Reconstruction of the heart and the aorta for radical resection of lung cancer

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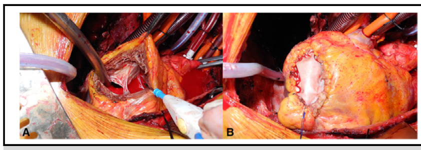
ABSTRACT

Introduction: We report a single-center experience of resection and reconstruction of the heart and aorta infiltrated by lung cancer in order to prove that involvement of these structures is no longer a condition precluding surgery.

Methods: Twenty-seven patients underwent surgery for lung cancer presenting full-thickness infiltration of the heart (n = 6) or the aorta (n = 18) and/or the supra-aortic branches (subclavian n = 3). Cardiac reconstruction was performed in 6 patients (5 atrium, 1 ventricle), with (n = 4) or without (n = 2) cardiopulmonary bypass, using a patch prosthesis (n = 4) or with deep clamping and direct suture (n = 2). Aortic or supra-aortic trunk reconstruction (n = 21) was performed using a heart-beating crossclamping technique in 14 cases (8 patch, 4 conduit, 2 direct suture), or without crossclamping by placing an endovascular prosthesis before resection in 7 (4 patch, 3 omental flap reconstruction). Neoadjuvant chemotherapy was administered in 13 patients, adjuvant therapy in 24.

Results: All resections were complete (R0). Nodal staging of lung cancer was N0 in 14 cases, N1 in 10, N2 in 3. No intraoperative mortality occurred. Major complication rate was 14.8%. Thirty-day and 90-day mortality rate was 3.7%. Median follow-up duration was 22 months. Recurrence rate is 35.4% (9/26: 3 loco-regional, 6 distant). Overall 3- and 5-year survival is 60.9% and 40.6%, respectively.

Conclusions: Cardiac and aortic resection and reconstruction for full-thickness infiltration by lung cancer can be performed safely with or without cardiopulmonary bypass and may allow long-term survival of adequately selected patients. (J Thorac Cardiovasc Surg 2023;■:1-8)



Prosthetic reconstruction of the heart after resection for lung cancer.

CENTRAL MESSAGE

Cardiac and aortic reconstruction for invasion by lung cancer can be performed safely with or without CPB and may allow survival benefit for adequately selected patients.

PERSPECTIVE

Lung cancer with deep and extended infiltration of the heart and the aorta has been generally considered not suitable for radical surgery. This single-center experience proves that neoplastic infiltration of these structures is no longer a condition precluding resection.

See Commentary on page XXX.

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Infiltration of the heart and the aorta by lung cancer (Figure 1, *A* and *B*) has been considered a condition precluding radical surgery for a long time due to technical and oncologic reasons. Most of literature data reporting the feasibility of surgical treatment in this setting refer to patients with limited left atrial infiltration from non–small cell lung cancer (NSCLC)[1-10] or marginal vascular involvement.[9-14] However, despite the disappointing results of oncologic options of cure, tumors with extended infiltration of the cardiac wall or the aorta that cannot be managed with marginal resection or limited cardiovascular repair have been generally considered not suitable for radical surgery, due to the technical complexity of the interventions required, concern about related major morbidity and mortality, and doubt regarding prognostic benefit. Our experience including patients undergoing complete resection of lung cancer deeply invading the heart or the aorta followed in most cases by their prosthetic reconstruction with or without cardiopulmonary bypass (CPB) proves that cardiac and aortic involvement is no longer a condition precluding radical surgery.

METHODS

Between October 2014 and January 2021, 27 patients (19 male, 8 female) with a mean age of 64.3 ± 10.5 years (range, 27-78 years) underwent radical surgery for lung cancer presenting with full-thickness infiltration of the heart (n = 6) or the aorta (n = 18) and/or the supra-aortic branches (subclavian n = 3). Patients undergoing marginal atrial resection with staple suture or subadventitial resection of the aorta or the supra-aortic trunks were

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Abbreviations and Acronyms

AA	= aortic arch
CPB	= cardiopulmonary bypass
CS	= circulatory support
CT	= computed tomography
DFS	= disease-free survival
FDG-PET	= fluorodeoxyglucose-positron emission tomography
LSA	= left subclavian artery
MRI	= magnetic resonance imaging
NSCLC	= non–small cell lung cancer
OS	= overall survival

not included in this study. Neoadjuvant chemotherapy was administered in 13 patients and adjuvant therapy in 24. Postoperatively, 18 patients received chemotherapy, 4 chemoradiotherapy, and 2 immunotherapy. During the study period, 5 other patients underwent reconstruction of the heart (1 right atrial patch) or of the aorta (2 conduits and 1 patch) or supra-aortic branches (1 conduit reconstruction of the carotid artery) for radical resection of mediastinal tumors, which are not considered in the present analysis.

