



# Pulmonary artery resections for lung cancer – when and how?

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**Abstract:** Resection and reconstruction of the pulmonary artery (PA), whether associated or not to a sleeve resection of the bronchus, allows complete resection of centrally located lung cancer, thus avoiding pneumonectomy. Despite initial concern related to technical difficulties, perioperative management and long term survival, recent studies showed continuous enhancement of the surgical technique and reconstruction materials, reduction of the complication rate and improvement in the survival. This allowed this procedure to gain widespread acceptance in the treatment of lung cancer.

**Keywords:** Pulmonary artery reconstruction; lung cancer; sleeve resection

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## Introduction

Centrally-located lung cancer often requires a multidisciplinary approach with either induction or adjuvant therapy. Historically pneumonectomy was the surgical procedure routinely performed for these tumors. However, over the last three decades a large number of studies demonstrated an improved outcome with parenchymal sparing procedures when compared to pneumonectomy, with lower postoperative morbidity and mortality, guaranteeing complete resection (1,2).

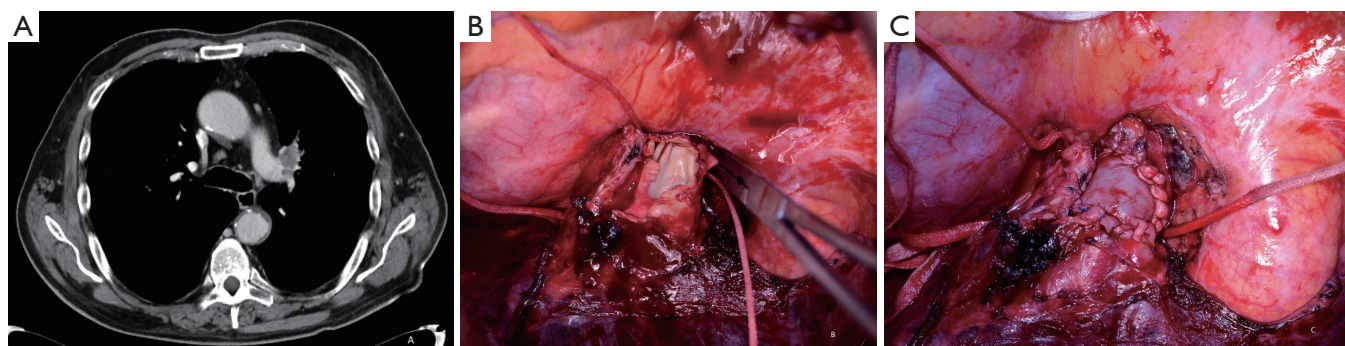
Resection and reconstruction of the pulmonary artery (PA) may be considered one of the most challenging and beneficial procedures in thoracic surgery. In addition to lobectomy, whether associated or not to a sleeve resection of the bronchus, this procedure allows centrally located lung cancer complete resection, thus avoiding pneumonectomy (3).

Moreover, pneumonectomy is often associated to a serious postoperative impairment of cardiac (4) and

lung function (5), and quality of life (6). For this reason, pneumonectomy is considered a disease itself, particularly when performed on the right side and after induction chemotherapy (7). Nowadays pneumonectomy is recommended only to achieve full oncological radicality when this cannot be obtained through parenchymal sparing procedures. Therefore, PA reconstruction should be carried out not only in case of cardiorespiratory impairment, but it should be always preferred when the procedure is technically feasible.

When performing a PA resection and reconstruction, patients need a preoperative clinical and radiological work-up not different from the other standard lung resection. This will vary according to the stage of disease, the patient's performance status and each single center policy. At our center preoperative workup usually includes total body contrast computed tomography (CT) scan, pulmonary functions tests, cardiac evaluation, blood gas analysis and routine blood tests.

The primary indication for PA resection is infiltration



**Figure 1** Pulmonary artery resection and reconstruction. (A) CT scan imagine. The illustration shows infiltration of origin of lobar branches of left upper lobe by metastatic hilar lymph nodes. (B,C) The patient required upper lobectomy and pulmonary artery reconstruction by an autologous pericardial patch.



