

The anticipation and management of air leaks and residual spaces post lung resection

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ABSTRACT

The incidence of any kind of air leaks after lung resections is reportedly around 50% of patients. The majority of these leaks doesn't require any specific intervention and ceases within a few hours or days. The recent literature defines a prolonged air leak (PAL) as an air leak lasting beyond postoperative day 5. PAL is associated with a generally worse outcome with a more complicated postoperative course and prolonged hospital stay and increased costs. Some authors therefore consider any PAL as surgical complication. PAL is the most prevalent postoperative complication following lung resection and the most important determinant of postoperative length of hospital stay. A low predicted postoperative forced expiratory volume in 1 second (ppoFEV1) and upper lobe disease have been identified as significant risk factors involved in developing air leaks. Infectious conditions have also been reported to increase the risk of PAL. In contrast to the problem of PAL, there is only limited information from the literature regarding apical spaces after lung resection, probably because this common finding rarely leads to clinical consequences. This article addresses the pathogenesis of PAL and apical spaces, their prediction, prevention and treatment with a special focus on surgery for infectious conditions. Different predictive models to identify patients at higher risk for the development of PAL are provided. The discussion of surgical treatment options includes the use of pneumoperitoneum, blood patch, intrabronchial valves (IBV) and the flutter valve, and addresses the old question, whether or not to apply suction to chest tubes. The discussed prophylactic armamentarium comprises of pleural tenting, prophylactic intraoperative pneumoperitoneum, sealing of the lung, buttressing of staple lines, capitonage after resection of hydatid cysts, and plastic surgical options.

KEYWORDS

Prolonged postoperative air leak; postoperative apical space; prevention; management; infectious conditions

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Air leaks

Definition and quantification of air leaks

A postoperative air leak is defined by air escaping the lung parenchyma into the pleural space after any kind of surgery in the chest. As simple as this definition may look like, its clinical implementation very often is based on pure individual

judgement. In fact it is not easy to quantify the amount of air bubbling through a water seal of any closed chest tube drainage system, which all go back to an invention made by Gotthard Bülau, a popular German internist, who lived and worked in Hamburg between 1835 and 1900 (1,2). Bülau used a pleural drainage system with a tube draining fluid and air under water in order to maintain a negative pressure inside the pleural cavity. Bülau used this method to treat pleural empyema since 1875 and published his technique 1891. Since surgery of the chest was not possible at the time, Bülau certainly could not anticipate the paramount importance of his idea for thoracic surgery.

Given the difficulty of a quantitative judgment, qualitative evaluation of air leaks can be attempted by differentiating active leaks-originating from bronchiolo-alveolar districts-from passive leaks due to limited lung compliance and space problems. If traditional closed chest tube systems with water-seal are used, this differentiation is quite susceptible to individual experience

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and expertise of medical and nursing personnel. In addition different opinions exist among physicians about qualitative and quantitative aspects of air leaks.

The most widely used technique for qualitative assessment of air leaks is asking the patient to cough while observing the water column and the water-seal. No air bubbles in the water-seal during this maneuver attest an air-tight lung; the presence of bubbles simply indicates air in the pleural space, but does not allow judgment regarding active or passive leakage. If the appearance of bubbles remains in the same intensity at repeated coughs the leak is very likely to be an active one. If the intensity is reduced with each cough and maybe stops after a few coughs the background may be a small active leak or a passive leak. Hence, before deciding to pull this tube the physician is well advised to repeat this test after about an hour to exclude any active leaks. If bubbles occur at normal breathing or while the patient speaks, there is a significant active air leak present.

To complement these considerations the strategy to apply suction to chest tubes varies among surgeons and institutions and puts drain management and drain removal algorithms even more on an intuitive basis.

A possible way out of this dilemma is offered by modern electronic chest tube systems allowing for a quantitative assessment of air leaks not just at a given moment, but over a defined period of time (3,4). The digital and continuous air leak measurement and the ability to plot the amount of air escaping the chest over a couple of hours provides solid information for quality assessment and straightforward clinical decisions leading to shorter hospital length of stay (LOS).

Different systems are available today, which directly measure air leaks or calculate the air loss from secondary parameters. Although the introduction of numerical data and trends has put chest tube management on a quantitative basis this quite young technology still has limitations and further development potential.

In order to anticipate and prevent air leaks intraoperative assessment is of importance. After any parenchymal resection the surgeon may want to check all resection lines and bronchial reconstructions for air tightness. This is realized through a water-submersion test. Warm sterile physiological saline solution is instilled into the chest cavity and the anesthesiologist is then asked to gently re-inflate the atelectatic lung gradually up to a peak pressure of 30 mmHg, which pressure is then held for a couple of seconds. All areas of interest are submerged and thoroughly inspected under water to identify major air leaks for further surgical measures. To facilitate the decision making for surgical interventions, a simple quantification test can be used during this assessment, which was suggested by Macchiarini *et al.* (5):

- grade 0 (no leak);
- grade 1 (countable bubbles);
- grade 2 (stream of bubbles);
- grade 3 (coalesced bubbles).