Preoperative Workup

Preoperative workup and staging included whole-body contrast-enhanced computed tomography (CT). Magnetic resonance imaging (MRI) was performed in case of doubt regarding cardiovascular infiltration or on brain metastasis; bone scintigraphy was performed if indicated. Fluorodeoxyglucose-positron emission tomography (FDG-PET) was performed if preoperative cytological or histological diagnosis of the primary tumor was not achieved or in case of doubt about the presence of metastatic lesions.

Bronchoscopy was performed in all patients to assess the potential involvement of the bronchial tree. Video mediastinoscopy or transbronchial needle aspiration was performed in the presence of enlarged peritracheal or subcarinal lymph nodes (long-axis diameter >1.5 cm) on CT scan. Patients with histologically or cytologically proven N2 disease underwent induction chemotherapy. Mediastinal restaging of patients with NSCLC after chemotherapy and before the operation was performed by FDG-PET with contrast-enhanced CT scan. Transbronchial needle aspiration was performed only in selected cases with doubt about N2 disease persistence after induction therapy. Induction therapy was also considered in some patients with the aim of primary tumor reduction.

The main criteria for patient selection included good performance status (Eastern Cooperative Oncology Group 0-1), clinical N0-1 status (even after induction therapy), and tumor infiltration not too extended to preclude a prosthetic reconstruction of the aorta or the cardiac chambers. All patients enrolled for surgical treatment presented with N0-1 preoperative clinical status, some after induction therapy, at the time of resection. Adjuvant therapy was considered indicated and administered to all patients except those who refused it (2).

Surgical Technique

Surgical access was lateral thoracotomy in 13 patients, posterolateral thoracotomy in 13, and median sternotomy in 1.

Tumors Invading the Heart

Interventions under CPB. For patients presenting with extended infiltration of the cardiac structures requiring prosthetic reconstruction (Figure 1, *A*), CPB was instituted via ascending aorta and right atrial or bicaval cannulation (N = 4), following full heparinization (Figure 2, *A*). Once CPB was started, the aorta was crossclamped and the heart arrested by means of cold blood cardioplegia, allowing for the excision of the mass and surgical reconstruction of the cardiac chamber involved (Figure 2, *A* and *B*). Reconstruction of the cardiac wall (left atrium in 3 cases and right ventricle in 1) was performed with a bovine pericardial patch fixed with a running 5-0 or 4-0 PROLENE suture (Figure 2, *B*).

Intervention without CPB. In patients (2) with the left atrium full-thickness infiltration who did not require prosthetic reconstruction, en bloc resection was accomplished by previous deep clamping of the atrium and subsequent direct 4-0 PROLENE running suture.

Tumors Invading the Aorta

Interventions with endovascular stent without crossclamping. For patients with tumor invading the descending aorta or the lower arch distally to the origin of the left subclavian artery (LSA), en bloc resection of the infiltrated vascular wall was planned after placement of an aortic endograft according to the previously described technique[15] (Figure 1, *B*). Endovascular stent placement was performed under general anesthesia using a retrograde femoral approach. Endografts of different types were used, including Zenith (Cook Medical), GORE TAG (W. L. Gore & Associates, Inc), and Valiant (Medtronic). Endovascular stent was inserted 2 to 10 days before resection. To avoid endograft dislocation after resection, proximal and distal landing zones were targeted, including approximately a 4-cm length of healthy aorta. Resection of the infiltrated aortic wall was performed en bloc with the planned lung resection.[15] The presence of the endovascular stent allowed safe resection with no blood leaks. Subsequent vascular reconstruction was accomplished covering the defect with the underlying endoluminal stent using a Dacron patch (fixed to the aortic wall with a 4-0 PROLENE running suture) or an omental vascularized flap transposed into the pleural cavity through the diaphragm according to a previously described technique.[16]

Interventions with crossclamping with or without circulatory support (CS). For patients showing tumor infiltration of the aortic arch (AA) close to the origin or with actual involvement of the LSA, direct crossclamping with or without a CS was required. In every case, arrangements for potential heart-beating circulatory assistance were made before the operation by positioning a guidewire in the left femoral artery for possible subsequent cannulation. CS, when required, consisted in left ventricular assistance to preserve blood flow to the lower body, keeping the heart beating. The circuit consisted of an inflow catheter inserted through the left atrial appendage using the thoracotomy approach, a venous reservoir, a centrifugal pump, and an arterial cannula directly into the descending aorta or peripherally into the left femoral artery. This allowed for a safe excision and reconstruction of the aorta. The actual use of CS was established on the basis of the estimated duration and complexity of the surgical procedure. At the end of the procedure, patients were weaned from the CS and operations completed in the usual fashion.