**Figure 2** CT scan imagines of infiltration of pulmonary artery.

of the origin of the lobar branches by primary lung cancer or by metastatic hilar lymph nodes (N1) (*Figure 1A,B,C*) with extracapsular extension or, after induction therapy, a desmoplastic reaction, scar tissue or fibrosis that linger on the site of the previous tumor infiltration. Thus, it could range from a partial infiltration of the vessel to a more extensive and even circumferential invasion that may require different resection and reconstruction techniques. PA reconstruction is more frequent on the left side, in association with upper lobectomy (70% of the cases) and with a right upper lobectomy (20%). Only in a 10% of the patients the procedure is performed on the main PA or in association with inferior lobectomy on both side (3).

The vessel infiltration can anticipated at preoperative imaging but the true status can be assessed only intraoperatively (*Figure 2*). If only a marginal, limited infiltration of the PA branches' origin is identified, a tangential resection with direct suture is performed. We consider this technique as a variation of standard lobectomy

and it is usually not classified as a reconstructive procedure. When up to 30% to 40% of the circumference of the vessel is involved by the tumor, a patch reconstruction, usually with biological materials, can be performed. In case of a more extended degree of infiltration a circumferential resection is required and the reconstruction can be performed by end to end anastomosis or by the interposition of a prosthetic conduit (biological or synthetic) (8).

### Operative technique

The operative technique includes two steps: the resection of the vessel and then the reconstruction of the PA.

Complete control of the proximal PA and distal PA is mandatory as well as both pulmonary veins (PVs) and the bronchus. The exposure of the PA can be more easily performed if the superior PV is completely dissected and retracted, but the transection of the vessel should be postponed until the feasibility of the procedure is

established. Before clamping the main PA low dose intravenous heparin is administered.

Over time we progressively modified the intra-operative management: we now tend to clamp the PA distally to the neoplastic infiltration, if possible. The intravenous dose of heparin is reduced to about 25 units/kg (1,500–2,000 units). The latter change contributes to prevent intra- and postoperative oozing, particularly from mediastinal lymphadenectomy, without any additional thrombosis events. At the end of the vascular reconstruction heparin is not reversed with protamine.

The proximal control of the main PA can be obtained both intra- or extrapericardially on a case by case basis particularly, on the left side the main PA is often involved close to its origin thus requiring an intrapericardial approach. In case of invasion of the interlobar artery only, it is possible to prepare it without opening the pericardium. On the right side usually the main PA is isolated extrapericardially, by retracting medially the superior vena cava.

After *en bloc* removal of the resected lobe with the portion of infiltrated PA the reconstruction phase may begin.

### **Patch reconstruction**

When the tumor infiltrated only the lobar aspect of the PA for not more than 30–40% of the circumference, a patch reconstruction is indicated. The defect may be of limited to large dimension on the longitudinal axis of the vessel and its shape is usually stretched in this direction. For that reason, the size and shape of the patch is tailored intraoperatively on the PA defect itself.

Different materials have been proposed for patch reconstruction: synthetic [polytetrafluoroethylene (PTFE) graft] (9), autologous (pericardium and PV) and heterologous (bovine and porcine pericardium).

Autologous pericardium is fresh, unpreserved, available on both sides of the chest and it can be harvested during the surgical procedure; it is generally sufficient to cover even large defects, it is cost-free and perfectly biocompatible. It is usually harvested anteriorly to the phrenic nerve, without any need of reconstruction of the pericardial defect (10).

In order to facilitate the patch's manipulation and suturing, intraoperative fixation by a glutaraldehyde-buffered solution is advisable (11). The fresh pericardium is fixed in diluted glutaraldehyde for few minutes, washed with saline and then adequately trimmed to the appropriate size; the patch's epicardial surface stays inside the lumen of the vessel. This technique contributes to minimize the tendency

of the harvested pericardium to curl and retract. The patch becomes more stiff, with a lower tendency to recoil during suturing and a lower risk of bleeding.

