Carinal surgery: A single-institution experience spanning 2 decades

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ABSTRACT

Objectives: Complete resection of neoplasms involving the carina are technically challenging and have high operative morbidity and mortality. This study examines the last 2 decades of clinical experience at our institution.

Methods: Medical records were retrospectively reviewed between 1997 and 2017 to identify all patients who underwent carinal resection. Primary outcome measures include risk factors for complications and overall survival.

Results: In total, 45 carinal resections were performed with a median follow-up of 3.4 years (interquartile range 0.8-8.5). Procedures included 21 neocarinal reconstructions (48%), 14 right carinal pneumonectomies (30%), 9 left carinal pneumonectomies (20%), and 1 carinal plus lobar resection (2%). Age ranged from 27 to 74 years, and 23 of 45 patients were female. Eight received neoadjuvant chemotherapy and 6 preoperative radiation. Extracorporeal membrane oxygenation and cardiopulmonary bypass were intraoperatively used for 4 patients with no mortality. Four patients underwent superior vena cava resection and reconstruction. Anastomotic complications occurred in 5 patients, all of which were managed conservatively: 1 required stent placement and a second underwent hyperbaric oxygen therapy. Postoperative events were observed in 26 patients (58%), including pneumonia ($n = 11$), blood transfusion ($n = 8$), and atrial arrhythmias ($n = 8$). More serious complications, such as acute respiratory distress syndrome, occurred in 3 patients. Postoperative events were most closely associated with pulmonary resection ($P = .040$). There were 3 deaths, yielding an overall operative 30- and 90-day mortality of 6.8% and 7%, respectively.

Conclusions: Despite advances in perioperative management, carinal resection poses challenges for both patient and surgeon. Preoperative chemotherapy, radiation, and concomitant pulmonary resection were associated with increased risk of complications. Patient selection and meticulous surgical technique contribute to reduction in morbidity and mortality. (*J Thorac Cardiovasc Surg* 2019;157:2073-83)

Right carinal pneumonectomy, reconstructed end-to-end anastomosis of trachea-left mainstem.

Central Message

Carinal surgery remains a high-risk, technically complex operation. Technical refinements and improved patient selection contribute to improved long-term survival with reduced mortality.

Perspective

Central airway neoplasms are rare, and patients undergoing carinal surgery are at a high risk for morbidity and mortality. Advances in perioperative management, anesthetic, and operative techniques in addition to careful patient selection have significantly contributed to improved patient outcomes. Patients with node-negative disease and/or adenoid cystic carcinoma histology have superior outcomes.

See Commentary on page 2084.

The first reports describing carinal resection and reconstruction were published nearly 65 years ago, citing mortality rates up to 30%.¹⁻³ Decades later, central

airway lesions continue to carry the same technical complexity with regard to airway reconstruction and management; however, recent literature has demonstrated

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Abbreviations and Acronyms

ACC	= adenoid cystic carcinoma
ARDS	= acute respiratory distress syndrome
CI	= confidence interval
CPB	= cardiopulmonary bypass
ECMO	= extracorporeal membrane oxygenation
HBO	= hyperbaric oxygen therapy
SCC	= squamous cell carcinoma

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a reduction in morbidity and mortality, supporting the notion that it is a safe and feasible operation.^{2,4-7} Advances in anesthesia, perioperative care, and careful patient selection are the pillars of improved patient outcomes and reduced morbidity and mortality. In 2013, Eichhorn and colleagues⁶ published a series of 64 patients who underwent carinal resection with an operative mortality of 3.1%. More recently in Asia, there have been small series suggesting that minimally invasive approaches may offer even further reduction in morbidity and mortality.⁸

Although the early evolution of tracheal surgery can be attributed to a select few surgeons,^{1,9,10} the technical aspects of modern-day tracheal surgery were pioneered by Hermes Grillo, MD,¹¹ who authored what is considered the definitive text on the subject entitled, “Surgery of the Trachea and Bronchi,” published in 2004.¹² One of the early reports of carinal resection was in 1950 by Abbott, in which 4 patients underwent right pneumonectomy with en bloc excision of the carina. Barclay and colleagues¹³ reported the first European experience of carinal resection with reconstruction in 1957. Three decades later, Grillo reported his experience on 36 patients who underwent carinal resection with primary reconstruction from 1962 to 1981 with an operative mortality of 13%.^{1,11} He also performed 5 staged reconstruction procedures that failed, and the staged procedure was subsequently abandoned because of their dismal outcomes. In 1999, Mitchell and colleagues¹⁴ published an update to this series consisting of a total of 143 carinal resections since 1962 with an operative mortality rate for primary reconstructions of 12.7%. The current study describes the next 20 years of patient outcomes in an era of more modern anesthetic techniques and improved patient selection.