Noninvasive cerebral monitoring (oximetry near-infrared spectroscopy) and renal blood perfusion monitoring were used. After complete dissection and exposure of the AA and supra-aortic trunks, the vascular segment infiltrated was crossclamped. The proximal clamp was placed on the AA between the origins of the left carotid artery and LSA, whereas distal clamping was usually at the level of the superior descending aorta. The LSA was clamped with a tourniquet on its distal and upper portion. After clamping, the portion of AA or LSA infiltrated was resected en bloc with the tumor enclosed within the lung parenchyma. Frozen section analysis was performed to confirm the radicality of resection. In case of limited aortic wall resection, subsequent reconstruction was performed by direct suture or patch prosthesis of polyethylene-terephthalate (Dacron) or bovine pericardium. For patients requiring a circumferential resection of the AA or LSA, a Dacron conduit reconstruction was performed (Figure 3, *A* and *B*). A running suture of 4-0 monofilament nonabsorbable material

FIGURE 1. NSCLC invading the heart (A) and the aorta (B). A, Right lung cancer with extensive invasion of the heart. B, Left lung cancer extensively infiltrating the aorta with endoluminal stenting.

(PROLENE) was used in every reconstruction. Due to the high pressure of the reconstructed vessels, heparinization was performed only when heart beating CS was used.

Postoperative Management

Patients who underwent vascular prosthetic reconstruction received antiplatelet agents postoperatively. Oral anticoagulation was not routinely used postoperatively due to high pressure of the reconstructed vascular structures. During hospitalization, patients undergoing patch reconstruction of the heart received subcutaneous low-weight heparin, which was shifted to oral anticoagulation after discharge until clinical control at 3 months in the absence of rhythm abnormalities. Pain management was performed according to standardized protocol in use for patients receiving thoracotomy: intraoperative intercostal blocks with 7.5 mg/mL ropivacaine to be repeated postoperatively "on demand" and continuous intravenous infusion of tramadol (10 mg/h) and ketorolac tromethamine (3 mg/h). Patients undergoing cardiac reconstruction were also evaluated by dynamic MRI or CT of the heart within the first month of the operation. Volume-rendering CT and MRI were used to assess the patency and flow of the reconstructed vessels. Postoperative oncologic follow-up was performed with contrast-enhanced total-body CT scan and FDG-PET scan. Follow-up evaluations were planned every 3 months for the first 2 years and every 6 months for the following 3 years. All living patients were available for follow-up for at least the first 5 years. The last date of follow-up was January 31, 2022.

The study was approved by the local ethics committee (institutional review board no.: 284-SA_2022; date of approval February 6, 2023; prot. N.7 SA_2023) and conducted in accordance with the Declaration of Helsinki. All patients provided written informed consent for the operation and inclusion of personal data in a scientific database.

Statistical Analysis

Continuous variables were reported as either the means and standard deviation or median and interquartile ranges according to their distribution, as assessed by the Shapiro–Wilk normality test. Categorical variables were reported as percentages.

To assess recurrence and mortality rates of patients undergoing complete resection, we used disease-free survival (DFS) analysis and overall survival (OS) analysis performed by the Kaplan–Meier approach. The DFS and OS differences in terms of resection type (eg, heart or aorta by NSCLC and reconstruction with or without CPB) were tested by log-rank test and are represented by Kaplan–Meier curves. The recurrence and mortality probability were computed at 36 and 60 months if data were available and 30 and 48 months otherwise. All statistical analyses were performed by R Studio statistical software, version 4.2.2 (The R Project for Statistical Computing).

RESULTS

Preoperative mean forced expiratory volume in 1 second of the 27 patients with NSCLC was $93.2 \pm 22\%$. All resections were complete (R0). Lung cancer histology is reported in Table 1. Cardiac reconstruction was performed in 6

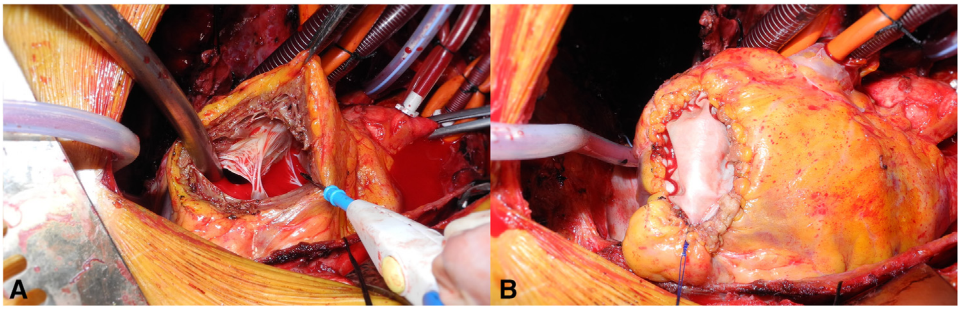

FIGURE 2. Prosthetic reconstruction of the right ventricle after resection of T4 NSCLC. A, The infiltrated portion of the right ventricle has been resected under CPB, leaving a large defect on the cardiac wall. B, Prosthetic reconstruction of the cardiac wall with a bovine pericardial patch has been completed.

