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How I do it: Bronchial Sleeve Resection and Pulmonary Angioplasty Techniques after Induction Chemo-Immunotherapy

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Informed consent statement: All patients were informed about the study and signed the informed consent.
Central message: Use of induction chemo-immunotherapy for locally advanced lung cancer is expected to increase surgical complexity. Bronchial sleeve and pulmonary artery patch plasty techniques are discussed.

Central Picture Legend
Technique to be performed on the PA could be decided after division of bronchus

Background
The incorporation of immunotherapy in neoadjuvant treatment of lung cancer has raised concerns about technical feasibility and safety of surgery, especially in complex cases involving pulmonary artery reconstructions and bronchial sleeve resections. The inflammatory response secondary to immunotherapy often lead to hilar fibrosis, making surgical dissection around the pulmonary artery more challenging, particularly in patients who have undergone neoadjuvant chemo-immunotherapy for locally advanced disease. While certain parameters like operative time and blood loss may not differ significantly from patients without neoadjuvant therapy, reported rates of conversion to open surgery can be as high as 54%, emphasizing the need for careful patient selection (1). Though some studies report much lower conversion rates of 3.2%, only a small proportion of patients within the series underwent a minimally invasive approach, further highlighting the importance of patient selection (2).
Adding to the complexity of surgery performed after neoadjuvant chemo-immunotherapy, is the sparsity of guidelines for the assessment of response or progression, following therapy. Also, the issue of pseudoprogression demonstrated by several authors, has not been studied in detail (1,3).

The rationale for use of chemo-immuno treatment in the neoadjuvant setting, lies in fostering diverse T-cell production, particularly if the tumor is not surgically removed before immunotherapy (4). Adjuvant immunotherapy post-tumor removal might be less effective due to reduced diversity in T-cell production (4). Hence, the use of immunotherapy in the neoadjuvant setting is expected to become more prevalent in earlier stages of lung cancer. Translating this to a surgical perspective, resection performed for locally advanced disease in a virgin mediastinum and hilum will decrease, whereas surgeries following neoadjuvant chemo-immunotherapy with a potential for pulmonary and hilar fibrosis, are expected to increase in patients.

In our current clinical practice and experience, we have noted that patients undergoing neoadjuvant chemo - immunotherapy may face different surgical challenges, classified into three groups:

I. Early-stage disease, lower lobes: Generally, there is minimal inflammation around the main pulmonary artery (PA), making lobectomy or segmentectomy feasible with minimally invasive techniques.

II. Locally advanced stage 3 patients, upper lobe disease: These cases may require more complex resections, potentially involving bronchial sleeve lobectomy and pulmonary artery angioplasty. Surgical techniques may vary based on the extent of the resection and degree of fibrosis. Minimally invasive surgery may be considered in experienced centers if only bronchial sleeve resection is needed.

III. Immunotherapy as part of definitive chemoradiation, with salvage surgery: These cases demand open surgery, proximal and distal control of the pulmonary artery, and may require intrapericardial access, necessitating expertise in salvage surgeries.
In the realm of pulmonary artery reconstructions, various techniques exist, each with distinct characteristics. In order of decreasing complexity, these include sleeve resection of the pulmonary artery with reconstruction, patch plasty of the pulmonary artery, tangential arterioplasty, and simple stapling of the pulmonary artery. The choice among these methods introduces not only technical challenges but also variations in outcomes and complications. Frequently, there is a concomitant need for bronchial reconstruction, which might involve sleeve bronchial resection and reconstruction, primary closure, or stapling of the bronchus. The primary focus of this manuscript is two-fold. Firstly, to emphasis the evaluation of pulmonary artery invasion by tumors and the subsequent decision-making process for selecting the appropriate surgical technique for the pulmonary artery. Secondly, to describe pulmonary artery reconstruction techniques, particularly patch plasty with bronchial sleeve surgery. The patients who had intraoperative videos included in this manuscript provided informed consent for recording and documenting the intraoperative findings; IRB approval was not required.

**Presurgical evaluation**

**Restaging**

The predominant focus has been on the necessity for invasive restaging procedures, driven by the fact that a majority of studies have chosen Major Pathologic Response (MPR) as a surrogate endpoint for evaluating clinical efficacy. Despite the acknowledged validity of MPR as a surrogate endpoint, there remains uncertainty regarding its association with Disease-Free Survival (DFS) or Overall Survival (OS). This ambiguity underscores the need for additional research to delve into the relationship between MPR and these critical clinical outcomes (5,6). Further exploration and investigation are essential to clarify the utility and predictive value of MPR in the context of patient survival and disease progression.