PATIENTS AND METHODS

This study protocol was approved by the institutional review board of Partners Healthcare (approval no. 2011P000633, date activated March 25, 2011). The institutional review board considered this retrospective chart review, including subject selection and confidentiality, and waived the need for patient consent. An institutional database was queried for all patients who underwent carinal resection at the Massachusetts General Hospital between 1997 and 2017. A detailed chart review of these 45 patients was performed. The Cancer Registry and Research Patient Data Registry databases were additionally queried for medical records and vital status. Follow-up was obtained from hospital charts and contact with patients. Indications for carinal resections include non-small cell lung cancer and other airway neoplasms, including carcinoid, mucoepidermoid and adenoid cystic carcinomas (ACCs), in addition to stricture revision and inflammatory lesions.

Preoperative Assessment

Patients were carefully evaluated for preoperative comorbidities and fitness for surgery, including cardiopulmonary evaluation and pulmonary function testing. Patients were strongly advised to discontinue smoking before surgery, and steroids were discontinued or tapered. A stair climb test of 2 to 3 flights was also employed as an adjunct measurement of pulmonary reserve. Ventilation-perfusion scans were liberally used in select patients to assess current and predicted postoperative function, particularly when planning pneumonectomy. In addition, all patients with planned pneumonectomies underwent transthoracic echocardiogram to assess right ventricular function and rule out pulmonary hypertension.

Patients were routinely evaluated with chest computed tomography to assess airway and mediastinal involvement of tumor and to evaluate for adenopathy. Metastatic disease was assessed with brain magnetic resonance imaging, bone scan (earlier in the series), and more commonly, positron emission tomography. Invasive mediastinal staging (primarily mediastinoscopy) was performed in most patients to rule out N2 disease. We favor the use of mediastinoscopy at the time of formal resection to avoid mediastinal scarring which can compromise tracheal mobility. All patients underwent preoperative flexible and/or rigid bronchoscopy for careful evaluation of the extent of tumor involvement and quality of tissue.

Anesthetic techniques varied depending on the degree of resection. All patients underwent preoperative placement of an epidural catheter. Because of the cumbersome nature of double-lumen endotracheal tubes, we often used an extra-long, wire-reinforced, single-lumen endotracheal tube (Phycon; Fuji Systems Corporation, Fukushima, Japan), which can be advanced into the mainstem bronchus with a low-profile balloon. As the surgical resection matures, the remaining mainstem bronchus is intubated across the field with a sterile endotracheal tube. Intermittent ventilation is then used to allow precise placement of interrupted, absorbable, anastomotic sutures. As the end-to-end tracheobronchial anastomosis is reapproximated and the sutures are tied, the original endotracheal tube is advanced into the bronchus, allowing uninterrupted ventilation. Cardiopulmonary bypass (CPB) or extracorporeal membrane oxygenation (ECMO) techniques were used in select cases exhibiting vascular involvement or the need for enhanced central mobility to achieve proper dissection and R0 resection.

Statistical Analysis

Patient characteristics were compared using Student *t* or Mann-Whitney *U* tests for continuous variables, and χ^2 or Fisher exact tests for categorical variables. Odds ratios for postoperative complications were estimated with univariate logistic regression using robust standard errors. Results are reported as odds ratio with 95% confidence intervals (95% CIs). Survival was estimated with the Kaplan-Meier method using the log rank test for significance of differences, and hazards ratios are estimated with Cox regression. All tests of association were 2-sided and *P* values below .05 were considered significant.

TABLE 1. Clinical and surgical demographics of carinal resection patients

Demographic	Overall (n = 45)
Age, y, median	45 (27-74)
Sex, n (%)	
Male	22 (49%)
Female	23 (51%)
Patient comorbidities, n (%)	
Diabetes	2 (4%)
Coronary artery disease	2 (4%)
Hypertension	10 (22%)
CVD	1 (2%)
COPD	9 (20%)
Steroids	0 (0%)
CHF	1 (2%)
PVD	1 (2%)
Previous thoracic radiation	6 (13%)
Chemotherapy	8 (18%)
Previous lung resection	8 (18%)
Smoking status, n (%)	
Never smoker	20 (44%)
Former smoker	16 (36%)
Current smoker	8 (18%)
Unknown	1 (2%)
Surgical demographics, n (%)	
Carinal resection with neocarina	21 (47%)
Left carinal pneumonectomy	9 (20%)
Right carinal pneumonectomy	14 (31%)
Carinal resection plus lobar resection	1 (2%)
Surgical approach	
Median sternotomy	15 (33%)
Right thoracotomy	26 (58%)
Left thoracotomy	2 (4%)
Median sternotomy + right thoracotomy	2 (4%)
Pathologic diagnosis	
Squamous cell carcinoma	19 (42%)
Adenocarcinoma	1 (2%)
Adenoid cystic carcinoma	12 (27%)
Mucoepidermoid carcinoma	4 (9%)
Carcinoid	4 (9%)
Stricture revision	2 (4%)
Other	3 (7%)

CVD, Cerebrovascular disease; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; PVD, peripheral vascular disease.

