1. Introduction

I would like to thank you for the honour of electing me as your President. My purpose will be today to share with you some considerations about an operation that has crossed the 20th century by typifying the greatness and servitude of thoracic surgery, while keeping many of its mysteries at the beginning of the 21st, I mean pneumonectomy.

The first pneumonectomy was performed in multiple stages by Macewen in 1895 in a patient with tuberculosis and empyema. Further attempts with one-stage pneumonectomy had not meet with success. In 1910, Kummel realised a pneumonectomy for lung cancer by clamping the pedicle and leaving the clamps in situ; the patient eventually died on the 6th operative day. The first individual hilar ligation was achieved by Hinz in 1922, and that patient succumbed to heart failure on day 3. Churchill in 1930, Archibald in 1931, and Ivanissevich in 1933 also attempted removal of a whole lung with no survivor beyond a few days. The first successful left-sided pneumonectomy as a two-stage procedure has been performed in Europe by Rudolf Nissen in 1930 in Berlin. In 1933, Graham and Singer reported the first successful en bloc left pneumonectomy, for lung cancer, followed by Overholt who reported the first successful en bloc right pneumonectomy in a patient with a carcinoid tumour in 1935 [1].

Since then, much has been written about the technique, risks, and indications of pneumonectomy, along with the development of our speciality. Obviously, thoracic surgery made great strides with endotracheal mechanical ventilation. The possibility of excluding the ventilation of the operated side was offered from 1935 by Magill. Carlens introduced the first double lumen tube for thoracic surgery in 1950. It needed to wait for the 1970s so that a new technological overhang transforms the daily surgical practice with the invention of surgical staplers, developed during the previous decade by soviet researchers. Finally, the advent of video-assisted surgery and the development of minimally invasive approaches end temporarily this chapter of the technological advances.

At the same time, as a better knowledge of cardiac and respiratory physiology was acquired, more and more sophisticated methods of evaluation were developed and provided reasonable guidelines for the relative risk of patient presenting for various sized pulmonary resection and for pneumonectomy. Furthermore, indications for pneumonectomy changed over time. Nowadays, the epidemic development of lung cancer makes the first application of it. Indeed, pneumonectomy for inflammatory lung disease, bronchiectasis, tuberculosis, and other non-malignant conditions is quite uncommon in modern-days medicine. With the advent of lung transplantation, the thoracic surgeon even learnt to replace the removed lung in selected cases. However, despite many efforts, pneumonectomy remains a challenging operation, carrying many complications and anatomic and physiologic changes.

2. Operative mortality

Reported postoperative mortality rates, defined as the fraction of patients dying before discharge or within 30 days after surgery, improved along with time. Twenty years ago, the Lung Cancer Study Group published their detailed analysis on 30-day operative mortality for lung resections in a large population of lung cancer patients in North America, and stated that mortality of pneumonectomy should be less than 8% to comply with modern standards [2]. During the past decade, mortality rates below 5% have been reported [3–5]. Although operative mortality seem to have declined, it is unclear whether pneumonectomy is becoming really
safer over time. Because available information is often limited to educated guesses or optimistic data from case series skewed by selection bias, current risks of pneumonectomy may be considerably higher than those typically reported. Indeed, some academic institutions worldwide still report on mortality rates exceeding 10% [6–9]. This is confirmed by studies using nationwide data such as cancer registries, multicenter or Medicare claims databases, testifying of similar in-hospital mortality, including in very-high-volume hospitals [10–12]. Furthermore, any attempt to assess the present risk of pneumonectomy should integrate the current features the ‘modern’ thoracic surgeon has to deal with:

1. constant ageing of the population;
2. development of multimodality strategies with induction chemo- and/or radiotherapy;
3. strong differences in postoperative outcome according to the side of the procedure, particularly in the context of post-induction surgery;
4. the rarity but the dangers of non-cancer indications for pneumonectomy.

It is however obvious that there is almost one out of ten patients who will die after such an operation, whatever the surgical group, the institution or the country may be. This risk, one of the highest that may be encountered by patients submitted to non-emergent surgery, may be prohibitive when it exceeds the expected benefit in survival, especially in lung cancer patients with advanced tumours.

