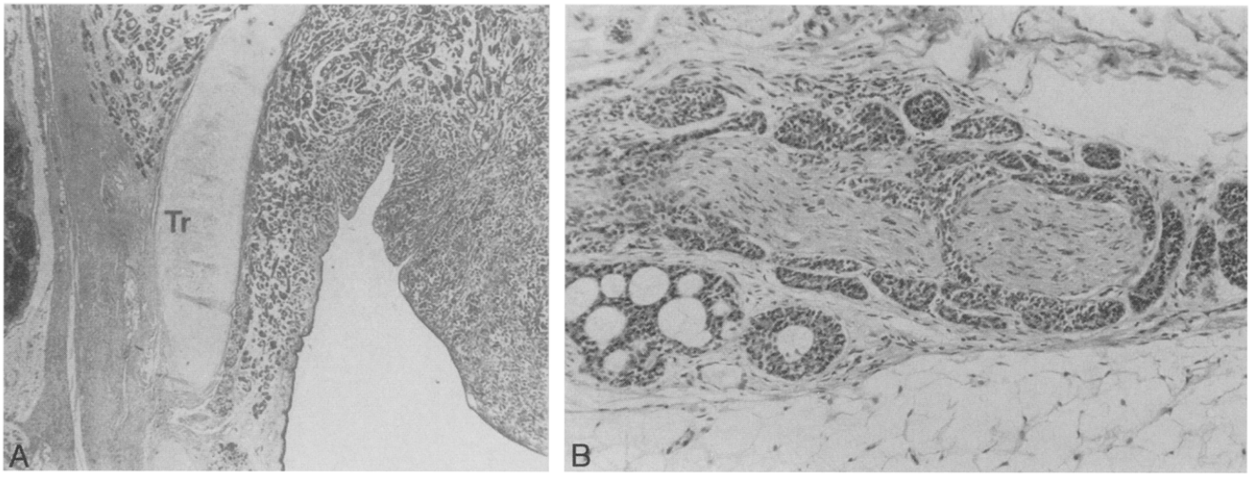

Fig. 3. A, Photomicrograph illustrating the extensive microscopic spread of adenoid cystic carcinoma. The spread occurs both longitudinally and circumferentially and is neither visible to nor palpable by the operating surgeon. *Tr,* Trachea. **B,** Photomicrograph illustrating adenoid cystic carcinoma, spreading longitudinally on the outer surface of the trachea, in the perineural lymphatic spaces.

Table II. *Complications of surgical resections*

	No. of patients	
Operative mortality (30-day)		3
Trachea–innominate artery fistula (Marlex mesh)	1	
Airway dehiscence, pneumonia (Marlex mesh)	1	
Pneumonia, cerebral hypoxia (possible pulmonary embolus)	1	
Morbidity		22
Recurrent nerve palsy	9	
Airway granulation	8	
Wound infection	5	
Dysphagia	4	
Stenosis	3	
Miscellaneous	6	

Table III. *Survival data for 38 patients with adenoid cystic carcinoma*

	No. of patients	*Mean survival (mo)*	*Median survival (mo)*
Overall	38	85	60
Primary resection	32	87*	73*
Complete resection, disease-free margins	16	118†	93†
Incomplete resection, diseased margins	16	90‡	61‡
Primary radiotherapy	6	74§	87§

*Survival in 29 patients excluding three operative deaths.

†Survival in 14 patients excluding two operative deaths.

‡Survival in 15 patients excluding one operative death.

§Two of six patients who had primary radiotherapy later underwent resection for local recurrence in the airway.

sumably complete resection in whom the resection margins were histologically free of disease on final pathologic examination and 16 patients in whom the final resection margins contained residual tumor. There were two postoperative deaths in the 16 patients with presumably complete resection, and mean survival in the 14 remaining patients was 118 ± 105 months (12 to 352 months). In the 16 patients with incomplete resection (residual tumor at the resection margins on final pathologic examination), there was one operative death, and mean survival in the remaining 15 patients was 90 ± 75 months (4 to 254 months). These survival data are presented as actuarial survival curves in Fig. 5. Although the survival differences do not reach statistical significance according to the log-rank test, there is a trend for increased survival in the group undergoing complete resection, particularly at 10 years: complete resection 69%, incomplete 30%.