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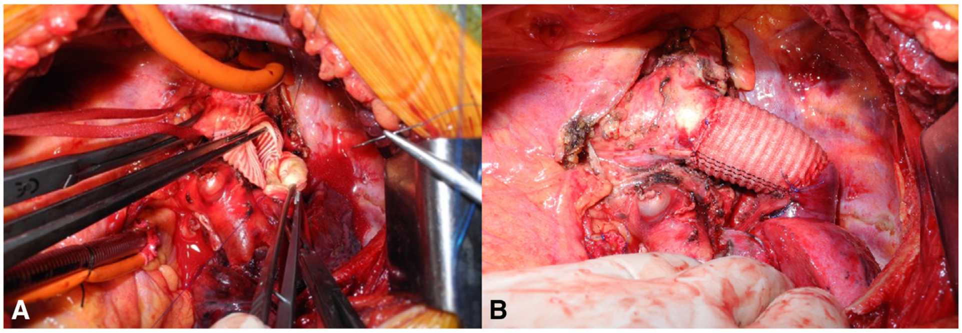

FIGURE 3. Prosthetic reconstruction of the aorta after resection of T4 NSCLC. A, Anastomotic conduit reconstruction of the distal aortic arch with cross-clamping under left circulatory support. B, Distal aortic arch replacement with a Dacron conduit has been completed.

patients with (n = 4) or without (n = 2) CPB, using a patch prosthesis (n = 4 with CPB) or with deep clamping and direct suture (n = 2; no CPB). There were 5 left atrial and 1 right ventricle reconstructions. Aortic or supra-aortic trunk reconstruction (n = 21) was performed using a heart-beating direct crossclamping technique in 14 patients (8 patch, 4 conduit, 2 direct suture), or without crossclamping by placing an endovascular prosthesis before resection in 7. Reconstruction and reinforcement of the aortic wall in this group of patients was accomplished in 4 cases with a Dacron patch and in 3 cases by an omental flap transposed through the diaphragm without additional surgical access. In the crossclamping group, patch reconstruction was performed using Dacron prosthesis in 6 patients and bovine pericardium in 2, whereas conduit replacement was performed with Dacron prosthesis in all cases. In 7 of 14 patients undergoing the heart-beating crossclamping technique, a left CS was used. Associated parenchymal resections are reported in Table 1. Overall mean operative time was 221.4 ± 49.1 minutes. For patients receiving aortic and supra-aortic trunk reconstruction, mean operative time was 214.3 ± 53 minutes with a mean clamping time of 29.3 ± 3.3 minutes. Mean operative time for patients undergoing cardiac reconstruction was 230.8 ± 41.6 minutes. Mean CPB time for patients who required it was 51.5 ± 12 minutes. No intraoperative mortality occurred. Thirty-day and 90-day mortality rate was 3.7% (1/27). The only postoperative death occurred 12 days after the operation in a patient who underwent right pneumonectomy associated with left atrial resection and patch reconstruction. It was due to cardiac failure occurring on postoperative day 3 during intensive care unit stay.

Postoperative hospital stay ranged between 6 and 20 days (mean, 9.8 ± 4.4 days). Patients undergoing cardiac reconstruction had a longer mean postoperative hospital stay (10.25 ± 3.7 days; range, 6-20 days) if compared with patients receiving aorta or supra-aortic trunk reconstruction (9.6 ± 4.8 days; range, 7-16 days). Overall mean intensive care unit stay was 3.08 ± 1.47 days.

Major complication rate was 14.8% (4/27: 1 bleeding requiring rethoracotomy, 1 laryngeal nerve injury, 1 chylothorax, and 1 cardiac failure resulting in death). Pathologic nodal staging was N0 in 14 patients, N1 in 10, and N2 in 3 (Table 1).

Median follow-up duration was 22 months (range, 5-72 months). OS at 3 and 5 years was 60.9% and 40.6%, respectively (Kaplan–Meier) (Figure 4). Patients with heart infiltration had an OS of 44.4% at 3 and 4 years, whereas patients with aorta infiltration had an OS of 65.4% at 3 years and at 4 years (Figure 5).