RESULTS

Patient's ages ranged from 27 to 74 years (23 females, 22 males). Chronic obstructive pulmonary disease (n = 9, 20%) and hypertension (n = 10, 22%) were the most common comorbidities. Fifty-three percent of patients (n = 24) were either current or former smokers (Table 1). The most common presenting symptoms were cough and shortness of breath followed by hemoptysis. The majority of patients had a performance status of 0 to 1 (Zubrod

scale). No patients were on steroids at the time of surgery, and one patient was weaned off steroids a month prior to surgery. Eight patients (18%) had a previous lung resection, including segmentectomy (n = 1), lobectomy (n = 2), or pneumonectomy (n = 5), before their carinal resection and reconstruction.

Surgical approach and pathologic diagnoses are depicted in Table 1. Forty-two percent (n = 19) of patients had a diagnosis of squamous cell carcinoma (SCC), whereas 27% were found to be ACC (n = 12); less common pathologies are listed in Table 1. Two carinal resections were performed as revisions for symptomatic strictures from carinal resection performed the previous year at outside institutions. One underwent carinal resection with creation of a neocarina for carcinoid involving the carinal spur, subsequently developing symptomatic right bronchial stenosis with multiple failed dilations, debridement and stenting. The second patient underwent left carinal pneumonectomy for mucoepidermoid carcinoma at an outside institution and developed a symptomatic anastomotic stricture. Eight patients received neoadjuvant chemotherapy and seven thoracic radiation. Six patients received radiation with induction chemotherapy within 1 year of surgery. One patient had received chemoradiation 5 years previously for a history of SCC of the right tonsil with nodal metastases.

Surgical Technique

Forty-five carinal resections were performed with a median follow-up of 3.4 years (interquartile range 0.8-8.5, range 0.2-15.9) from 1997 to 2017. Twenty-one patients (47%) underwent neocarinal reconstruction without pulmonary resection. Fourteen patients (31%) underwent right carinal pneumonectomy. Nine patients (20%) underwent left carinal pneumonectomy. There was only 1 patient (2%) who underwent carinal plus lobar resection due to limited lung function for a tumor of the right mainstem bronchus which extended into the superior segmental bronchus and 1 mm from the carinal spur. The lateral wall of the left mainstem bronchus was anastomosed to the bronchus intermedius, one centimeter below the tracheal anastomosis. This patient was the only one to require surgical intervention for anastomotic dehiscence and was stented.

Median sternotomy was performed in 15 patients (33%), thoracotomy in 28 patients (62%), and combined thoracotomy/median sternotomy in 2 patients (4%). Four patients had a right carinal pneumonectomy with superior vena cava resection and reconstruction, of which 2 were approached via median sternotomy. The other 2 patients (4%) had a combined anterior thoracotomy/median sternotomy due to tumor involvement of the superior vena cava requiring en-bloc caval resection and prosthetic reconstruction of the vessel.

TABLE 2. Postoperative complications of patients undergoing carinal resection and reconstruction

Total postoperative events	N = 26 n (%)	95% CI (%)
Pneumonia	11 (24)	14-38
Pleural effusion requiring CT drainage	2 (4)	1-14
ARDS	3 (7)	2-17
Pulmonary embolism	2 (4)	1-14
DVT requiring treatment	1 (2)	0.2-10
Blood transfusion	8 (18)	9-31
Atrial arrhythmia	8 (18)	9-31
Anastomotic complication	5 (11)	4-23
Requiring medical treatment	4 (9)	3-20
Requiring surgical treatment	1 (2)	0.2-10
Respiratory failure	5 (11)	4-23
Reintubation	3 (7)	2-17
Tracheostomy	3 (7)	2-17
Mechanical ventilation >48 h	2 (4)	1-14
Pericarditis	3 (7)	2-17
Vocal cord paresis	2 (4)	1-14
Localized BPF	1 (2)	0.2-10
Deaths	3 (7)	2-17

CI, Confidence interval; CT, chest tube; ARDS, acute respiratory distress syndrome; DVT, deep-vein thrombosis; BPF, bronchopleural fistula.

Bronchial anastomoses were buttressed with a single vascularized tissue flap: 9 omental, 3 pleural, 12 intercostal muscle, 10 autologous pericardial, 1 latissimus dorsi, 4 thymic. In 5 patients, 2 different types of flaps were used, pericardial/thymic ($n = 2$), pleural/pericardial ($n = 2$), pleural/intercostal ($n = 1$). Of the 15 median sternotomies that were performed, we employed a thymic flap in 4 patients, 2 with a combined pericardial and thymic flap, 7 with an omental flap, and 1 with a pericardial flap. All patients who had received previous thoracic radiation underwent omental mobilization via extension of the incision to the upper abdomen to buttress the anastomoses.