Primary radiotherapy. Six patients had tumors that were judged to be unresectable, and they were treated primarily with radical radiotherapy. The mean survival in these six patients was 74 ± 64 months (1 to 172). Two of these six patients ultimately had airway obstruction as a result of local recurrence and were operated on 7 and 8 years after

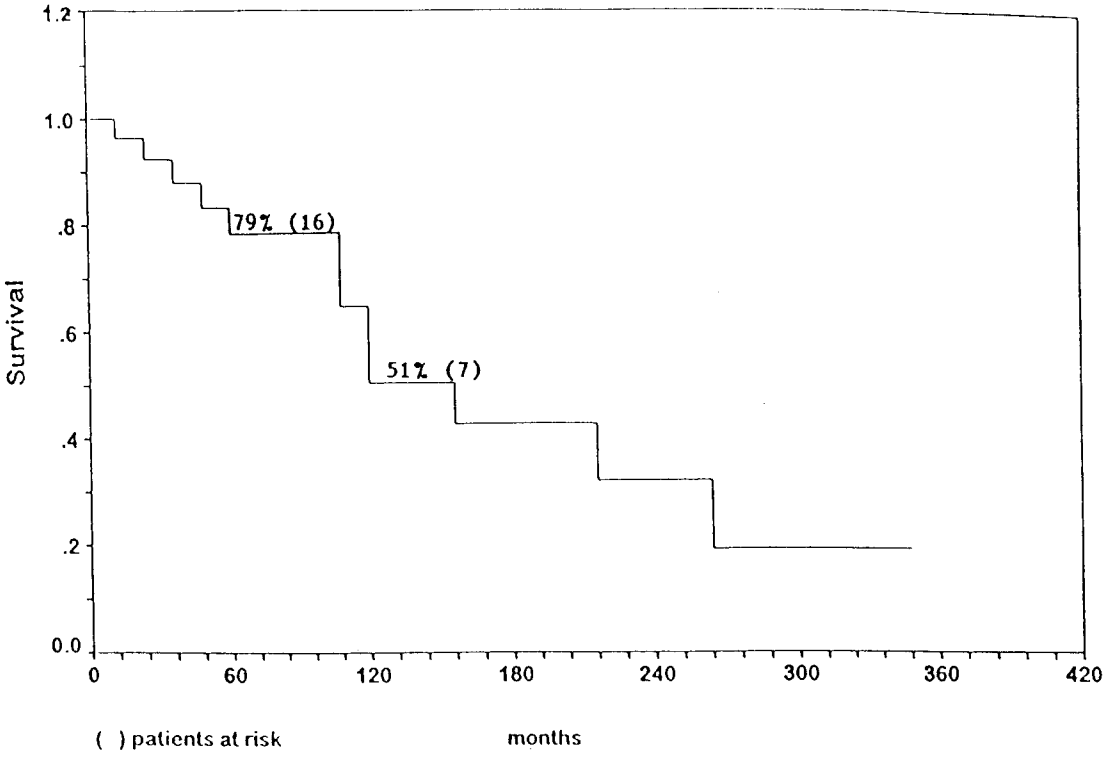

Fig. 4. Actuarial survival curve in 32 patients treated by primary resection. Because of three operative deaths, 29 patients were at risk.

initial radiation. In both cases a palliative operation was done, with known residual tumor remaining after the procedure. These two patients survived for 33 and 25 months, respectively, after surgical resection.

Adjuvant radiotherapy. Twenty-five of the 32 patients undergoing resection received adjuvant radiotherapy: postoperative radiation, $n = 16$; preoperative radiation, $n = 9$. In the group of patients receiving adjuvant radiation (23 patients excluding two operative deaths), the mean survival was 88 ± 76 months (11 to 263 months). Six of the seven patients who had no adjuvant radiotherapy had had complete resection. There was one operative death in the group of seven patients who did not receive any adjuvant radiotherapy. Mean survival in the six remaining patients was 131 ± 131 months (5 to 352 months). There was no significant difference in mean survival between these two categories.