Recurrence rate was 34.6% (9/26:3 locoregional, 6 distant). DFS was 68.3% at 3 years and 51.2% at 5 years. Patients undergoing pneumonectomy had a trend toward worse survival without reaching statistical significance ($P = .06$) at univariate analysis (Figure 6). There was no difference in survival related to histotype (squamous vs other; $P = .14$) or the use of CPB ($P = .18$) or CS ($P = .24$) at univariate analysis. A multivariate analysis for risk factors influencing long-term survival was not performed due to the too-limited statistical sample. Complete long-term patency of the reconstructed vessels (aorta or supra-aortic trunks) has been shown in all patients by dynamic MRI performed 1 month and 1 year (for living patients) after surgery.

DISCUSSION

Heart and aorta can be infiltrated by T4 lung cancer. Invasion of these structures has been considered a contraindication for radical surgery for a long time. This is principally due to technical reasons related to the complexity of the cardioangioplastic procedures required to achieve a radical resection but also due to the weak evidence of related oncologic benefit on long-term outcome available in the literature. Over the last decades, only few limited experiences worldwide have reported the feasibility and safety of extended operations for radical resection of T4-NSCLC invading the aorta or the heart (usually the left atrium).[1-15] If considering resection of tumors invading the thoracic aorta, most of the interventions reported in published series include subadventitial dissection procedures. So far, there are only small case series reporting angioplastic

TABLE 1. Patients' characteristics, interventions, and survival

Patient	Age, y	Neoadjuvant therapy?	cT stage	cN stage	Cardiac/ vascular resection	Cardiac/ vascular reconstruction	Parenchymal resection	Histology	pT stage	pN stage	Adjuvant therapy?	Recurrence?	DFS, mo	Overall survival, mo	Death?
1	77	No	4	0	Aorta	Suture	Left upper lobectomy	Squamous cell	4	1	Yes	Yes	10	25	No
2	71	Yes	4*	0*	Aorta	Suture	Left upper lobectomy	Squamous cell	y4	y0	No	Yes	8	10	Yes
3	78	No	4	0	Aorta	Patch	Left upper lobectomy	Squamous cell	4	1	No	No	5	5	Yes†
4	59	Yes	4*	1*	Aorta	Patch	Left pneumonectomy	Adenocarcinoma	y4	y1	Yes	Yes	8	20	No
5	65	No	4	0	Subclavian artery	Conduit	Left upper lobectomy	Adenocarcinoma	4	0	Yes	Yes	17	29	No
6	62	Yes	4*	0*	Aorta	Patch	Left upper lobectomy	Adenocarcinoma	y4	y0	Yes	No	12	12	No
7	69	Yes	4*	0*	Aorta	Patch	Left upper sleeve lobectomy	Squamous cell	y4	y0	Yes	No	6	6	No
8	71	Yes	4*	0*	Aorta	Conduit	Left upper sleeve lobectomy	Squamous cell	y4	y1	Yes	No	30	30	No
9	60	Yes	4*	0*	Subclavian artery	Conduit	Left upper lobectomy	Adenocarcinoma	y4	y0	Yes	No	24	24	No
10	75	Yes	4*	0*	Aorta	Stent + omentum	Left lower lobectomy	Squamous cell	y4	y2	Yes	Yes‡	21	21	Yes
11	71	Yes	4*	0*	Aorta	Stent + omentum	Left lower lobectomy	Adenocarcinoma	y4	y1	Yes	Yes‡	44	55	Yes
12	63	No	4	1	Aorta	Stent + omentum	Left pneumonectomy	Adenocarcinoma	4	1	Yes	No	22	22	Yes†
13	60	No	4	0	Aorta	Stent + patch	Left lower segmentectomy	Sarcomatoid	4	0	Yes	No	72	72	No
14	73	Yes	4*	1*	Aorta	Stent + patch	Left lower lobectomy	Adenocarcinoma	y4	y1	Yes	No	69	69	No
15	65	No	4	0	Aorta	Stent + patch	Left pneumonectomy	Squamous cell	4	2	Yes	No	12	12	No
16	63	Yes	4*	0*	Subclavian artery	Patch	Left upper lobectomy	Adenocarcinoma	y4	y1	Yes	Yes	6	22	No
17	59	No	4	0	Aorta	Stent + patch	Left pneumonectomy	Squamous cell	4	2	Yes	No	14	14	No
18	78	Yes	4*	1*	Aorta	Patch	Left lower lobectomy	Adenocarcinoma	y4	y1	Yes	No	24	24	No
19	74	No	4	0	Aorta	Patch	Left upper sleeve (PA) lobectomy	Adenocarcinoma	4	0	Yes	No	34	34	No
20	67	Yes	4*	1*	Aorta	Conduit	Left upper sleeve lobectomy	Sarcomatoid + adenocarcinoma	y4	y1	Yes	Yes	12	14	No
21	59	No	4	0	Aorta	Patch	Left upper lobectomy	Adenocarcinoma	4	0	Yes	Yes‡	15	28	Yes
22	62	Yes	4*	0*	Heart left atrium	Patch	Right pneumonectomy	Adenocarcinoma	y4	y0	Yes	No	12	12	Yes†
23	57	No	4	0	Heart left atrium	Patch	Right pneumonectomy	Adenocarcinoma	4	0	No	No	1	1	Yes§
24	27	No	4	0	Heart left atrium	Suture	Right pneumonectomy	Sarcomatoid	4	0	Yes	No	51	51	No
25	53	No	4	0	Heart left atrium	Patch	Right pneumonectomy	Squamous cell	4	0	Yes	No	15	15	No
26	67	No	4	0	Heart left atrium	Suture	Right pneumonectomy	Squamous cell	4	0	Yes	No	23	23	Yes†
27	52	No	4	0	Heart right ventricle	Patch	Sublobar (wedge)	Lung cancer recurrence (neuroendocrine)	–	0	Yes	No	30	30	No