The incidence of postoperative air leaks depends on the timely distance to lung resection. While an air leak is present in 28% to 60% immediately after completion of the surgery, it is reported in 26% to 48% of patients on postoperative day 1 (POD1), 22% to 24% on POD2 and still 8% on POD4 according to the literature (6-10).

Prolonged air leak (PAL)

Generally about 50% of all patients present with at least minor air leaks after lung resections and the majority of these leaks stop spontaneously after a few hours up to three days. The definition for the term PAL varies in multiple published studies and proposed definitions of PAL range from an air leak lasting four days to greater than ten days postoperatively (11). Based on recent literature several authors have recommended defining a PAL as an air leak lasting beyond postoperative day 5, which is an average LOS after pulmonary lobectomy. This definition is consistent with The Society of Thoracic Surgeons (STS) database definition for a PAL as an air leak exceeding the otherwise necessary LOS.

Clinical impact of PAL

There is no amount of air leak that is ever good, says the thoracic and cardiovascular surgery team from the Cleveland Clinic Foundation. The presence of air leaks predicts a worse outcome with prolonged hospital stay and more complicated postoperative course. As a consequence any air leakage should be considered as a surgical complication, not simply those lasting seven days or more (6).

PALs are the most prevalent postoperative complication with a reported occurrence of 18-26% (12,13) up to higher rates of 45-58% of surgeries (6,14). PAL is the most important determinant of length of postoperative hospital stay (12).

Its effect on LOS is significantly stronger than that of any other causes including suboptimal pain control, nausea and vomiting (15,16).

Prolonged postoperative air leak has been and still is considered a complication only when it persists five days or beyond the normal hospital stay. This ignores the potential impact of the vast majority of air leaks (6). Despite the fact that it is the most common postoperative pulmonary complication followed by pneumonia, acute respiratory failure and hemorrhage, the mortality rate of PAL is surprisingly high

and has been reported between 1-12% (12,17,18). Brunelli A and colleagues have reported a significantly increased rate of empyema in patients with air leaks lasting more than seven days as compared to patients with lesser air leaks (8.2% to 10.4% versus 0% to 1.1%) (19). In addition to empyema Varela G *et al.* have found air leaks lasting longer than five days associated also with other kind of pulmonary complications like atelectasis and pneumonia (20).

These conditions led to a prolonged hospital stay of up to six days and a financial loss to the health care provider of approximately 39,000 Euros. The relation of PAL, LOS and costs is confirmed by a number of other publications (6,19,21,22). The consequences for the individual patient and the whole healthcare system are manifold:

- prolonged chest tube drainage causes prolonged pain (15,23,24);
- restricted ventilation leads to increased risk of pneumonia (22);
- decreased mobility through chest tubes and related pain (25);
- decreased mobility results in increased risk of thromboembolism (24);
- necessity of pleurodesis, mechanical ventilation, and reoperation (25);
- higher readmission rate to intensive care units (22);
- prolonged hospital stay (6,12,15,22) and related higher overall costs (12,23).

Risk factors for prolonged air leakage

In a very recent study from Liverpool, UK, the authors have retrospectively analysed a total of almost 2,000 patients undergoing lung resections between 2002 and 2007 with the aim to define risk factors for the development of postoperative air leaks (14). A logistic regression model including various potentially relevant factors revealed a low predicted forced expiratory volume in 1 second (ppoFEV1, $P < 0.001$), upper lobe lobectomy ($P = 0.002$) and surgical technique ($P = 0.02$) as significant risk factors for developing prolonged postoperative air leak. The consequences of PAL were increased LOS ($P < 0.0001$), higher in-hospital mortality ($P = 0.003$) and more ICU readmissions ($P = 0.05$).

Gómez-Caro A and coworkers have found incomplete or fused fissures to be a risk factor for PAL (26). In a prospective study enrolling 119 patients after lobectomy those with incomplete or fused fissures ($n = 63$) were intraoperatively randomly assigned to receive either the traditional technique or the fissureless technique to approach the fused fissures. The incidence of PAL was significantly higher among patients with incomplete or fused fissures, however, the application of the fissureless preparation technique avoiding dissection of the lung

parenchyma over the pulmonary artery was significantly superior in terms of preventing PAL and reducing hospital stay.

Emphysema and other underlying lung disease have been identified as significant risk factors involved in developing air leaks (27). The severely rarefied lung tissue may be a too weak support for the staples during lung volume reduction surgery (LVRS) and the increased negative pleural pressure together with higher mechanical forces in the proximity of the staple lines predispose the lung to rip. In the NETT trial (22) the occurrence and duration of PAL was higher in patients with lower diffusing capacity ($P = 0.06$), upper lobe disease ($P = 0.04$) and important pleural adhesions ($P = 0.007$), whereas surgical variables were not found to be predictors.