Influence of metastatic tumor. The incidence of metachronous hematogenous metastasis is summarized in Table IV. No patient had clinically identified hematogenous metastases at the time of initial or primary treatment. Hematogenous metastases were identified during follow-up in 17 of the 38 patients. In 13 of these 17 patients, pulmonary metastases were present, and seven of the 13 patients with pulmonary spread had no documented metastasis at other sites. After initial therapy, this group of 17 patients remained clinically free of disease for a mean of 100 ± 79 months (12 to 300 months). After the recognition of metastatic disease, mean survival continued for an additional 37 ± 26 months (4 to 84 months). Pulmonary metastases often remained asymptomatic for long periods. Two patients with pulmonary metastasis were treated with combination chemotherapy without any observable clinical response.

Metastatic tumor was identified in the regional lymph nodes of five patients. These five patients had a mean survival of 42 ± 46 months (4 to 120 months). In contrast, those patients without documented lymph node involvement survived for a mean of 111 ± 91 months (12 to 348 months) ($p = 0.11$). Spread in the perineural lymphatic spaces was seen in eight patients who had a mean survival of 71 ± 70 months (12 to 233 months). There was no statistically significant difference in survival between patients with and without perineural lymphatic spread.

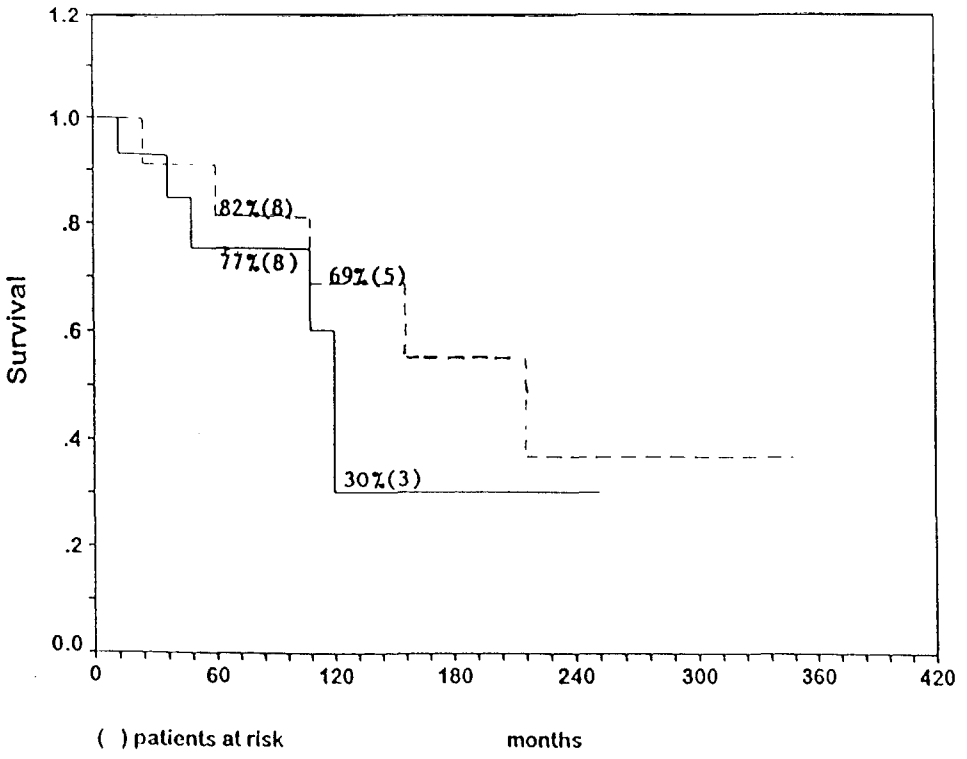

Fig. 5. Actuarial survival curve comparing the results of complete and incomplete resection. *Dashed line,* Complete resection (15 patients at risk); *solid line,* incomplete resection (14 patients at risk).