Operative Morbidity

Postoperative events (inclusive of major and minor complications, of which 12 experienced more than 1) were observed in 26 patients (58%), highlighted by pneumonia ($n = 11$), blood transfusion ($n = 8$), and atrial arrhythmias ($n = 8$) (Table 2). More serious complications included acute respiratory distress syndrome (ARDS) ($n = 3$, 7%) and anastomotic dehiscence ($n = 1$, 2%). Nineteen (42%) patients experienced no postoperative events. There were no bronchovascular fistulas and one localized bronchopleural fistula in the patient who experienced an anastomotic dehiscence, which was managed with a chest tube. Postoperative events were most closely associated

TABLE 3. Univariate analysis of factors associated with operative morbidity and mortality after carinal resection and reconstruction

Factor	Operative morbidity	
	OR (95% CI)	P value
Age	1.06 (1.01-1.14)	.015
Female sex	1.30 (0.272-7.40)	.767
BMI	0.940 (0.814-1.07)	.245
Poor performance status score	0.327 (0.001-1.90)	.498
Smoking history*	2.00 (0.590-6.78)	.359
COPD	5.40 (0.708-12.00)	.211
Preoperative FEV ₁ (% predicted)	0.997 (0.968-1.03)	.848
Preoperative DLCO (% predicted)	0.956 (0.914-0.979)	.014
Preoperative chemotherapy	11.2 (1.84-24.08)	.014
Preoperative radiotherapy	†	.016
Previous pulmonary resection	0.833 (0.170-4.48)	1.00
Concomitant pulmonary resection	3.78 (0.825-23.18)	.065
Positive margins (R0 vs R1/2)	0.587 (0.139-1.80)	.537
Postoperative complications	—	—
Pneumonia	—	—
ARDS	—	—
PE	—	—
Mechanical ventilation >48 h	—	—
Reintubation	—	—
Pericarditis	—	—
Atrial arrhythmia	—	—
Transfusion requirement	—	—
Anastomotic complications	—	—

OR, Odds ratio; CI, confidence interval; BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 second; DLCO, diffusion capacity of the lungs for carbon monoxide; ARDS, acute respiratory distress syndrome; PE, pulmonary embolism. *Current ($n = 8$) or past ($n = 16$) smokers compared against never-smokers. †Odds ratio cannot be calculated. P value given is the result of Fisher exact test.

with age ($P = .015$), preoperative chemotherapy ($P = .014$) and preoperative thoracic radiation ($P = .016$) and lower preoperative diffusion capacity of the lungs for carbon monoxide ($P = .014$). A history of previous lung resection, was not associated with operative morbidity ($P = 1.00$), while concomitant lung and carinal resection may confer an increased risk of postoperative events ($P = .065$) (Table 3).

Five patients suffered respiratory failure postoperatively; 3 of whom ultimately died. Two required reintubation followed by subsequent tracheostomy but eventually recovered and were decannulated. One tracheostomy was placed preemptively during the index surgery, given the patient's history of severe delayed laryngospasm from a recent thoracic operation. Two patients experienced recurrent nerve palsy with vocal cord paresis. One patient required diet modification for recurrent aspiration, whereas the second underwent vocal cord injection.

Five patients had anastomotic complications. Intact anastomosis with eschar was observed in 3 patients treated conservatively with no intervention and ultimate improvement. Another patient improved following multiple treatments of hyperbaric oxygen therapy (HBO) therapy after surveillance bronchoscopy demonstrated ischemia (without exposed cartilage or necrosis). The only patient in this cohort who underwent carinal resection plus lobar resection required stenting of the airway for anastomotic dehiscence. Three months later, she developed a stricture prompting dilation and stenting. The stent was removed 3 months later and the anastomosis remained patent.

Mechanical Support

CPB was planned electively for 3 patients undergoing left carinal pneumonectomy due to tumor extension into central structures, proximity to major vessels, and the need for airway and cardiac mobilization and retraction (Table E1). Two patients had tumor extensively adherent to or abutting the aorta and pulmonary artery, 1 of whom was also 13 weeks pregnant. She subsequently delivered a healthy baby 6 months later. Veno-arterial ECMO was electively used for 1 patient who underwent left carinal pneumonectomy, given the concern for the ability to ventilate the right lung due to a short right mainstem bronchus. All 4 patients suffered only minor postoperative events: 3 required postoperative blood transfusions, 2 demonstrated focal anastomotic ischemia managed conservatively, and 1 experienced vocal cord paresis. ECMO was used for 2 other patients postoperatively in the setting of hypoxemic respiratory failure and cardiogenic shock. One patient experienced an arrhythmia and arrested, whereas another patient developed a hemodynamically significant pulmonary embolism. These 2 patients ultimately died with multiorgan dysfunction.

Operative Mortality

There were 3 deaths within 30 days of the index operation during the 2-decade experience reported in this study, yielding an operative 30-day mortality of 6.8% (95% CI, 1.9%-16.7%). All 3 patients died during the primary admission for carinal resection ranging 8 to 11 days following their operation. One patient died of right heart failure following pulmonary embolism, 1 patient arrested intraoperatively with a refractory cardiac dysrhythmia, and 1 patient developed renal failure and ARDS leading to multiorgan dysfunction. At 90 days, 40 patients were known to be alive, yielding a 7% 90-day mortality.