DFS, Disease-free survival; *PA*, pulmonary artery. *After neoadjuvant. †Other cause. ‡Local. §Thirty-day mortality.

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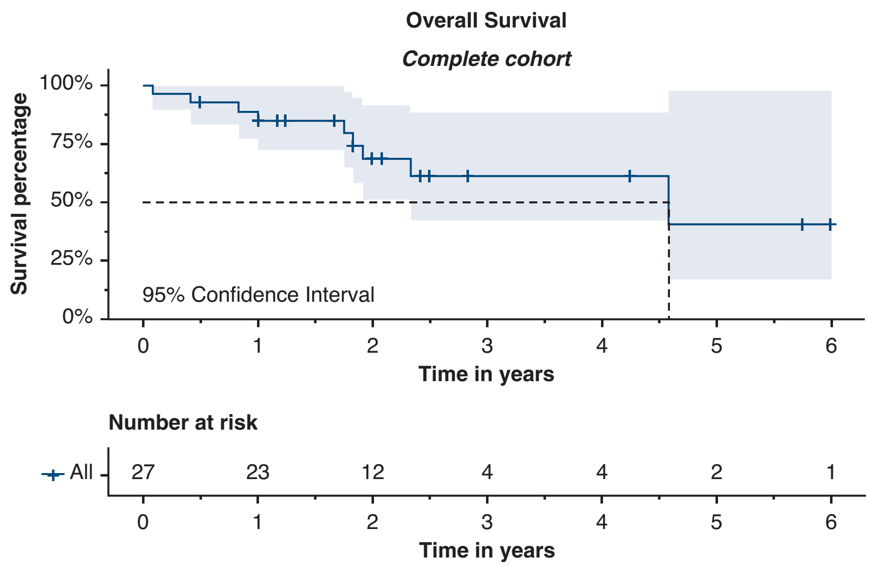

FIGURE 4. Overall survival: Kaplan–Meier curve.

procedures in this setting.[9-14,17] The reported perioperative mortality ranges between 2.9% and 12.5%[12,13,17] and major morbidity between 7% and 37%.[10-14,17] Published studies reporting results of lung resection extended to the left atrium over the last 2 decades include limited number of patients, frequently with tumor invasion confined to the base of the pulmonary veins and heterogeneous data in terms of perioperative mortality ranging from 0% to 20%. Very few experiences of en bloc radical resection have been reported also for anterior mediastinal tumors invading the aorta or the heart.[18-20]

At present, according to current clinical practice guidelines,[21,22] patients with biopsy-proven T4-N0 NSCLC should be considered surgical candidates if a radical resection is potentially achievable. However, when considering tumors with deep and extended infiltration of the aorta or the heart, the possibility to achieve a complete resection of the disease is principally related to the technical expertise of the center in cardiovascular reconstructive procedures and may require CS in most cases.