Although our choice remains the use of autologous pericardium, other biological options have been reported as venous patches: superficial femoral vein (12), azygos vein, saphenous vein, and, recently, the superior PV patches and bovine and porcine pericardium patches (13). Among these options, the azygos vein can be found only on the right side, while the saphenous vein and the superficial femoral vein need another surgical procedure to be harvested, both providing a little amount of tissue for the reconstruction. These procedures are also time consuming and may be traumatic for the patients. The superior PV can provide enough material for the reconstruction (14–16), but it is usually obtained, due to anatomical reasons, only when it is associated with left upper lobectomy; it is more difficult on right side. During the preparation for upper lobectomy, in case the extra-parenchymal portion of the PV is not infiltrated by and sufficiently far from the tumor, the vessel can be prepared from the atrial confluence intrapericardially to its extrapericardial portion, up to proximal branches. The superior PV is then closed proximally, at the atrial confluence, by a TA stapler and is ligated distally at the extralobar origin of the branches; a 1.5 to 2.5 cm long conduit is obtained. After obtaining frozen sections of the specimen PV margins, the conduit can be trimmed to obtain a suitable PA patch oriented with the endovascular layer looking inside the artery (13).

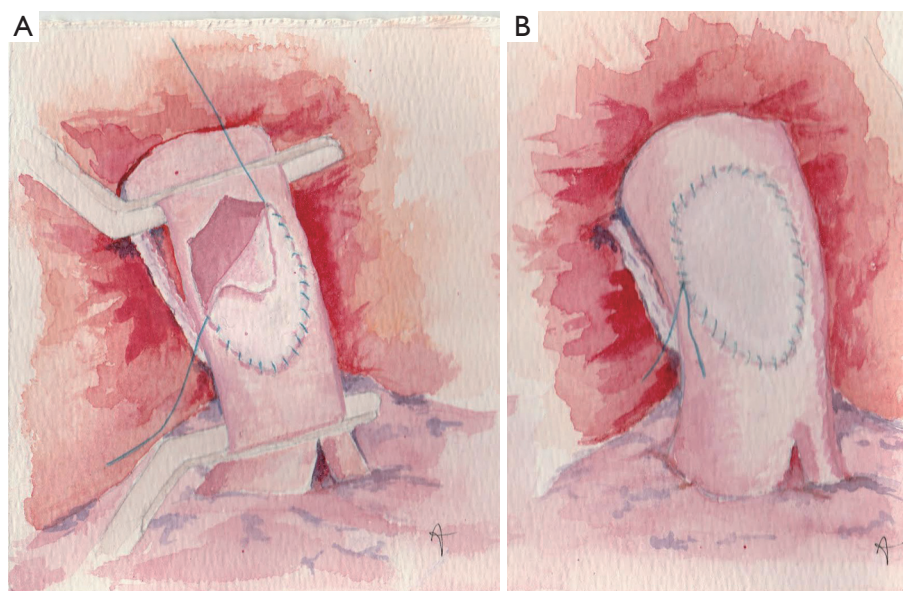
The bovine pericardium has been used as a valid alternative to autologous pericardium over the years. It reduces the harvesting and trimming time allowing more regular margins, but it also shows very little elasticity; however the edges are stiffer and easy to suture. The porcine pericardium shows similar properties, but it is thinner and more flexible.

Whatever patch we choose, two stay sutures are usually placed at the opposite sites of the patch. Then, while the assistant stretches and holds the patch in place, a 5–0 monofilament non-absorbable suture is used to anastomose it (*Figure 3A,B*). The inferior stay suture is removed when the suture line reaches it.

The patency of the vessel is assessed after expansion of the residual lobe, to prevent kinking due to elevation of the parenchyma (3).

If a bronchial sleeve resection is required, the patch reconstruction is usually performed before the bronchial anastomosis to reduce the arterial clamping time.





**Figure 3** Drawing of pulmonary artery patch reconstruction. (A) While the assistant stretches and holds the patch in place a non-absorbable running suture is completed; (B) once the suture is completed the blood flow can be restored.