All 3 patients who died suffered at least 1 respiratory postoperative event. All deaths (n = 3) occurred in patients who had undergone a carinal pneumonectomy as compared with no pulmonary resection. The 2 patients requiring continued ventilator support accounted for two-thirds of operative deaths. All patients who developed ARDS

(n = 3) had undergone pneumonectomy. Only 1 patient who developed ARDS subsequently recovered after undergoing continued treatment for pneumonia, frequent bronchoscopies for secretion management and aggressive diuresis. She ultimately required reintubation and tracheostomy but was eventually weaned from mechanical ventilation.

Survival

Median overall survival for the entire cohort was 8.4 years (95% CI, 4.3-12.5 years). Overall survival was 83% at 1 year and 58% at 5 years (Figure 1). Median survival in patients with ACC (n = 12) was 6.4 years (95% CI, 0-13.8 years) versus 2.8 years in patients with SCC (n = 19, 95% CI, 0-10.1 years). Five-year survival was 62% for patients with ACC versus 46% for patients with SCC (Figure 2). For patients with pN0 disease (n = 20), 5-year survival was 78% compared with 34% in patients with pathologically node-positive disease (N1, n = 6; or N2 disease, n = 13) (hazard ratio, 0.35; $P = .005$) (Figure 3). Median survival of patients with pN0 disease was 11.9 years (95% CI, 8.4-15.4 years) compared with 2.6 years (95% CI, 1.5-3.8 years) in patients with node-positive disease ($P = .005$).

Forty-four percent of patients (n = 20) had R0 resections, whereas 22 patients had an R1 resection. Although frozen sections were sent in every operation, the inability to resect more airway due to concern for increased anastomotic tension frequently prevented complete resection. No significant difference was found when comparing resection margin status as a predictor of anastomotic complications ($P = 1.00$), morbidity ($P = .397$), or mortality ($P = .092$). Eleven of 22 of the R1 resections and the only R2 resection were ACC. When comparing ACC R1 or R2 resection (n = 12) against R0 resections of all

FIGURE 1. Extended Kaplan-Meier curve for overall survival of all carinal resections.

FIGURE 2. Overall survival comparison of the most common histologies that underwent carinal resection in this cohort. ACC, Adenoid cystic carcinoma; SCC, squamous cell carcinoma.

histology (n = 33), there was no difference in survival ($P = .799$). Sixty-two percent of ACC patients with positive margins were alive at 5 years compared with 60% of those patients with negative margins.

DISCUSSION

Despite nearly 70 years of growing experience since the first published cases, carinal resection and reconstruction continues to be a technically complex operation with potential for significant morbidity and mortality. Advances

FIGURE 3. Overall survival of the cohort stratified by nodal status.

in anesthetic technique and improved intensive care have improved outcomes, but patient selection remains paramount. We describe an operative mortality rate of 6.8% in this recent 20-year experience with carinal surgery. This marks a reduction from our previously reported mortality rate of 12.7% in an earlier cohort of patients from 1962 to 1996,¹⁴ although the CI in the current study includes the previous estimate. At 5 years, 58% of patients were alive from this recent cohort. These data add to the small body of published series (Table 4)^{1,2,4,6,7,11,14-19} composed of at least 30 patients in whom the reported mortality rates range from 29% to as low as 3% in recent years, with 5-year survival rates peaking at 51%.^{4-7,17,20,21}

In addition to a reduced mortality rate, these data support improved safety of central airway surgery from our previous series. Although postoperative events affected greater than one half of our patients, many were minor complications. Importantly, in our previous series, late deaths were secondary to anastomotic complications,¹⁴ whereas we report here only 5 patients suffering anastomotic complications, 4 of whom were treated conservatively. The available literature reports anastomotic strictures following carinal resection in 2.5% to 7.4% of patients,^{4,7,15} of which our experience is just below this reported range (2%). Core principles that have evolved from our previous experience include avoiding anastomotic tension, careful preservation of tracheobronchial blood supply, liberal use of release maneuvers, and buttressing airway anastomoses with vascularized tissue flaps. These are tenets that support the low observed rate of anastomotic complications in this study.^{22,23} We continue to employ a “rule of thumb” that resected trachea plus left mainstem bronchus should not exceed 4 cm when performing left carinal pneumonectomy. We routinely employ surveillance bronchoscopy at 5 to 7 days postoperatively to identify anastomotic problems that would alter management. Other considerations include in patients who have received previous thoracic radiation (n = 6), omental flaps are preferable for buttressing airway anastomoses.^{22,24} We also explored the use of HBO therapy as a salvage method to treat airway anastomoses that exhibit some degree of cartilage ischemia, or partial necrosis after tracheal resection and reconstruction.²⁵ Since we observed some improvements in anastomotic healing of the trachea, HBO has been judiciously implemented at our institution for tracheal and carinal resections associated with suboptimal anastomotic healing, or repair of complex tracheoesophageal fistulas.