Infectious conditions and chronic inflammation like tuberculosis and aspergillosis (28-30) but also cystic fibrosis (31) have been reported to increase the risk of PAL. Of 23 out of 71 patients with PAL and/or residual air space after resections for pulmonary aspergillosis, complications were observed more frequently in patients with greater cavitation near the chest wall (32).

Some authors have found a different prevalence of PAL for different lobes. Okereke and coworkers retrospectively analysed 319 patients after lobectomy and found PAL less frequently after left lower lobectomy ($P < 0.0001$) (6). In contrast to other studies the occurrence of PAL was clearly surgeon dependent in their series ($P = 0.007$) and not associated with lung function parameters.

Prediction of air leaks

Specific analyses of clinical data performed by different groups revealed a prevalence of PAL exceeding seven days postoperatively of 14% to 18% of lung resections. Knowing the quantitative risk of this complication beforehand may assist the surgeon in deciding on preventive intraoperative measures such as the use of sealants, buttressing staple lines, or pleural tenting.

In their paper published 2004 in the *Ann Thorac Surg* Brunelli and coworkers found a prevalence of 15.6% PAL in a cohort of 588 patients operated on between 1995 and 2003 (33). Logistic regression analysis led to the identification of a set of risk factors for the development of PAL, which was used to further generate a score for the prediction of PAL. This set of predictors consisted of ppoFEV1, presence of pleural adhesions and upper lobe resections.

In 2010 Brunelli *et al.* published a second paper with an updated version of their scoring system based on the analysis of 658 patients undergoing lobectomies between 2000 and 2008 without the use of sealants, pleural tent, or buttressing material (34). Again potential predictors were identified by univariate analysis and subjected to stepwise logistic regression analysis to generate a scoring system, which was then validated on

patients operated on in a different center.

The set of predictive variables and their scores were:

- age greater than 65 years, 1.0 point;
- presence of pleural adhesions, 1.0 point;
- FEV1 less than 80%, 1.5 points;
- body mass index less than 25.5 kg/m², 2.0 points.

Four risk classes according to their aggregate scores were significantly associated with incremental risk of PAL in the validation process in 233 patients.

Another recent paper by Lee and coworkers from Montreal, Canada, analysed single institutional data from 580 patients after pulmonary resection between 2002 and 2007 following a similar algorithm to establish a predictive risk model for PAL (35). They validated their scoring system in a consecutive set of 381 patients operated on at their institution after 2007. The rate of PAL was 14% in the derivation set and 18% in the evaluation set, which is in good accordance with other reports.

Their set of predictors building a simple scoring system, with the total number of points indicating the probability of PAL, consisted of:

- pleural adhesions, 2 points;
- FEV1, 1 point per 10% below 100%;
- DLCO, 1 point per 20% below 100%.

Concluding from the published evidence it becomes clear that lung function as expressed by preoperative (FEV1) or predicted postoperative (ppoFEV1) is the strongest predictor of PAL. This view is supported by another recent paper from the UK by Elsayed H and coworkers (14).

However, individual prediction of air leaks is difficult even after considering the proposed scores and may not be very useful in a day-to-day setting at a thoracic surgery clinic. The delayed decision to reoperate on a patient to close a significant air leak which didn't stop within a week leads to unnecessary prolongation of the postoperative hospital stay in the referring patient.

Only few publications have specifically addressed this issue in order to assist surgeons in this decision. At least modern digital chest drainage systems with air leak meters allow for quantifying the air loss over time and visualisation of a trend. Billé A *et al.* from Torino have reported that 75% of patients with an air leak greater than 180 mL/min had PAL exceeding five days, however the number of patients studied is too small to serve as a reliable basis for clinical decisions (36).

Cerfolio and colleagues found that patients with an early postoperative air leak of 5 or greater on a 7 graded scale are more likely to develop PAL ($P < 0.001$) (37). In the absence of a clear cut-off magnitude of an air leak each surgeon or institution has to base their indication to reopen upon own experience with a certain drainage system (15).

Apical spaces

Ethiology and pathogenesis of PAL and apical spaces

There is surprisingly sparse literature addressing postresection spaces, probably because this condition is an expected finding after lobectomy and rarely clinically significant unless infected or large enough to cause symptoms. Furthermore there is no standard definition of postresection apical spaces.