#### *End-to-end anastomosis*

When more than one-half of the PA circumference is involved by the tumor, a circumferential resection is required with end-to-end anastomosis of the stumps. In this case, it is better to complete the bronchial anastomosis first, as the bronchial axis is shortened so that the two vascular stumps can be approximated with less tension and the surgeon can minimize manipulation. Usually, two key factors help to solve the size discrepancy of the two sides of the anastomosis: the elasticity of the PA and careful stitches placement. Nevertheless, it is important to obtain regular margins when transecting the PA on both sides to facilitate the caliber correction and to avoid stenosis. Another trick to reduce tension on the anastomosis after completion of the bronchial reconstruction is to elevate the lower lobe with a sponge while suturing the PA. The anastomosis is completed with a running 5-0 or 6-0 monofilament non-absorbable suture (*Figure 4A,B*). At the end of the anastomosis, the removal of the proximal clamp usually relieves the residual tension (17).

#### *Prosthetic conduit reconstruction*

Despite all the expedients mentioned before, if the distance between the PA stumps is judged excessive interposition of a prosthetic conduit is mandatory. This is an infrequent

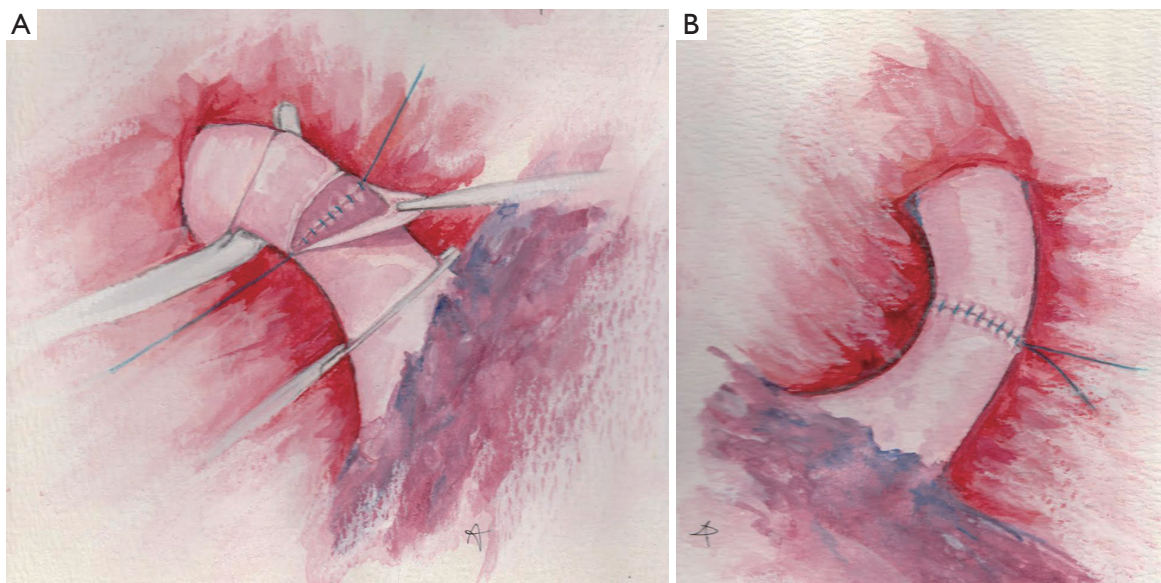
condition usually occurring on the left side, when a left upper lobe tumor extensively infiltrates the PA without the involvement of the corresponding lobar bronchus, thus not requiring a bronchial sleeve resection.

Over the years, different techniques and materials have been employed for this procedure. Although the use of PTFE has been reported with good results (18,19) as well as other synthetic materials, it might increase the risk of thrombosis, especially for a low-pressure vessel, and it may require long-term anticoagulation.

In the literature numerous biological materials have been proposed for PA conduit replacement: the autologous pericardium, the bovine pericardium (20,21) and, more recently, the cryopreserved allograft (PA or aorta) (22), the porcine pericardium (13) and the superior PV (14-16).

The pericardial conduit can be easily prepared by harvesting a relatively large pericardial patch that is trimmed in a rectangular shape and wrapped around a chest tube drainage with the epicardial surface inside; the longitudinal suture is completed with a running 6/0 monofilament non-absorbable material, creating an approximately 1.5–2 cm long conduit (20).