When the tumor invades the aorta, technical options to reconstruct this vascular structure depend on the depth, the extension, and the site (AA or descending aorta) of the neoplastic infiltration. In case of tumor invading the descending aorta, the placement of endografts (commonly employed for aneurysm treatment) has been successfully used to allow a safe resection of the infiltrated vascular wall without need for crossclamping and CS because of full protection guaranteed by the endoluminal stent across the infiltrated area.[15] Furthermore, it helps reduce intraoperative bleeding due to the exclusion of adjacent intercostal arteries. After the first description of this off-label use of aortic endografts,[15,23] we have confirmed the safety and efficacy of this technique in a series of 8 patients so far (7 with lung and 1 with mediastinal tumor). Placement of endovascular prosthesis is generally preferred within 7 to 10 days of the planned resection based on histologic evidence reported in experimental studies, which show inflammatory reaction of the aortic wall causing progressive graft embedment with consequent increase of technical difficulty when performing vascular wall resection after longer time.[24] One-stage graft insertion soon before resection is discouraged by some authors due to possible complications related to stenting procedure (paraplegia, endoleaks), but in other investigators' opinion, it can offer some advantages, since it allows avoiding additional anesthesia and potential useless procedure if actual invasion of the aortic wall is not confirmed at thoracic surgical exploration.[15] The maximal possible extent of the aortic wall resection with this technique has still not completely defined. In our series, we have proven the safety of aortic wall resection up to about one half of the vessel circumference. The use of endografts with long margins of uninvolved aorta has ensured safety in cases of partial-thickness vascular wall resection with no patch reconstruction avoiding endoleaks and aneurysm formation.[15,17] However, for more extended aortic infiltration and full-thickness resection, we prefer to perform a vascular reconstruction using a synthetic patch (usually Dacron) or a vascularized omental flap applied over the defect. The latter option is preferred, especially if a concurrent bronchial stump reinforcement is required due to previous induction therapy. Reconstruction of the aortic wall confers increased protection and stability to the resected area, preventing the occurrence of aortic narrowing or proximal dilatation as reported by other authors.[24] This endograft procedure for radical resection of lung cancer

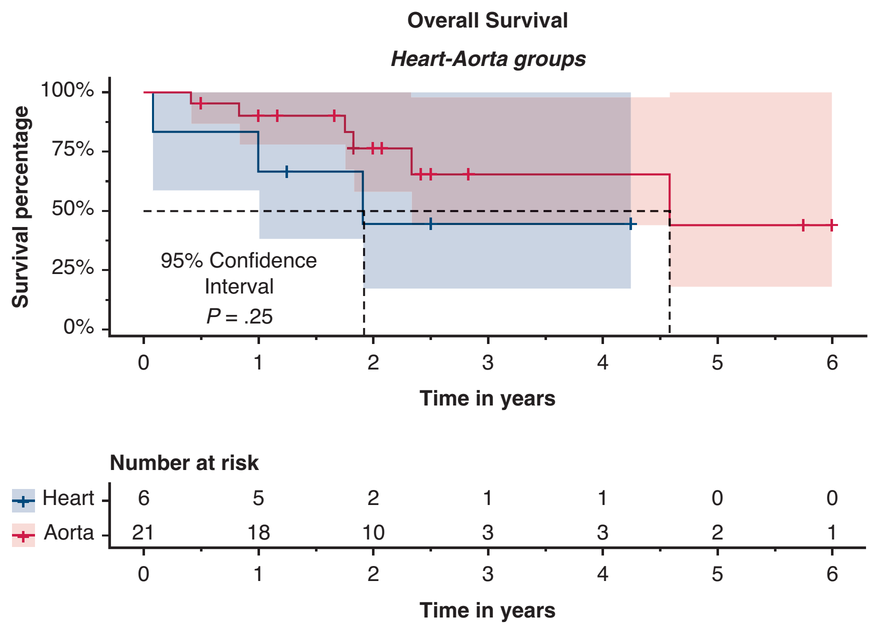

FIGURE 5. Survival curve (Kaplan–Meier) of patients undergoing resection of tumor invading the heart (*blue*) or the aorta (*red*).

invading the descending aorta has been performed with limited major complication rates, no perioperative mortality, and no local recurrence in our and other selected centers' experience.[15,17,23] Conversely, in the case of tumor invading the AA and the supra-aortic trunks, the cross-clamping technique still remains the option of choice.[25] This can be performed with or without CS. The present experience proves that vascular resection and reconstruction can be performed safely with both options either with prosthetic patch, conduit technique, or with tangential suture repair.

Concerning interventions for tumors invading the heart, only limited experiences of small partial cardiac chamber resection, generally on the left atrium, without prosthetic reconstruction have been reported in the English literature so far. There are only few published studies including series ranging between 12 and 46 patients, most of which with fewer than 25 patients. A recent systematic review and meta-analysis[26] has analyzed all the published studies in this setting (18) up to 2021, collecting a total of 483 patients worldwide. Reported operative mortality ranged between 0% and 20%, and complication rates ranged from 7.1%