Following most lobectomies a variable volume of the pleural space is initially unfilled by extension of the remaining lung tissue. This is a common finding on plain chest radiographs and can almost always be seen by CT scan. After lung resection different physiologic mechanisms including expansion and hyperinflation of the remaining ipsilateral lung, mediastinal shifting, narrowing of the intercostal spaces and elevation of the diaphragm contribute to minimize the residual pleural space consequently. Hence, any restrictive process of the lung and chest wall like restrictive lung disease, previous thoracic operations or induction chemo- or/and radiotherapy may increase the likelihood of postoperative residual pleural space.

Persistent residual air spaces are more common in restrictions for inflammatory or infectious diseases, LVRS, upper lobe resections and resections of any type performed in patients with emphysema or fibrotic processes. In these processes the rarefied or poorly compliant remaining lobes fail to regularly fill the void left in the hemithorax (38). If allowed to persist large undrained postresection fluid collections may lead to trapping of the remaining lobe preventing adequate re-expansion and resulting in a fixed space even when drainage is ultimately attempted. Shields and colleagues in 1959 reported an incidence of persistent residual air space after resection for the management of tuberculosis as high as 21% and 33% in patients with pulmonary segmentectomy for TB. Upper lobectomies and bilobectomies have a higher incidence of postoperative air leaks and residual pleural spaces (15,38).

The vast majority of apical spaces may be unproblematic without impacting on the clinical course of the patient. Asymptomatic spaces usually resolve through resorption of the air, better expansion of the remaining lung, mediastinal shifting, elevation of the diaphragm and diminution of the intercostal spaces. However, in the presence of a significant broncho-pleural fistula spontaneous healing and resolution of an apical space is unlikely, especially when complicated by an empyema. In these cases surgical reintervention including filling of the space with viable material like muscle flaps or omentum, sometimes upper thoracoplasty or combinations may be indicated (39).

Barker WL emphasizes in his review paper of 1996 (40) a

cautious, thoughtful and more conservative approach to residual apical spaces for mainly two reasons. Firstly premature surgical interventions may lead to iatrogenic complications and secondly, surgical intervention will not be required for several months after the occurrence of an apical space in most cases, irrespective of cause. He proposes careful observation based on appropriate clinical, physiologic, and radiologic criteria to achieve a favorable outcome in these patients, who may be widely asymptomatic over long periods of time even with persisting vented or unvented spaces. Decision making may not always be easy and straight forward and requires an individualised approach. Like in any other kind of surgery a number of factors have to be taken into account before surgical treatment is considered, including performance status, respiratory reserve, quality of lung tissue, underlying disease and prognosis, problems with maintaining the drainage, local or systemic effects of chronic infection as well as social and even economic aspects.

This view is in part contradicted by a more recent publication. In a prospective study from Istanbul, Solak O and coworkers identified 58 patients who had a postresectional residual pleural space on the first postoperative day and followed them by chest X-ray, recording any complications and reoperations up to twelve weeks (41). The majority (76%) of residual spaces were completely resorbed within the observation period. 10% had an uncomplicated persistent apical space and 14% developed complicated residual spaces requiring re-drainage or reoperation. The authors identified persistent air leak and infection as the major complications of residual pleural spaces and favour early surgical intervention for complicated spaces. Since the onset of infectious complications was not observed after four weeks postoperatively, routine follow-up of uncomplicated spaces beyond the first month may not be necessary.

Treatment of PAL and apical spaces

Before considering any surgical measures in the initial management of PAL it is of paramount importance to separate two clinical entities: does the leak originate from the alveoli through a peripheral lesion in the visceral pleura or from bronchial structures, or in other words do we face an alveolar air leak or a bronchopleural fistula. If a significant air loss is encountered and there is suspicion of a problem at the bronchial anastomosis or stump early bronchoscopy should be indicated. The management of bronchopleural fistulas is substantially different from that of alveolar air leaks, however, in the vast majority of PAL the background is an alveolar air leak and initial management should be aimed at treating this entity (11).

Cerfolio RJ and coworkers have based their prospective

algorithm for the management of air leaks after pulmonary resection on four qualitative categories of air leaks (7):

- grade 1: forced expiratory only;
- grade 2: expiratory only;
- grade 3: inspiratory only;
- grade 4: continuous.

Initially all chest tubes were put on 20 cm H₂O of suction until POD2 and were then converted to water seal. If an air leak was present together with a pneumothorax on POD3, suction was installed again with 10 cm and with 20 cm if a pneumothorax was present without an air leak. 25% of patients presented with air leaks on POD1. A low FEV1/FVC ratio, increased age, increased RV/TLC ratio, increased RV, and an increased FRC were predictors of having an air leak on postoperative day 1. The majority of patients with air leaks on POD4 still had air leaks on POD7 and were effectively treated with talc slurry. This group recommends conversion from suction to water-seal to allow spontaneous sealing of expiratory PALs without significant pneumothorax.