Table IV. *Sites of metastases in 17 patients*

Site	*No.*
Pulmonary	13
Liver	4
Bone	3
Brain	2
Renal	1
Heart	1
Skin	1
Abdomen	1

Local recurrence. Local recurrence of the primary tumor in the airway was documented in eight of 38 patients. Only three of these local recurrences occurred in the 32 patients treated by primary resection. In contrast, five of the six patients treated with primary radiotherapy had local recurrence, which was the ultimate cause of death in all five.

The interval between primary treatment and documented local recurrence may be of astonishing duration (see Figs. 6 to 8). The mean disease-free interval before local recurrence in these eight patients was 88 months (4 to 324 months). After clinical recognition of local recurrence, the mean survival was 33 months (4 to 81 months). Seven of the eight patients with local recurrence also had hematogenous metastasis during the period of follow-up.

Discussion

Adenoid cystic carcinoma is a rare primary tumor of the upper airway, which is frequently amenable to resection and reconstruction by primary anastomosis. At present, such surgery can be accomplished with a reasonably low operative mortality rate and remarkably good long-term survival, particularly if survival is compared with that observed with the more common primary lung cancers. Our reported results are summarized in Table V and compared with observations reported in previous publications by Grillo and Mathisen,[2] Perelman and Koroleva,[7] and Regnard and associates.[9] Long periods of follow-up were obtained in all four of these reports: 20, 23, 26, and 32 years. Operative mortality was close to 10% in three of the four reports in which operative mortality was specifically identified. Most important, actuarial 5- and 10-year survivals, calcu-

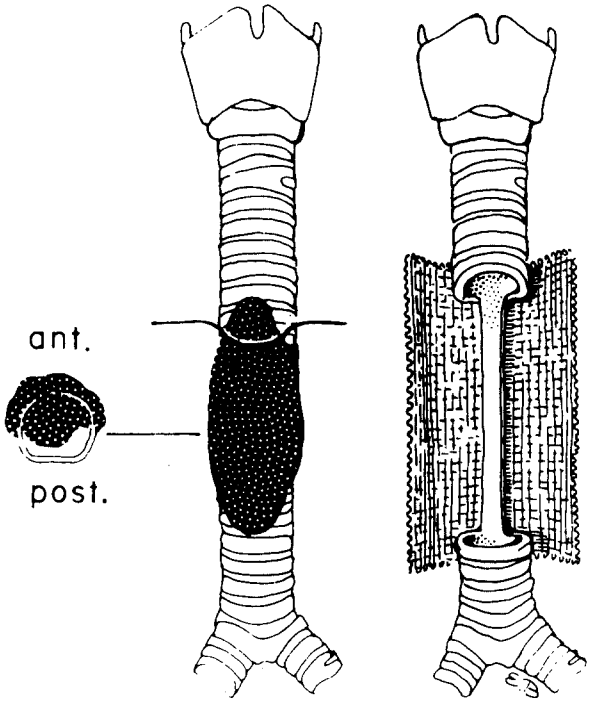

Fig. 6. Tumor in the upper mediastinal trachea of a 15-year-old girl. The tumor was resected and replaced with a cylinder of Marlex mesh in 1963.

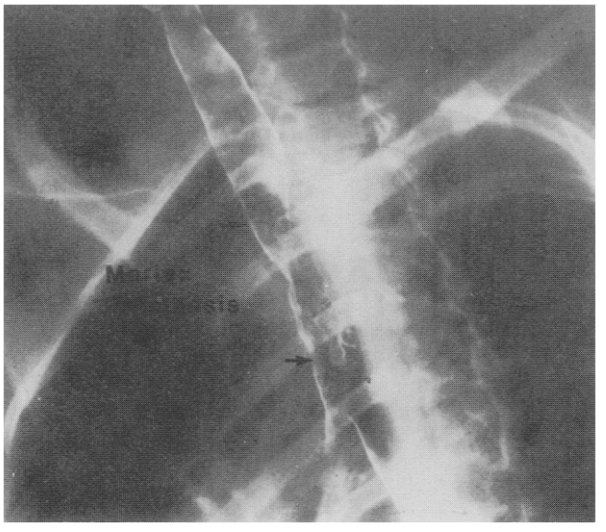

Fig. 7. A contrast tracheogram in the same patient, 4 years after prosthetic replacement. The prosthetic airway is indicated by the black *arrow* and is widely patent. Beginning at 4½ years, progressive narrowing developed at the upper ends of the prosthesis.

lated by the Kaplan-Meier method, were between 65% and 79% at 5 years and between 53% and 57% at 10 years.