Underlying lung disease, particularly chronic obstructive pulmonary disease, has been consistently shown to be a very important risk factor. One of the biggest challenges for the thoracic surgeon currently is still trying to predict which patients would survive a pneumonectomy and not become a respiratory cripple. The purpose of all the studies on preoperative assessment reported in the literature was to predict invariably surgical mortality, but not quality of life after pneumonectomy. As thoracic surgeons, we know that all pulmonary function tests should be used as guidelines in decision-making only. Apart from spirometry and blood gases analysis, many sophisticated, and sometimes aggressive, function tests have been used. Preoperative FEV₁ remains probably the main prognosticator. Ventilation and perfusion lung scan allow to calculate a predicted post-operative FEV₁ at best. However, an absolute value of FEV₁, does not take into account the patients age, sex, body weight and co-morbidities. Use of exercise testing and VO₂ max measurement was reported by several studies. But it seems that new solutions for these very old problems do not exist really! A kind of ‘back to the future’ has been illustrated by the recent rediscovery of more simple and older tests such as 6 min walk or stair climbing tests [13]. Moreover, these tests can be easily repeated during the preoperative period to evaluate the improvement of pulmonary function after rehabilitation and physiotherapy.

The type of surgical procedure appears to affect mortality. Patients undergoing pleuropneumonectomy are at increased risk for death. Completion pneumonectomy, as well, is also associated with a higher mortality rate. These statements are widely accepted because are based upon good sense. Conversely, the fact that patients undergoing a right-sided pneumonectomy have a higher mortality than those undergoing a left one has not always received great attention both in the past, and currently. Present day mortality rates for right-sided procedures range from 10 to 12%, while rates for left-sided procedures range from 1 to 3.5% [14]. A recent report from the Memorial Sloan Kettering Cancer Center in New York showed that mortality rate for right pneumonectomy can reach 24% when a preoperative induction therapy has been performed [15]. There are multiple possible reasons for this substantial difference. The first is that patients undergoing right pneumonectomy are more likely to experience bronchopleural fistulas and postpneumonectomy oedema, which in turn can increase mortality.

3. Bronchial fistula

Frequency of broncho pleural fistula after right pneumonectomy ranges from 4 to 8%, whereas it ranges from 1.5 to 3% after left pneumonectomy [14]. This is believed to be due mainly to anatomical characteristics with the right bronchial stump remaining in the pleural space after surgery while the left stump retracts into the mediastinum, potentially protecting it from inflammation and potential breakdown. Other risk factors include preoperative radiation, chemotherapy, residual tumour at the bronchial margin, impaired wound healing in relation with various conditions (steroid, nutritional status, associated diseases …). Technical factors believed to increase the risk include over or under tightening sutures and devascularisation of the bronchial stump from excessive peribronchial and peritracheal dissection on the occasion of mediastinal lymphadenectomy. There is no evidence in the literature that use of stapler to close the bronchial stump decrease the risk of fistula when compared to the hand sewn method. The best method to close the bronchial stump after pneumonectomy is still an unresolved issue. However, since the mortality rate of BPF ranges from 30 to 80%, prevention is of paramount importance. Bronchial reinforcement with autogenous tissue should be considered. Multiple flaps have been described. In my department, we tend to favour pedicled intercostal muscle flaps or the use of mediastinal fat tissues harvested in the thymic area (Figs. 1 and 2). In some circumstances, a pedicled diaphragmatic flap can provide a good procedure to buttress the bronchial stump suture. It appears to be a very suitable flap in case of previous radiotherapy because this muscle is located outside of the field of radiation. Finally, each time possible, mediastinal pleura should be partially or totally closed.
Immediate postpneumonectomy oesophagopleural fistula is an unusual complication, occurring with a frequency of approximately 0.5% and may coexist with bronchopleural fistula [16]. These are believed to be the result of direct trauma to the oesophagus at the time of surgery. Most esophagopleural fistulas occur after right sided pneumonectomies, and in our experience, following extrapleural pneumonectomy for mesothelioma. This is explained easily by the anatomic location of the oesophagus in close connection with the mediastinal pleura. Closure of the fistula can be attempted after adequate treatment of the empyema. Closure of the fistula can be attempted after adequate treatment of the empyema. Its treatment is challenging for the surgeon and the patient, and include direct suture of the oesophagus, buttressing by omentoplasty and large thoracoplasty (Fig. 3). There are also reported cases of successful closure of the fistula with less invasive procedures such as tissue glue application or expandable endoprosthesis, which always failed in our experience. Despite appropriate treatment, mortality rates are far over 50%.