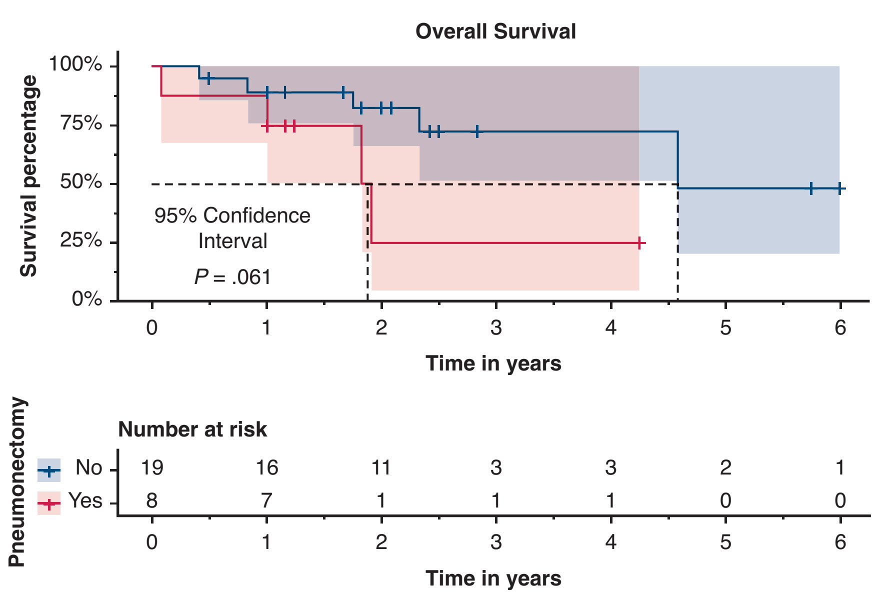

FIGURE 6. Survival curves (Kaplan–Meier) of patients undergoing pneumonectomy (*red*) versus other resections (*blue*).

to 52.6%. Pneumonectomy was performed in the vast majority of patients (84%), neoadjuvant treatment (chemotherapy or chemoradiotherapy) was administered in 36% of cases, and adjuvant therapy was administered in 56%. CPB was used only in 1.2% of patients. Estimated pooled 5-year OS rate was 19.9%. Estimated 3-year OS was 23.1%. Median OS ranged from 10 months[10] to 29 months.[9] Unanimously, good survival rate can be achieved in very well-selected patients (according to general status), with N0-1 disease if a complete resection is achieved.

Differently, patients with lung cancer showing more extended infiltration of the cardiac chambers that cannot be completely resected with limited atrial wall resection and direct suture have been considered unresectable so far. Our here-reported experience including 6 patients with NSCLC undergoing resection of a wide portion of the atrium or the ventricle, 4 of whom requiring prosthetic reconstruction under CPB, proves that even this condition should not be considered an absolute contraindication for radical surgery and that patch repair of large portions of the cardiac chambers can be performed safely under CPB without early oncologic recurrence.

There is a controversial approach in the literature concerning the use of CPB for oncologic interventions. No increase of distant metastases and tumor recurrence has been reported in a systematic review by Muralidaran and colleagues.[27] Conversely, Tsukioka and colleagues[6] have reported early relapse resulting in death in both patients receiving atrial resection under CPB in their experience. These authors hypothesize that increased intraoperative tumor cell dissemination promoted by the extracorporeal circulation could have been responsible for the early relapse, as previously advocated by other authors.[28] However, both the aforementioned patients in the latter study presented with pathologic N1-N2 disease, representing a factor of increased tumor recurrence risk itself. In our series, none of patients who underwent cardiac reconstruction under CPB showed locoregional recurrence or distant metastasis within 6 months of the operation, and 2 of the 3 patients who did not experience perioperative fatal complications are still alive, with no evidence of disease at 15 and 30 months, respectively. This evidence does not confirm the hypothesis of increased rate of early recurrence for tumors resected under CPB.

The role of neoadjuvant therapy on long-term prognosis, which has been well defined in other categories of locally advanced NSCLC (ie, N2 disease), is still object of debate for T4-NSCLC and in particular for patients showing infiltration of the heart and the aorta. Looking at literature data,[26] only 36% of patients undergoing atrial resection received induction therapy, and although some authors have observed better survival in this group of patients,[5] clear evidence of prognostic benefit has still not been proven. In the present series, induction therapy was administered in approximately one half of patients with NSCLC without showing a significant improvement of long-term survival. Several reports in the literature have advocated a potential detrimental effect of induction treatment from a technical point of view affecting the perioperative risk of morbidity, especially if a reconstructive procedure is required. The present authors have confirmed even in the series here reported the safety of extended resections and reconstructive procedures after neoadjuvant therapy, as already reported in previous studies.[29]

The main limitation of the present study is represented by the small statistical sample, which is justified by the rarity of the complex interventions included and by the restrictive indications for resection in patients with such oncologic status. Strengths are related to the homogeneity concerning indications for surgery, intraoperative technical management, and perioperative management of a single-center experience. In conclusion, the present experience proves that cardiac and aortic resection and reconstruction for full-thickness infiltration by lung cancer can be performed safely with or without CPB and may allow long-term survival for adequately selected patients.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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