Although the objective in resectable cases is to obtain a complete and potentially curative operation, it is frequently impossible to safely extend the resection far enough to obtain histologically disease-free margins at the transected ends of the airway. It is again worthy of emphasis that adenoid cystic tumors of the upper airway frequently spread 1 cm or more beyond the palpable and visible confines of the neoplasm. This determination can be made only during the operation by means of frozen section assessment to evaluate the resection margins. At this stage in the operation, the gross tumor has already been resected, and the surgeon is faced with the options of either leaving tumor at the resection margin or further extending the resection, which may be incompatible with a safe reconstruction by primary anastomosis. In our series, there were 16 patients who were treated primarily by resection in whom the final resection margins contained residual tumor. These patients had a mean survival of 90 months after an incomplete operation. This is not greatly different from the survival observed in 16 patients with complete resections and negative margins at final pathologic examination, who had a mean survival of 119 months. The numbers in each group are small, and there is no statistically significant difference in these survival data. Furthermore, only three instances of local recurrence were documented in the patients treated by primary resection. These observations suggest that an incomplete resection, in which the gross tumor is entirely removed but microscopic disease remains at the margins, may still provide the best treatment, or palliation, in selected patients.

Six patients in this report were treated primarily with radical radiation therapy. In some of them long periods of remission were obtained, ranging between 1 and 172 months, with a mean survival of 74 months. However, five of these six patients ultimately had a fatal local recurrence.

The role of adjuvant radiotherapy is impossible to evaluate with any certainty. Adjuvant radiation in a variety of dosages was used in 25 of the 32 patients managed by primary resection. There was, however, no statistically significant difference in survival between the 25 patients receiving adjuvant radiation and the seven patients who did not. It appears logical, nevertheless, to assume that adjuvant radiotherapy may be beneficial and likely to delay or reduce the incidence of local recurrence in the airway.