4. Postpneumonectomy oedema

Postpneumonectomy oedema is an uncommon complication (2–5%) but it carries a mortality rate of more than 50%. It occurs mostly during the first 3 days after surgery. Postoperative pulmonary distress is associated with pulmonary oedema on chest X-rays (Fig. 4) while there is no evidence of cardiac dysfunction, pneumonia, sepsis or aspiration [17]. It is more common after right pneumonectomy and this may be due to the greatest lymphatic drainage of the right lung that must be compensated by the left lung. True pathogenesis is unknown but fluid overload is considered to play an important role as well as transfusions, micro aspirations and micro embolisms. In my department, we hypothesised that routine one lung ventilation during surgery using tidal volume of 10 ml/kg (as recommended) may increase the risk. The clinical relevance of experimental ventilator-induced lung injury has recently received a resounding illustration by the Acute Respiratory Distress Syndrome Network trial that showed a 22% reduction of mortality in patients with acute respiratory disease syndrome when lung mechanical stress was lessened by tidal volume reduction during mechanical ventilation [18]. This clinical confirmation of the concept of ventilator-induced lung injury has also undisputedly substantiated the experimental observation that excessive tidal volume and/or end-inspiratory lung volume is the main determinant of ventilator-induced lung injury, including on healthy tissues. More recently, attention has focused on the roles and implication in the pathogenesis of ventilator-induced lung injury of inflammatory cells and mediators that may be activated and released either in the alveolar space or in the systemic circulation because of the rupture of the alveolar-capillary barrier and on the cellular response to mechanical stress [19]. That is why we started a prospective clinical trial using ‘protective’ low Tidal volume of 5–7 ml/kg during one lung ventilation. Prevention is of paramount importance because treatment is mainly supportive. It should include judicious use of IV fluids, diuretics, and adequate oxygenation. A short course of systemic steroids in the absence of clinical evidence of infection at the very early beginning of the process may be useful in some patients. Immediate institution of inhaled nitric oxide (10–20 parts/million) may improve ventilation/perfusion mismatching and should be continued in responder patients, together with postural changes if needed. When treated with invasive endotracheal mechanical ventilation (ETMV), acute respiratory insufficiency after lung resection is fatal in up to 80% of cases. Non-invasive positive-pressure ventilation has been proved to reduce the need for ETV, thereby improving survival on the basis of a clinical randomised study conducted by the Marie Lannelongue group [20].
5. Early mortality

Even high, in-hospital mortality may reflect the risks of the procedure insufficiently, somewhat being the tree disguising the forest. In that way, 90-day mortality was used recently to emphasise on the risks of right pneumonectomy after neoadjuvant therapy for lung cancer [15]. In our experience (unpublished data), the incidence of sudden deaths in otherwise ‘healthy’ discharged patients are not rare within the first 3 months following pneumonectomy. Some of them may be due, in my opinion, to pulmonary embolism, the origin of which should also be searched ‘in situ’. Indeed, patients may develop thrombus in the pulmonary artery stump that may embolise in the remaining lung (Fig. 5). Most of the time, these thrombi develop after right pneumonectomy and may be due to the greater length of the right pulmonary artery stump. Thus any surgical effort should be made to shorten the arterial stump. Ligation of the vessel could be more at risk for thrombus than closure with continuous suture or staplers. In most cases these thrombi are discovered as an incidental finding on follow up CT scan. Routine thrombosis prophylaxis must be administered postoperatively, and perhaps prolonged a while after such surgery.