Although preoperative thoracic radiation is no longer considered a contraindication to resection,²⁴ the associated risk to anastomotic healing continues to be reported in each series with conflicting rates.^{16,23,26} In our series, preoperative chemoradiotherapy was associated with

TABLE 4. Summary of published series of carinal resections with n > 30

Author, y	n	Morbidity (%)	Mortality (%)	5-y survival (%)
Grillo, ¹¹ 1982	31	–	13	–
Jensik and colleagues, ¹ 1982	34	–	29	15
Dartevelle and colleagues, ² 1995	55	10.9	7.2	40
Mitchell and colleagues, ¹⁴ 1999	143	38.8	12.7	–
Porhanov and colleagues, ⁴ 2002	231	35.5	16	25
Regnard and colleagues, ¹⁵ 2005	65	50.8	7.7	26.5
de Perrot and colleagues, ⁷ 2006	119	47.1	7.6	44
Roviaro and colleagues, ¹⁶ 2006	53	11.3	7.5	33
Macchiarini and colleagues, ¹⁷ 2006	50	36	4	51
Rea and colleagues, ¹⁸ 2008	49	28.6	6.1	27.5
Eichhorn and colleagues, ⁶ 2013	64	40.6	3.1	31
Galetta and colleagues, ¹⁹ 2018	32	59.1	9.1	30.3

increased postoperative morbidity; however, 7 of these 8 patients required concomitant pneumonectomy and suffered mainly postoperative respiratory complications. Concomitant pneumonectomy carries significant additional risk for operative morbidity ($P = .040$) and mortality.^{4,14,27} All 3 of the 30-day deaths in this experience appeared to result from early cardiopulmonary complications, and all 3 had undergone pneumonectomy. Lung-sparing procedures, whenever anatomically feasible, are favored over pneumonectomy. Careful consideration of pulmonary reserve, comorbidities, and disease extent optimize selection of patients who require pneumonectomy with carinal resection.

Our recent series describes the contemporary use of CPB or ECMO as a planned operative strategy in 4 patients with low morbidity and no operative mortality. Given the rarity of complex tracheobronchial cases even at high-volume centers, the literature describing extended resections which use CPB or ECMO is limited by small cases numbers. We believe each case must be evaluated individually, attributing careful consideration to the technical challenges of the procedure against the risks associated with CPB or ECMO, including systemic anticoagulation, oncologic consequences of circulatory support,^{28,29} and longer operative time. We believe that circulatory support strategies can be advantageous in carefully selected patients harboring complex airway tumors, and in some cases for emergent, life-threatening complications.^{21,30-33} Specifically, planned CPB may be helpful to achieve R0 resection in cases in which tumor approximates central vascular structures including aorta, superior vena cava, and atria. ECMO can be useful when standard cross field or jet ventilation may be insufficient, or too cumbersome, to achieve adequate oxygenation during a complex tracheobronchial resection and reconstruction, particularly in the setting of pneumonectomy. Systematic review of

small series with carinal involvement paired with larger series of ECMO use in pneumonectomy patients, suggest that mechanical support may be safely used in highly selected patients with acceptable long-term survival rates.^{29,34} Accordingly, advances in mechanical support have paralleled improvements in integrated perioperative care, including anesthetic ventilation techniques to avoid barotrauma and sequelae of ARDS, as well as improved intensive care management.

Despite the complex technical challenges and risks associated with carinal resection, it offers patients a chance at long-term survival when alternatives are simply palliative. Histologic diagnoses should be given close consideration when considering technical limitations and feasibility of the operation. Our observations demonstrate that patients with node-negative disease and/or ACC histology have superior outcomes. Our series supports previous observations in the literature that the presence of nodal disease portends a poor prognosis with significant limitations to long-term survival.^{4,5,21,26} In contrast, in patients with ACC, long-term survival can be achieved despite positive microscopic resection margins when employing adjuvant radiation in patients undergoing carinal resection with reconstruction.³⁵

Despite being one of the larger contemporary series for carinal resection, our retrospective study is limited by its retrospective design and small case numbers. The small sample size precluded the use of robust standard errors and may make the analysis more vulnerable to type II errors than type I. Central airway tumors are rare, and the few published single-center series (Table 4) are still too small for robust statistical conclusions. Furthermore, comparing survival in patient cohorts that span several decades remains challenging because advances in perioperative management, improved anesthetic techniques, and patient selection have significantly evolved over time.