Conservative approaches include prolonged chest tube drainage, provocative chest tube clamping or permissive chest tube removal, physiotherapy, application of various agents for pleurodesis like tetracycline, talcum or silver nitrate through the chest tube, or outpatient management with a chest tube and a Heimlich valve (42).

Pneumoperitoneum

The principle of using pneumoperitoneum to treat PALs and space problems after lung resections is not new and has been described since the 1980s (43-45).

In the era of fast-tracking surgery its value has been rediscovered and the technique adapted. Unlike the more commonly used percutaneous method designed for basal spaces after lower lobe lobectomies as described by Carbognani *et al.* (46), a paper by Alper Toker (47) describes a method to induce pneumoperitoneum intraoperatively through a transdiaphragmatic route in patients with insufficient filling of the chest cavity by the remaining lung. After the resection, in these series mainly upper lobectomies, the lung is ventilated at a peak pressure of 30 mmHg and expansion is monitored. If full expansion and complete filling of the chest cavity is considered unlikely, the anterolateral part of the diaphragm is punctured with a Veres needle and 800 mL of air are injected into the abdomen. The small diaphragmatic lesion is closed by a prepared purse-string suture. No complications related to this method were observed, all air leaks and apical spaces resolved in a few days and the peritoneal air was reabsorbed within 3.5 weeks. If

not applied intraoperatively, these authors recommend making use of this measure at an early postoperative phase when the lung still is mobile enough to shift to the apex of the chest cavity.

Blood patch

Instillation of autologous blood into the pleural space through the chest tube is another nonsurgical option to induce pleurodesis in the management of postoperative PAL. The sclerosing effect of blood may not be as potent as that of other agents and may be explained by non-infectious inflammatory reactions of the pleura together with the occlusion of alveolar leaks by fibrin formation leading to early re-expansion of the lung with an additional sealing effect.

In 1987 Robinson (48) reported an 85% success rate with this method in the treatment of chronic and recurrent spontaneous pneumothorax. This first report was followed by several reports published in the 1980s. In 1998, Cagirici *et al.* (49) demonstrated the efficacy of autologous blood pleurodesis in a prospective study in 32 patients following tube thoracostomy for spontaneous pneumothorax. 84% of air leaks closed within 72 h and no recurrence was seen in the 48-month follow-up. Only minor complications like fever and pleural effusion were observed in one third of patients. However, this paper does not focus on PAL after lung resection. Rivas de Andrés (50) reports a 100% success rate using a blood volume of 100 mL to induce pleurodesis to treat PAL after surgery for non-small cell lung cancer in a small group of six patients. Similar results are reported in a prospective analysis by Lang-Lazdunski and Coonar (51), who assessed the effect of 50 mL of blood for pleurodesis after lung resections in 11 patients. The aspired result was achieved in 72.7% within 12 h and in 100% within 48 h. In a series of 21 patients with PAL mainly after lobectomies and LVRS Droghetti (52) reported a 100% success rate in all patients with blood pleurodesis. After a single injection of blood the air leak ceased in 81% within 12 h and in 100% within 24 h. The authors recommend an instillation of 150 mL of blood in a 32F chest tube and raising the tube above patient niveau instead of clamping in order to avoid chest tube occlusion.

The first prospective randomized controlled study comparing blood pleurodesis with conventional management in 22 patients after lobectomy was published by Shackcloth *et al.* (53) 59% of the observed air leaks were successfully treated, with no statistical differences between both groups. However, blood pleurodesis significantly reduced the time to air leak cessation, chest tube removal, and hospital discharge by six days. Similar results were found by Andreotti and colleagues (54) who compared 50 and 100 mL of blood instillation with conventional chest

tube placement for the management of air leaks after lobectomy. 50 mL of blood reduced the time to air leak cessation by four days, 100 mL by five days. Most recently, Ozpolat (55) reports the efficacy of blood patch pleurodesis for PAL following pulmonary hydatid cyst operations. Air leaks ceased in 21 of 24 patients with chest tube removal within 24 h if no leak was observed (20 patients).

In a meta-analysis of the relevant literature and a best evidence article to answer the question whether blood pleurodesis was an effective measure in the management of PAL, Chambers A *et al.* (56) found more than 43 papers addressing this topic, of which ten represented the best evidence to answer the clinical question. They conclude that autologous blood pleurodesis has a superior outcome as compared to conservative management of postoperative PAL. 70-81% of PAL resolved within 12 h and 95-100% within 48 h *vs.* a mean of 3-6.3 days with simple chest drainage. These rates did not differ between lung resections compared to surgery for pneumothorax. Blood patching decreased the rate of recurrent air spaces from 35-41% for conservative chest tubes to 0-29%. Complications including pleural effusions, fever and empyema occurred in only up to 18%. In patients with ARDS and pneumothorax, blood patching reduced overall mortality as well as duration of ICU stay.