Berthet reported the use of cryopreserved allografts harvested from multi-organ donors, implanting both PA and thoracic aorta. The ABO blood group and human leucocyte antigen group biocompatibility were not required. The



**Figure 4** Drawing of pulmonary artery end-to-end anastomosis. (A) While completing the non-absorbable running suture; (B) after removal of vascular clamps.



**Figure 5** Drawing of pulmonary artery prosthetic conduit replacement. After completion of conduit replacement the blood flow can be restored.

appropriate graft is selected on the basis of morphologic preoperative CT scan data (22).

Among the biological materials, the porcine pericardium has recently been used by our group. The conduit can be intraoperatively trimmed and wrapped on a chest tube or a syringe of the correct size (23) (Figure 5).

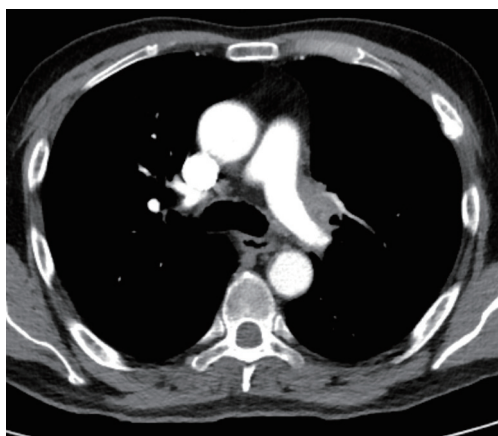
D'Andrilli proposed that an effective autologous conduit can be obtained with the superior PV (15,16). When the extra-lobar PV branches are free from tumor, the vessel can be used as a valid alternative for PA reconstruction. The similarity of the two vessels' wall confers the perfect thickness to the conduit, thus allowing an easy anastomosis. The PV conduit harvesting procedure has been previously described.

The appropriate length of the conduit should be tailored on the resected arterial segment. Usually, a 1.5- to 2.5-cm long conduit is sufficient enough to fill the gap between the vascular stumps.

The proximal anastomosis is initially completed with a running 5/0 monofilament non-absorbable suture and after a check of the conduit length, the distal one is completed with the same technique. Two points are crucial in completing the vascular replacement: the need to avoid an excessive conduit length that could lead to kinking of the vessel and the necessity to avoid any tension at the level of the anastomosis. The latter point can be achieved with the section of the inferior pulmonary ligament and, on the right side, by the opening of the pericardium around the inferior PV.

#### ***Reconstruction of the main PA***

The involvement of the main PA is a rare condition caused by a proximal invasion of left hilar tumors (Figure 6). It usually required pneumonectomy. Median sternotomy is



**Figure 6** Main pulmonary artery infiltration. When the vessel infiltration is confirmed intraoperatively a left pneumonectomy with patch reconstruction is indicated.

performed and the pericardium is opened. The main PA as well as the right and left PA branches are dissected free from the surrounding structures. Cardiopulmonary bypass is instituted. The right PA is clamped and the involved vessel is removed *en bloc* with the left lung. The defect is repaired with a patch (3).

### **Perioperative management**

When a sleeve lobectomy is associated with a PA reconstruction, it is recommended to perform the positioning of soft tissue between the bronchial and the vascular anastomosis. The interposition of a pedicled intercostal flap has been used by our group with excellent results; the intercostal artery supplies an ideal easily revascularization (24,25). The muscle flap is wrapped around the bronchial anastomosis to protect and revascularize the suture line and to prevent direct contact between the two structures; it is secured to the bronchus by interrupted absorbable 4-0 sutures. Other means of protection such as the pericardial flap, the pleural flap, or the mediastinal fat pad have also been proposed (2,26,27). In addition, in case of double sleeve lobectomy the use of low dose steroids during the early postoperative course has been suggested to reduced edema and improve healing (28).

When a biological patch or conduit is employed no long-term anticoagulation is recommend if no other disorders coexist; subcutaneous low-molecular weight heparin is administrated according to standard protocols of prevention of pulmonary embolism (21).

### **Outcome**

Outcome usually depends on the choice of the most appropriate reconstruction procedure on a case by case basis. Patency, cardiac and pulmonary function, and completeness of resection are the keys for long-term survival.