CONCLUSIONS

Importantly, our 6-decade experience in central airway surgery has taught us several important guiding lessons. (1) Patient selection is paramount where candidacy for complex central airway surgery is predicated on medical fitness, status of mediastinal lymph nodes prompting aggressive mediastinal staging modalities, and thoughtful technical planning to evaluate safe limits of resection and reconstruction; tumor size is not a contraindication unless a tension free anastomosis cannot be achieved. (2) R0 resection should be attained whenever possible, however, not at the expense of anastomotic tension, particularly in the setting of ACC. (3) Advances in mechanical and circulatory support including CPB and ECMO provide novel strategies to achieve an R0 resection in even more technically challenging and comorbid patients with reasonable risk profiles. (4) Because of the rarity of cases and technical expertise required, these cases should be referred to high-volume centers for evaluation. These “lessons learned” have contributed to a marked reduction in morbidity (particularly anastomotic complications and incidence of ARDS) and mortality in the last 2 decades, which improves the chance for long-term survival in patients harboring central tumors.

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Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: carina, neocarina, carinal pneumonectomy, carinal resection, carinal reconstruction

Discussion

Dr Betty C. Tong (Durham, NC). Congratulations on an excellent presentation and study. You and your colleagues have provided a comprehensive strategy for addressing these challenging patients and continued the series at the Massachusetts General Hospital that was last presented by

Dr John Mitchell 20 years ago at this meeting. So, in 2038, 20 years from now, I hope that you will continue the tradition as an endowed chair and chief of an academic thoracic center. But for now, I have a few questions.

First, over your series, the average case volume declined from nearly 4 cases a year in Dr Mitchell's series to just over 2 per year in your series. You have highlighted in your manuscript the need for meticulous and tailored perioperative care, which undoubtedly requires deliberate practice and experience. And in fact, 2 of your cases were revisions of carinal resections that were done previously at other institutions. So, given those volumes, how can any of us expect to be good at this operation if the greatest-volume center in the country, arguably yours, much less surgeons, are doing only about 2 cases per year?

Dr Christina L. Costantino (Boston, Mass). Thank you, Dr Tong. This is certainly a challenge for both experienced surgeons and trainees alike. The techniques are the same for airway surgery but of course require more considerations regarding available airway length and proximity

or involvement of vital structures. We do recommend that these cases be done at higher-volume centers, given that some of these patients can be offered long-term survival if selected appropriately, as they require an experienced multidisciplinary team to achieve resection with low morbidity.

Dr Tong. Second, it was striking to me that all 5 deaths in the series were in patients who underwent carinal pneumonectomy. So, with a total of 25 patients who underwent carinal pneumonectomy and 5 deaths, that's a mortality rate of 20%. I think it's important that we consider not only overall survival in our patients but disease-free survival as well. So, if we put our patients through a big operation, profoundly affect their quality of life with a pneumonectomy, and they recur very shortly thereafter and thus requires systemic treatment with or without radiation, then I wonder how much we have really helped them.

Can you comment a little bit on the patients in this series that were operated on for non-small cell lung cancer?

Dr Costantino. First, regarding your point about disease-free survival and adjuvant therapy, this is certainly a limitation of our study and a data point we would have liked to include to get a full picture of disease course following resection. As you might expect, many of the patients were referred from all over the country, and for this reason, the follow-up data over this 20-year series following their return home are not complete.

Still, however, even in the case of non-small cell lung cancer, these patients would have progressed to become symptomatic, given the location of their tumor and limited palliative medical options available. We certainly agree that the risk of morbidity and mortality associated with pneumonectomy is substantial, and we perform lung-sparing operations whenever possible; however, we do believe there is a benefit of operating in select patients.

Dr Tong. My final question is in this area of targeted immune therapies, photodynamic therapy, laser ablation, airway stenting, all the local therapies, if you will, plus the immune therapies, do you think we should even be doing these operations at all? You have obviously carefully selected your patients. Can you tell us a little bit about how that's done?

Dr Costantino. Even in the era of new immune therapies, I think that we certainly should be performing these operations in select patients, particularly in the setting of N0 disease, where R0 resection can be achieved. Many of these patients received laser ablation, stenting, or coring out of the lesion, and they were all temporizing measures before they became symptomatic again with dyspnea, cough, or hemoptysis. If you exclude patients with adenoid cystic carcinoma, the median survival of those with N0 disease is still 11.9 years (75% of patients are alive at 5 years). Of course, with node-positive disease, the median survival was 2.6 years, but perhaps we can extend survival further with resection and these newer adjuvant regimens. Temporizing procedures and medical therapy at this point cannot achieve these survival rates.

So I do think that we should be operating on these patients, but they should be carefully selected for at

experienced centers. Careful consideration must be paid to technical feasibility, pulmonary reserve, comorbidities, and disease extent to optimize selection of patients who require pneumonectomy with carinal resection.

Dr Tong. Very good. Congratulations.

Dr Costantino. Thank you.

Dr Malcolm M. DeCamp (*Madison, Wis*). Congratulations on a timely update. I really enjoyed the presentation. I have a specific question about the patients with adenoid cystic carcinoma. If I understood the presentation, margin didn't really matter in terms of long-term survival, and I wondered how you managed the decision about adjuvant radiation. Obviously, the patients with positive margins received adjuvant radiation. Did you withhold adjuvant radiation from the patients with R0 resections, or did they all undergo radiation?