In conclusion, few studies mostly comprising a small number of patients suggest blood pleurodesis to be beneficial though there is no consensus on the optimal volume of blood instilled as well as on the usage of antibiotics to prevent possible complications such as infection and empyema.

Suction or no suction

It is common practice among many surgeons to apply suction of -20 cm H₂O to chest tubes directly after pulmonary resections to enhance pleural apposition and to switch to a plain water seal as soon as there is no further evidence of an air leak. However, this routine has been questioned by evidence from patients undergoing LVRS in whom suction of -20 cm H₂O was found to prolong air leaks (57,58). This is probably due to increased air flow preventing leaks from sealing as well as by possibly creating new tears in the emphysematous lungs of those patients. In uncomplicated cases many experts nowadays use water seals without suction in LVRS.

These findings of a possible negative effect of suction in LVRS prompted interest on the application of suction also after other pulmonary resections in patients without severe emphysema.

In 2005 Alphonso *et al.* (8) published data on 239 patients undergoing lobectomy or wedge resection either via thoracotomy or VATS who were randomized to receive either water seal alone

or low-pressure suction (2 kPa). The protocol started directly after the operation in the operating room, so that patients in the water seal group never received any suction. The cumulative persistence of air leaks showed no significant difference between the groups by Kaplan Meier curves and log rank test, prompting the authors to adopt an algorithm without routine application of suction unless clinically indicated. However, a multivariate analysis to identify possible factors associated with PAL was not performed in this trial.

Brunelli *et al.* (59) report similar findings in a prospective randomized study on 145 patients who underwent lobectomy due to lung cancer and were assigned either to water seal or -20 cm H_2O suction on the morning after surgery. There was no statistically significant difference between groups concerning duration of air leak and number of cases with PAL, also after correction for site of resection and length of stapled parenchyma. The complication rate tended to be higher in water seal patients (32%) than in the suction group (18%), but the difference did not reach statistical significance. The authors conclude that the use of water seal only was safe but did not improve outcome.

In contrast to the findings of Alphonso and Brunelli, Cerfolio *et al.* (37) published a prospective study in favour of a non-suction protocol in a small number of patients [33] without severe emphysema. Patients with an air leak on the first postoperative day were randomly assigned to receive water seal only or -20 cm H_2O suction. The difference between groups concerning air leak sealing was highly significant favouring the water seal group (67% by postoperative day 3) to the suction group (7%). However, 22% in the water seal group had to be switched to at least -10 cm H_2O suction due to a clinically relevant pneumothorax.

Similar favourable data for a non-suction protocol were provided by Marshall *et al.* (9) They prospectively randomized 68 patients to water seal or -20 cm H_2O suction after leaving the operation theatre, with all patients receiving at least a short time period of suction inside the OP. The time to air leak sealing was significantly shorter in the water seal group (1.5 days) compared to the -20 cm H_2O group (3.3 days). However, time to chest tube removal did not differ between groups unless corrected for length of stapled parenchyma, then also favouring the water seal group. 27% of patients in the water seal group had to be switched to -10 cm H_2O due to a pneumothorax of at least 25%. In these patients, suction continued only for up to 24 hours before returning to water seal.

The different results of these studies may be explained by various facts. Brunelli *et al.* (59) studied lobectomies and bilobectomies only, while Cerfolio (37) and Marshall (9) included also lesser parenchymal resections. Hence, water seal

may be efficient only in small parenchymal resections. However, Alphonso *et al.* (8) included a wide range of procedures from lobectomy to lung biopsy and surgery for pneumothorax showing no benefit for either water seal or suction, but there was no subset analysis provided. Concerning the type of procedure, no definitive recommendation can be based upon the data currently available. Another difference between the studies discussed is the performance of pleural tenting in 80% of Brunelli's patients, which has not been routinely done by the other authors. Since pleural tenting is an effective method to avoid air leaks, it might superimpose a possible benefit of water seal versus suction for air leak sealing. Furthermore, the time point of randomization to water seal or suction varied between studies from directly after closure of the thorax inside the operating theatre with patients on water seal never receiving suction to the morning of the first postoperative day. Thus, initial application of suction varied.

Finally, Brunelli *et al.* did not routinely perform chest X-rays after switching to water seal and might have missed a not negligible number of relevant pneumothoraces with the need for intermittent suction, which was around 25% in Cerfolio's and Marshall's trials. That might account for the negative outcome of the Brunelli trial as well as for the slightly increased complication rate among patients with water seal only. Alphonso *et al.* performed chest X-rays on days 1, 3 and 7, but only report 1.6% of patients in the non-suction group to have been switched to suction due to clinical considerations. As in Brunelli's trial, they might also have missed some relevant pneumothoraces, possibly accounting for the missing effect in the water seal group. The fact that patients in the water seal group in this study did not even receive a short period of initial suction since randomization to water seal or suction was already done in the operating theatre, might also have influenced the negative result of this trial. Furthermore, the different and often not clearly defined radiographic and clinical criteria for applying intermittent suction in the water seal group may be another factor explaining the inconsistent results of the four studies cited.