6. Functional impairment and quality of life

Quality of life after pneumonectomy has not been yet very well taken into account although it is undoubtedly one of the most important endpoint for our patients. Nature of the anatomic changes that occur in the remaining lung appears to depend on the age of the patient at the time of surgery. If true regeneration with growth of normal alveoli

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Fig. 3. (A) Contrast swallow showing an oesophagopleural leak following right extrapleural pneumonectomy for mesothelioma. (B) Same patient treated by direct suture, omentoplasty and 8-rib thoracoplasty.
and respiratory units can occur in young patients, older have simple dilatation and hyperinflation of the remaining lung. Normally, 55% of overall lung function is contributed by the right lung, and 45 by the left. Most studies confirm the presence of reduced lung function after a pneumonectomy, but the functional amputation does not always correlate in proportion. Indeed, the postoperative values depend also largely on the age of the patient at the time of surgery, how much compensatory hyperinflation developed postoperatively, how long after surgery the tests were performed, and which lung was removed.

One should kept in mind that functional impairment is not always due to the sole amputation of parenchyma. Postpneumonectomy syndrome is a rare complication due to severe anatomic changes in the postoperative chest consequently to the hyperinflation of the remaining lung. Mostly occurring after right pneumonectomy, it is associated with a major mediastinal displacement towards the empty pleural space resulting in: (1) the compression of the distal trachea and main bronchus by the block constituted by the great vessels and the vertebral bodies like the wire of a stringed instrument on its bridge; and (2) a marked reduction of the venous blood flow to the heart due to the dynamic skewing of the caval systems on the occasion of polypnea. Symptoms include dyspnea, restriction at exertion, cough, inspiratory stridor, recurrent pneumonia and bronchectasis. Pulmonary function tests shows airflow obstruction. We encountered such syndrome recently in the follow-up of a young woman who had to undergo an salvage left pneumonectomy for massive hemoptysis due to a congenital abnormality with absence of the left pulmonary artery and right-sided aortic arch, that we reported elsewhere [21]. Rather than the endoluminal stenting of the main bronchus which does not palliate at all the hemodynamic consequences of the
mediastinal shift, there is an elegant and effective surgical solution that consists in thoracotomy for freeing adhesions and filling the postpneumonectomy space with an expandable prosthesis, whose volume may be controlled by injection or withdrawal of up to 1 l of saline solution (Fig. 6A and B).

There has been a great hope to reduce chronic chest pain by the use of VATS, thus resulting in improvement of quality of life. In fact, only cosmetic benefits have been demonstrated to date, and VATS does not allow better quality of life neither in terms of pain nor respiratory function [22]. This conclusion is probably of evidence nowadays for most thoracic surgeons. As thoracic surgeons, we have to apologise for this initial ‘naivety’ because 10 years of investigations were needed to reach this obvious conclusion.

7. Conclusions

Undoubtedly, extensive experience with pneumonectomy has been gained along with time. However, if much has been written, little has been learnt. It appears clearly that standard right pneumonectomy remains a high risk procedure, even if not thoroughly explained. In that sense, lung sparing resections should be encouraged whenever possible. Extended lobectomies associated with bronchoplastic and angioplastic procedures allow to perform surgical resection in good oncological conditions with a lowered risk. The risk of right pneumonectomy should be taken into account especially with the development of combined therapeutic strategies against lung cancer. Indeed, to minimise the operative risk is a constant concern of the surgeon. Clearly, a nearly 25% mortality following induction therapy and right pneumonectomy is unacceptable. In my opinion, to perform surgery on first intention, whenever a complete resection is thought to be technically possible may be still justified even in case of locally advanced disease in some instances. Any attempt to downstage the disease in these particular patients introduces a new dilemma for the surgeon concerning the type of resection to be performed: the one that was required initially to remove all the disease, or the one dictated by the residual disease? As far as early morbidity is concerned, one may reasonably suppose that a non-dramatic difference could be anticipated following pneumonectomy performed on first intent, when compared with lobectomies associated with reconstruction of hilar and mediastinal structures performed after the induction therapy. Furthermore, to resect the residual disease leads to the consideration of surgery as an adjuvant modality treatment to oncological regimen, which is not the least of the paradox. Pragmatism, however, would probably lead us to deny that paradox when the tumour is left-sided, but to comply with it when the tumour is right-sided.

References

[16] Massard G, Wihlm JM. Early complications. Esophagopleural fistula. This conclusion is probably of evidence quality of life neither in terms of pain nor respiratory function [22].
[17] Reference