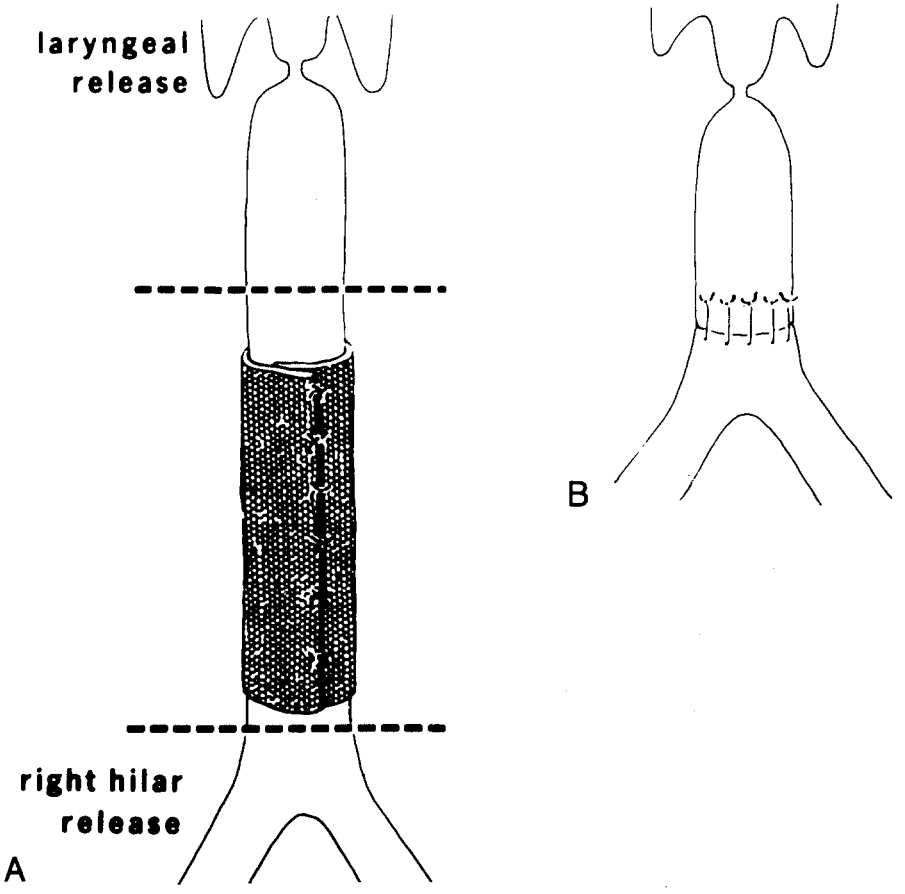

Fig. 8. A, In 1968, 5 years after the initial resection, the patient was again operated on. The prosthesis and adjacent tracheal ends were resected. **B,** The airway was reconstructed by primary anastomosis. Release procedures were used at the upper and lower ends of the airway.

Table V. *Reported results of resection for adenoid cystic carcinoma of the airway*

	Grillo[2]	*Perelman*[7]	*Regnard*[9]	*Pearson*
No. of patients	60	56	65	38
Years of follow-up	26	20	23	32
Operative mortality	8 (13%)	8 (14%)		3 (9%)
Actuarial survival (%)				
5 yr		66	73	79
10 yr		56	57	51
Mean survival (mo)				
Radiation only	39			74
Resection and radiation	108			88

Hematogenous metastases occurred in more than half of our patients, and by far the commonest site of metastatic disease was the lungs. However, these metastases often occur long after initial diagnosis of the primary tumor (12 to 300 months with a mean interval of 100 months). Furthermore, these patients survived for as long as 7 years after the diagnosis of hematogenous spread, with a mean survival interval of 3 years (37 months). To date, there is no evidence that chemotherapy is useful in the management of these metastases. Lymphatic metastases are relatively uncommon and did not significantly alter survival in the small number of cases reported here.

In summary, adenoid cystic carcinoma of the upper airway is a rare primary tumor that occurs in all adult age groups and is frequently slow to

progress and late to metastasize or recur locally. Many cases are amenable to a segmental resection of the airway with removal of all gross disease and reconstruction by primary anastomosis. Most tumors will respond to radiotherapy, which often results in long periods of remission in patients treated with radiotherapy alone. Given the limitations of this nonrandomized comparison, from our review it seems reasonable to recommend adjuvant radiotherapy in all patients undergoing resection, and certainly in those patients in whom the final pathologic examination identifies residual tumor at the resection margins. Both complete and incomplete resections can be done with an acceptably low operative mortality and with the expectation of long periods of survival in a majority of patients.

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Discussion

Dr. Douglas E. Wood *(Seattle, Wash.).* I compliment Dr. Maziak, Dr. Pearson, and their colleagues for an excellent review of a rare tumor. Dr. Pearson is one of the world leaders in the development of indications and techniques for airway surgery and presented one of the earliest experiences of adenoid cystic carcinoma of the trachea in 1974 and of other primary tumors of the trachea in 1984 at this Association. Dr. Maziak is to be especially commended for achieving 100% follow-up in these patients accrued over a 32-year period.

I would like to emphasize two points from this paper. Adenoid cystic carcinoma of the trachea has a protracted natural history with patients, recurring up to 29 years after tracheal resection. These patients can have excellent palliation with a combination of surgery and radiation. Microscopically diseased margins and diseased regional lymph nodes appear to have a minimal effect on survival in this series, as well as the series published by Grillo and Mathisen. Even patients with metastatic disease have a mean survival of 3 years and therefore require aggressive treatment for their tracheal primary tumor to provide palliation.

Reports on alternative therapies for adenoid cystic carcinoma, namely, radiation therapy, usually present 5-year data; however, they need to present similar lengths of follow-up as well as diligence in surveillance to compare with the surgical results from Toronto and elsewhere. As surgeons, we may underestimate the effectiveness of radiation and unfairly compare it with surgery when we refer patients with the more advanced, unresectable tumors to the radiation oncologists. We must be cautious not to draw conclusions regarding the efficacy of different treatment modalities in these retrospective nonrandomized reports.