**Assessment of PA invasion:**

After neoadjuvant chemo-immunotherapy, radiologic and pathologic responses may differ, emphasizing the importance of assessing CT imaging for arterial invasion. All patients should undergo a CT chest with IV contrast after induction therapy, to assess primary tumor response, degree of pulmonary artery involvement, and feasibility of surgery. Although we do not routinely
obtain a PET-CT for restaging, progression of the primary tumor after induction therapy, prompts a thorough evaluation for distant metastases, and a PET-CT may be useful in this circumstance. To augment the precision of the assessment, fiber optic bronchoscopy becomes an indispensable adjunct. This procedure allows for a detailed examination of the bronchus and the extent of endobronchial tumor infiltration, if present. It also provides additional information that contributes to a more comprehensive understanding of the disease extent. Integrating these imaging modalities and techniques in the pre-operative assessment process ensures a thorough evaluation of both arterial and bronchial involvement, aiding in the formulation of an informed and tailored surgical approach.

**Assessment of cardio pulmonary reserve**

Assessing cardio-pulmonary reserve is crucial, and standard measurements apply, the caveat being cases of complete bronchial or arterial obstruction which could be corrected with the reconstructive surgery. In such circumstances, lower than usual reference levels may be acceptable. With regards to pulmonary function tests, our thresholds for lobectomy are predicted FEV-1 and DLCO values > 40%. However, we do consider certain patients with predicted FEV-1 and DLCO ranging 30-40% if upper lobectomy is planned, and the patients are able to complete a 6-minute walk test or stair climb test without limitation. All patients should undergo a transthoracic echocardiogram to assess cardiac function and pulmonary artery pressures (PAP). Patients with pulmonary hypertension, specifically those with mean PAP > 45 mmHg are deemed high risk for surgical intervention.”

**Selection of the pulmonary artery resection and reconstruction technique**

Various approaches to managing the pulmonary artery range from simply stapling the pulmonary artery to sleeve resection with end-to-end anastomosis. In between these two ends of the spectrum, are pulmonary artery tangential angioplasty and pulmonary artery patch plasty. Although it is preferable to know which approach will be required beforehand, the degree of pulmonary artery involvement may not be apparent until the time of surgery, after division of the bronchus, either standard division or by a sleeve resection (Figure 1) (Video 1 – Video 2).
Surgical technique

The basics of our surgical plan involve the following. The surgical technique prioritizes radical lymph node dissection in the mediastinum and hilum and staging with frozen sections before proceeding with lobectomy, with a preference for keeping pulmonary artery resection as the final hilar structure to be divided. Pulmonary artery sleeve resection is reserved for more extensive involvement, with a preference for patch plasty.

In detail, we prefer the division of the main hilar structures from the easiest to the most difficult one. Whenever there is hilar involvement by a tumor or extensive fibrosis, opening the pericardium and dividing the vein intrapericardially, or performing a sleeve resection to the bronchus may be required before exploring the most involved structure which is the PA (Video 1). After division of the vein and/or bronchus, (we call this point “burning the bridges”), there can be no bail out from surgery. At this stage, the type of pulmonary artery resection and reconstruction is decided. We believe any circumstance that a surgeon can place vascular clamps proximally and distally on the pulmonary artery, could be managed with pulmonary artery tangential angioplasty or with a patch plasty. In the situations of vascular sleeve and in some of the patch plasty techniques, we prefer to place one of the vascular clamps to the inferior pulmonary vein to prevent back bleeding. Videos 1 and 2 demonstrate intra-operative assessment of pulmonary artery involvement during both right and left upper lobectomies, in patients who received neoadjuvant chemo-immunotherapy. In the left side, the PA was amenable to stapling, whereas in the right side, the PA required a sleeve resection due to margin positivity after an arterial patch plasty. (Video 1 and Video 2).

Surgical technique: Right upper lobe bronchial sleeve resection and pulmonary arterial patch plasty after neoadjuvant chemo immunotherapy.