Brunelli *et al.* conducted a second study (60) introducing an alternative algorithm of intermittent suction termed "alternate suction". This algorithm consisted of -10 cm H_2O during the night and water seal only during daytime and was studied against water seal only in 94 patients after lobectomy with an air leak at the morning of the first postoperative day. There was no difference concerning duration of air leaks and complications, but chest tube duration and duration of hospital stay were significantly shorter in the "alternate suction" group. However, chest X-rays were not routinely performed, hence a not negligible number of pneumothoraces in the water seal only group may have been missed as in the previous trial by Brunelli.

The possible advantage of the “alternate suction” algorithm might be comparable to a switch to intermittent suction in case of a pneumothorax as performed in the studies of Cerfolio (37) and Marshall (9).

In conclusion, from the five cited prospective randomized trials the optimal algorithm concerning the application of suction in patients without severe emphysema undergoing lung resection remains unclear. There is evidence that an initial short period of suction followed by water seal only or the “alternate suction” protocol proposed by Brunelli (60) are safe and can reduce air leak or chest tube duration in the absence of a relevant pneumothorax, progressive subcutaneous emphysema or cardiorespiratory deterioration. In a water seal only protocol, a chest X-ray is mandatory after switching to water seal to detect a relevant pneumothorax, which is an indication for applying suction of at least -10 cm H₂O. A water seal protocol might not be advisable or even contraindicated in patients with highly restrictive lung disease and in those with a substantial risk of bleeding. In restrictive lung disease re-expansion of the lung will probably be not achieved without suction. In bleeding, tube patency is of utmost importance and should not be risked by avoiding suction.

In patients with severe emphysema and FEV₁ <40% predicted undergoing other procedures of lung resections than LVRS, clinical evidence and expert consensus suggest a water seal protocol in the absence of clinical conditions that require suction. In these cases, a level of suction not exceeding -10 cm H₂O is reasonable.

Intrabronchial valves (IBV)

Endoscopic valve therapy has been recently introduced as a potential less invasive treatment option. After initial case reports of the successful use of one-way endobronchial valves designed for the treatment of emphysema in the closure of a persistent distal bronchopleural fistula this idea was studied and further developed by other authors (61).

In a multicentric analysis of 40 patients over a period of four years the “Endobronchial Valve for Persistent Air Leak Group” reported a complete resolution of the air leak in almost 50% of patients and an improvement in 45% after placing one to nine endobronchial valves per patient (62). However, this early series comprised patients with different underlying diseases with a majority of recurrent spontaneous pneumothorax. Only seven patients had prolonged postoperative air leaks.

Although in 2001 an ACCP consensus statement did not see a role for bronchoscopy in the treatment of PAL, today numerous reports provide ample evidence that endobronchial

valve treatment of prolonged postoperative air leaks can be successfully used in selected patients (63).

More recently a larger single center experience specifically focussing on PAL was published by Firlinger *et al.* (64). In patients with high comorbidity where a second operation has to be avoided transbronchial selective deflation of the leaking lung segment was successfully used in clinically relevant PAL exceeding seven days. The source of the air leak was identified by stepwise blocking subsegmental bronchi by a ballon catheter and monitoring of the air leak using a digital chest tube system. Endobronchial one-way valves were then deployed into the orifice of the referring segment or subsegment resulting in an immediate improvement or cessation of the air leak. Valves were removed some weeks after successful management of PAL.

Flutter valve (Heimlich valve)

In order to reduce the length of hospital stay strategies have been developed and successfully used by many surgeons during the past decades allowing early discharge and home care management of PAL. The chest tube is left in place, shortened properly and attached to a so called flutter valve, named Heimlich according to its inventor. Henry Jay Heimlich (born 1920) was an American physician. In 1963, Heimlich introduced a chest drainage flutter valve. He claims his inspiration came from seeing a Chinese soldier die from a bullet wound to the chest during World War II.

The principle of the flutter valve is a one-way valve and bases on a rubber sleeve within a plastic case where the rubber sleeve allows air passing through the valve in one direction when the sleeve opens and prevents air flowing backwards when the sleeve closes off. The patient has to be checked up regularly for air leak dynamics and possible complications in the outpatient service. Data from six trials comprising a total number of 148 patients show that all but five (3.4%) air leaks resolved with an outpatient one-way valve system. Hence, the usage of a one-way valve in the outpatient setting is safe and effective in handling a stable and uncomplicated PAL.