I have three questions for Dr. Maziak. Neutron beam irradiation provides a threefold increase over photons in local/regional control of adenoid cystic carcinoma of the head and neck. Should patients with tracheal adenoid cystic carcinoma undergo surgical resection followed by neutron rather than photon adjuvant therapy, or perhaps should these patients even be referred for primary neutron beam irradiation?

You described five patients with a Marlex mesh prosthesis for reconstruction of the trachea. What were the long-term results in this group of patients, and is this a technique that you would still consider for extensive tracheal tumors?

Finally, could tracheal homografts be used in adults to achieve a more radical resection, and do you think that this might provide an increase in survival?

Dr. Maziak. Thank you for your comments, Dr. Wood. The first question posed is about different forms of radiation. All of our patients received photon radiation supervised by the radiotherapists. Whether neutron beam irradiation would be preferable I cannot comment.

With regard to the five patients in this series (adenoid cystic carcinoma of the airway) who had the Marlex mesh prosthesis reconstruction, two died of complications within 30 days relating to the Marlex prosthesis; trachea–innominate artery fistula in one and carinal dehiscence in the other. The other three patients had good long-term

palliation with the prothesis: 2 years, 5 years, and 8 years. Three of the five operations were done before 1967 and knowledge of the current techniques for extended resection were not known. In retrospect, these three tracheal tumors could now be reconstructed by primary anastomosis. At present there is rarely if ever an indication for prosthetic replacement. A majority of cases that might warrant tracheal replacement beyond the limits which can be managed by primary anastomosis are technically inoperable.

Dr. Wood also asked about the role of tracheal homograft. That would require preservation of a strip of the host membranous trachea. This will rarely be possible in patients with extensive tracheal neoplasms and has yet to be used as a means of long-term tracheal reconstruction.

Dr. Hermes C. Grillo *(Boston, Mass.).* The Toronto group provided what we really need in looking at this disease, namely, some long-term data.

I will just make an amplifying comment or two. You have the figures from the French series, in which there were 65 resections from 26 different institutions. I had a recent communication from Professor Perelman in Moscow, who has been at this for 31 years, as have you and we. His group has a total now of 66 patients and 50 resections, which is about a 76% resectability rate. This is close to our resectability rate for this particular tumor, in contrast to squamous tracheal cancer, for which it is about 66%. Bryan Meyers is currently reviewing our cases at Massachusetts General Hospital. Of 103 patients, only 75 were operated on, about a 73% resection rate. Survival, and I hesitate to mention it because it is very preliminary, seems to be about 79% at 5 years and about 42% at 10 years. So it is a disease that keeps recurring. It is very unlike squamous cancer of the trachea, which behaves like lung cancer in terms of recurrence. If we add the figures from Canada, Russia, France, and the United States, from these major series, we find about 220 resected cases of adenocarcinoma in 30 years, which shows how hard it is to accumulate data. We are just beginning now to collect enough data to say what the clinical pattern is. What is clear is that we are all coming out with about the same findings.

In our 75 resected cases there were three staged resections, which we no longer do, and ten laryngectomies. Among the patients who underwent resection with reconstruction, there were 26 lesions in the trachea and 36 in the carina. Twenty were in the carina alone, six necessitated removal of the right upper lobe, and 10 necessitated pneumonectomy, usually left pneumonectomy, with carina. I wonder if you saw the same amazing frequency in the carinal level, which requires the most complicated resections, with the highest mortality rate.

Dr. Maziak. Thank you for your kind comments Dr. Grillo. In 36 of 38 patients the tumor arose in the trachea, with extension into the cricoid or subglottic level in six, larynx in four, and carina in 13. Among the 32 patients who underwent primary resection of the airway, there were 12 carinal resections, nine of which required additional resection of lung: sleeve resection of the right upper lobe (5), left pneumonectomy (2), sleeve lobectomy of the right upper and middle lobes (1), and right pneumonectomy (1). In the two patients requiring left pneumonectomy, a normal left lung was sacrificed because it was impossible to perform a primary anastomosis. Two of our three operative deaths followed carinal resection.