Dr Costantino. Thank you for your question. Regarding the patients with adenoid cystic carcinoma, there were actually no patients in cohort who had R0 resections for the adenoid cystic group. They all had R1 and one had an R2 resection. These resections were mainly limited by length of the airway and concern for anastomotic tension, as we found late anastomotic complications were a major source of morbidity and mortality in our previous series. Of the patients with adenoid cystic carcinoma in the current series, some of these patients did receive adjuvant radiation, and the others we don't have complete follow-up data regarding therapy. However, based on a study that we have previously published on a larger cohort of patients who had adenoid cystic carcinoma, resection even in the presence of advanced disease offers extended survival in addition to adjuvant radiation for residual disease.

Dr Decamp. So if you had an R0 resection, would you administer radiation to that patient?

Dr Cameron D. Wright (*Boston, Mass*). No.

Dr Alain Chapelier (*Paris, France*). I would like to congratulate you and your group for your excellent presentation and very good results you reported, especially in the group with carinal resection without lung resection with 24 patients.

I have a question. You have well detailed in your presentation of the 4 cases of left carinal

resection, pneumonectomy with the use of ECMO, which is sometimes a perioperative choice. Would you recommend systematic sternotomy for left carinal pneumonectomies now?

Dr Costantino. I'm sorry, you said a systematic?

Dr Chapelier. Would you recommend now a systematic median sternotomy for left carinal pneumonectomies?

Dr Costantino. In recent decades, our preference at our institution for both neo-carinal and left or right pneumonectomy has been a median sternotomy.

Dr Shaf Keshavjee (*Toronto, Ontario, Canada*). What about hyperbaric oxygen (HBO)? You alluded to it a little bit. How do you make your decision on that? Is it just some holy water stuff, or does it really work?

Dr Costantino. It's a good question. Certainly, at our institution it is an observational—

Dr Keshavjee. Holy water.

Dr Costantino. We survey our anastomoses by surveillance bronchoscopy while they are still in the hospital to try and identify any anastomotic complications early, and we have seen this in our study of our tracheal resections as well. We have seen improvement in patients with daily HBO who previously had ischemic injuries that were not improving. It is certainly observational but it is definitely something that we believe helped.

Dr Keshavjee. Okay, both big guns are coming to the mike. Tell us about it, Cam.

Dr Wright. So it is holy water, but there is no question that there is tension on any airway resection we do, especially these kinds of cases, and with tension, there is ischemia. As you know, when you do airway surgery, you can see the signs of ischemia, and it gets better as you go away from the anastomosis. So, Dr Mathisen is the one that really latched onto the idea, and luckily, we have an HBO center right next to us that accepts these patients. So nowadays we do bid HBO for 7 to 10 days if we detect significant ischemia or impending dehiscence.

And I will just say anecdotally, it seems to make sense and I think it salvaged a couple of my patients after a tracheal resection.

We are never going to have randomized trials, so it's all voodoo. It doesn't hurt and it might help.

Dr Keshavjee. I think when you start to see impending trouble with a patient like that, it's probably good to have a few tricks up your sleeve and things to help you out. And I think also your improvement in survival of the pneumonectomies, like all pneumonectomies, I think we need to think more about nitric oxide early, which most people have access to, but also extracorporeal membrane oxygenation early so that you try and not get into a

position where you are beating up one lung on a ventilator and then starting extracorporeal membrane oxygenation 10 days later when you have missed the boat. So I think a lot of these things that we used to bail these patients

out will help us get more of these patients to a chance of a curative resection. So I certainly think that the centers of excellence should keep trying to do these operations.

TABLE E1. Details of patients selected for cardiopulmonary bypass

Patient	Indication	Surgery	Approach	Histology	Support
53-y-old man	Mobility for airway anastomosis. Tumor extended into left mainstem causing total occlusion with contiguous annular involvement of the entire tracheal wall.	Left carinal pneumonectomy	Median sternotomy	Adenoid cystic carcinoma	Cardiopulmonary bypass
35-y-old woman	Vascular proximity. Tumor extensively abutted the undersurface of the aorta and the pulmonary artery. 13 wk' pregnant: avoiding hypoxia	Left carinal pneumonectomy	Median sternotomy	Adenoid cystic carcinoma	Cardiopulmonary bypass
41-y-old woman	Vascular proximity. Tumor adherent to aorta with esophageal invasion. Avulsion of vessel needing repair.	Left carinal pneumonectomy	Median sternotomy	Adenoid cystic carcinoma	Cardiopulmonary bypass
50-y-old man	Tumor extends to the junction of left mainstem and trachea and then up distal trachea. Patient had very short right mainstem bronchus and felt may be difficult to ventilate right lung. Hemodynamic instability with cardiac retraction for long periods.	Left carinal pneumonectomy	Median sternotomy	Squamous cell carcinoma	Central VA ECMO (RA to ascending aorta)

VA ECMO, Veno-arterial extracorporeal membrane oxygenation; RA, radial artery.