When the procedure is correctly performed, complications could be anticipated in less than 5% of the patients; moderate leakage from the suture line, kinking or vessel thrombosis are the most frequent (3). Technical improvements and the widespread use of biological materials have significantly reduced thrombosis. Recently a rate of 0 to 2% of thrombosis requiring completion pneumonectomy has been reported (10,21,29). Contrast CT scan and three dimension (3D) volume rendering or an Angio-magnetic resonance are useful noninvasive tools to detect patency defect, both early and late in the postoperative course (30).

When PA reconstruction is associated to a bronchial sleeve lobectomy, bronchopleural or bronchovascular fistulas rarely occur. Intraoperative protection of the anastomosis (31) and prompt conservative treatment of the fistula reduces the risks of empyema and mortality (32,33).

It has been shown that, after PA reconstruction, the functional parameters are comparable with those reported for standard lobectomy (34-36). Our group previously showed that right heart morphology and function are also comparable with standard lobectomy (10).

These reconstruction lung sparing procedures can be performed also after induction chemotherapy (37,38). The procedure gained a widespread consensus for the treatment of centrally located lung cancer and a number of studies supported both functional and survival advantages when compared to pneumonectomy (1,2,39,40). Initial concerns on the PA reconstruction were raised due to its long-term patency and effects on cardiopulmonary function, and, later, on its oncological accuracy and survival. Nevertheless, over the past thirty years a number of studies reported continuous enhancements of surgical technique, reduction in complication rate and improvements in the survival rate (10,18,34,41). *Table 1* reports several studies over last decade and it includes series with more than 20 patients receiving PA resection and reconstruction.

The role of reconstructive parenchymal sparing procedures, albeit proved to be advantageous for survival of stage I and II patients, still produce uncertain effects in case of stage III lung cancer, particularly N2 disease. When



**Table 1** Results of main series of PA reconstruction comparing morbidity, mortality and long-term survival

References	Patients (concomitant bronchial sleeve)	Type of PA reconstruction	Complications (%)	Technical complications (n)	Mortality (%)	5-year overall survival	Disease free survival (%)
Cerfolio <i>et al.</i> 2007 (25)	42 [6]	TR [31]	26	0	2.3	60	NR
		Patch [7]					
		EE [4]					
		Conduit (-)					
Alifano <i>et al.</i> 2009 (26)	93 [23]	TR [88]	29	NR	5.4	39.4	NR
		Patch [3]					
		EE [2]					
		Conduit (-)					
Venuta <i>et al.</i> 2009 (21) <sup>‡</sup>	105 [65]	Patch [55]	28.5	1	0.95	44	43.1
		EE [47]					
		Conduit [3]					
Berthet <i>et al.</i> 2013 (22)*	32 [3]	Patch [2]	50	1	0	66.7	NR <sup>§</sup>
		EE [20]					
		Conduit [10]					
Ma <i>et al.</i> 2013 (29)	118 [41]	TR [26]	52.2	1	0	50.2	NR
		Patch [51]					
		EE [41]					
		Conduit (-)					
Galetta <i>et al.</i> 2015 (19)	150 [56]	TR [80]	30.7	0	3.3	50.4	49.1
		Patch [66]					
		EE (-)					
		Conduit [4]					
D'Andrilli <i>et al.</i> 2017 (16)	24 [1]	Patch [4]	29.1	0	0	69.9	52.7
		EE (-)					
		Conduit [20]					

Figures calculated from data reported in article. NR, not reported. \*, data collected only on patient underwent pulmonary artery replacement; <sup>‡</sup>, survival analysis calculated excluding 3 patients underwent pneumonectomy and patch reconstruction under CPB; <sup>§</sup>, reported estimated median disease free survival =42 months. TR, tangential resection; EE, end-to-end anastomosis.

an analysis of the survival rate is performed for the PA reconstruction, both stage by stage and on the impact of the nodal status on survival, its oncologic reliability is found to be comparable to that of a large series of bronchial sleeve resection studies as well as to those found within the lung cancer literature (10,21,41).

In conclusion PA reconstruction, when correctly performed is a safe, feasible and oncologically effective procedure.

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