Prior to surgery, pulmonary function tests and echocardiography are conducted to assess the patient's physiological suitability for the procedure. Pre-treatment and post-treatment contrast-enhanced CT scans are also compared to determine the necessity for reconstructive pulmonary artery surgery. The patient is intubated with a left-sided double-lumen tube, regardless of the surgical side preference. An anterior thoracotomy is the preferred approach, initiated from the 4th intercostal space and extending to the mid-half of the scapula posteriorly, along the lateral side of the pectoralis major, by dividing the serratus anterior muscle and preserving the latissimus dorsi muscle. We begin with a meticulous lymph node dissection, performed in the mediastinum.
including stations 2R, 4R, 10R, 7, and 11R. The hilar structures are then divided in the following order: azygos vein, if required, (which was infiltrated with the tumor in the case of our video) and superior pulmonary vein, with use of a vascular staple load. The bronchus is then divided with a scalpel behind the interlobar pulmonary artery, specifically at the level of the origin of the intermediate bronchus. Attention must be paid to identify the orifices of the middle lobe bronchus and the superior segmental bronchus of the lower lobe (Video 3).

Proximal division of the right main bronchus is then performed at a level, generally leaving 2-3 cartilages towards the carina. The pulmonary artery is then clamped proximally under the superior vena cava (SVC), and the inferior pulmonary vein is clamped either extra- or intrapericardially, three minutes after administration of heparin (2500-5000 IU). The pulmonary artery is then resected with scissors, maintaining at least 2-3 mm margins from the area of tumor infiltration. The specimen is sent for frozen section analysis for arterial and bronchial margins. It is important to assess the arterial vascular margins prior to placing the specimen in formalin, due to potential shrinkage of the PA, once fixed (Video 3).

The patch size is then tailored to the resected pulmonary arterial dimensions rather than the defect itself. Various patches, including bovine pericardium, autologous pericardium (treated with glutaraldehyde for 5 minutes), PTFE graft, superior pulmonary vein or saphenous vein grafts, may be used. In this patient, we used 1 mm PTFE graft. The tailored patch is sutured proximally and distally with 5/0 prolene sutures onto the defect. By placing continuous sutures on both sides of the patch, the patch is circumferentially sutured over the pulmonary artery. Unlike previous recommendations, we opt to perform pulmonary artery reconstruction before bronchial reconstruction, considering it a more time-efficient approach to decrease the duration of PA clamping (Video 4).

After completing the arterial patch plasty, the inferior pulmonary vein is mobilized to decrease the tension on the bronchial anastomoses. The thymus is mobilized to cover the patch entirely over the main pulmonary artery to decrease the potential risk of bronchovascular fistula development in the future. Subsequently, the bronchial anastomosis is performed with 4-0 PDS sutures. An air leak test of the bronchial anastomosis is then performed by inflating the lobe, without additional support around the bronchial suture line (Video 5).

In cases with more extensive involvement of the main pulmonary artery, we prefer intrapericardial control of the proximal pulmonary artery, between the SVC and the aorta (Video
Conclusions

With more frequent use of induction chemo-immunotherapy for locally advanced lung cancer, surgical complexity is expected to increase. Pre-operative and intra-operative assessment of the extent of pulmonary artery involvement is crucial for surgical planning. Various bronchial sleeve and pulmonary artery patch plasty techniques may be required during lobectomy, and should be part of the thoracic surgeon’s armamentarium when facing cases after chemo-immunotherapy.

References


**Figures:**

Figure 1: In the left Picture, assessment of PA after division of bronchus, In the right Picture sleeve resection was performed to assess the right main PA. Both patients after neoadjuvant chemo immunotherapy.

**Videos:**
Video 1: Robotic surgery and stapling of artery after left upper lobe bronchus division.

Video 2: Robotic right upper lobe sleeve resection was performed in order to adequately assess the degree of pulmonary artery involvement. Once the bronchus was divided, the right upper lobe arterial branches were safely encircled and stapled. Bronchial anastomosis was then completed.

Video 3: Division of all hilar structures after mediastinal lymph node dissection.

Video 4: Reconstruction of PA with patch plasty.

Video 5: Pericardial release and separation of the arterial patch plasty with mediastinal fatty tissue and bronchial anastomosis.

Video 6: Performance of bronchial sleeve and pulmonary arterial patch plasty by placing PA clamp between SVC and Aorta.