The efficacy of the flutter valve has been studied in a recent systematic review screening nine electronic databases for studies reporting the use of HV for adults with pneumothorax. Eighteen studies were included comprising 1,235 patients with primary or secondary spontaneous pneumothorax (SSP). The authors concluded that high-quality data to support the use of the Heimlich valve for ambulatory treatment of pneumothorax is sparse, however was successful in about 80% of patients with very few severe complications (65).

Surgical revision

If a significant PAL persists in a patient despite above mentioned conservative measures surgical revision may be considered. In order to minimize the risk of pleural space infection or partial obstruction this decision should be made as early as possible within a few days, when it becomes evident that bedside pleurodesis is ineffective. VATS may be used to accomplish pleural symphysis with application of sclerosing agents under vision, pleural abrasion or pleurectomy. Early surgical reintervention also increases the chance of completing any procedure by VATS including over stapling of parenchymal lesions and application of sealants. In delayed surgical reinterventions and complicated PAL or apical spaces thoracotomy together with muscle or omental flaps are good options to obliterate the pleural space.

Prevention of PAL and apical spaces

PALs are a common problem following lung resections and have led to the development of various surgical methods to prevent this complication. However, routine performance is not advisable since not all patients are expected to profit from these rather costly and time-consuming adjuncts. A careful selection of patients and the most reasonable method to be performed is recommended.

Pleural tenting

The idea of using a pleural tent to seal possible parenchymal air leaks is not new and was first proposed by Miscall in 1956 (66) and Hansen in 1957 (67). A few more recently conducted prospective randomized trials have renewed the interest in this method. Okur *et al.* (38) published data on 40 patients undergoing upper lobectomies or upper bilobectomies randomized 1:1 to pleural tenting being performed or not. In the pleural tenting group, chest tube duration and mean hospital stay were significantly shorter than in the non-tenting group. Furthermore, cumulative drainage volume was significantly less. PAL with the need for intervention (apical chest tube) only occurred in the non-tenting group in 15% of cases. In the tented group, 15% of patients had an asymptomatic apical space. A more recent study by Allama (68) had a similar protocol for upper lobectomies, assigning 23 patients to pleural tenting and 25 to no tenting. There was a significantly lower incidence of air leaks from postoperative day 3 on in the pleural tenting group. However, chest tube duration and hospital stay did not differ between groups in this study. PALs occurred significantly

less in the pleural tenting group. Regression analysis showed pleural tenting to be associated with decreased risk for PAL, while COPD increased the risk. Brunelli *et al.* (69) investigated pleural tenting in 200 patients undergoing upper lobectomy, with a 1:1 randomization to the tenting or no tenting group. In this study, the mean air leak duration, chest tube duration, length of hospital stay, and hospital costs per patient were significantly reduced by pleural tenting. Regression analysis identified pleural tenting to be the best predictive factor for occurrence and duration of PALs. The beneficial effect of pleural tenting manifested before POD4.

In conclusion, pleural tenting seems to be a safe and effective method to prevent air leaks in upper lobectomies and bilobectomies.

Prophylactic intraoperative pneumoperitoneum

Prophylactic intraoperative pneumoperitoneum has been suggested as another method to prevent PAL. This procedure involves a catheter to be placed under the diaphragm intraoperatively to allow for air insufflation into the peritoneal cavity. In a recent prospective randomized study by Okur *et al.* (70) 60 patients undergoing lower lobectomy or bilobectomy were assigned to either achieve interoperative pneumoperitoneum or not. Chest tube duration and hospital stay were significantly shorter and drain volume lower in the pneumoperitoneum group. Furthermore, residual air spaces occurred in only one case in the pneumoperitoneum group compared to eight in the control group. Though the trial involved only a small amount of patients, data suggest intraoperative pneumoperitoneum to be a safe and effective method of preventing PAL in lower lobectomy and bilobectomy.

Sealing of the lung

Different sealing material has been studied for preventing air leaks after lung resections, and each of these different products has its specific properties and indication fields. A huge number of randomized and non randomized studies were performed with every single product over a period of at least 40 years demonstrating variable feasibility of these products for routine clinical use.

The indications for the use of surgical sealants are controversial. In the absence of consistent evidence for the efficacy of these products for preventing air leaks after pulmonary resections in patients with lung cancer three Cochrane Reviews were undertaken in 2001, 2005 and 2010. For the recent Cochrane Review to this topic published in 2010 (71) the electronic databases were screened from 1966 to 2008 including randomized controlled

clinical trials in which standard closure techniques plus a sealant were compared with the same intervention with no use of any sealant in patients undergoing elective pulmonary resection. Sixteen trials with a total of 1,642 randomized patients were included. Only six trials were able to demonstrate a significant reduction of postoperative air leaks by the use of sealants and three trials showed a significant reduction in time to chest drain removal in the treatment group. In two trials the percentage of patients with PAL was significantly smaller and in three trials a statistically significant reduction in length of hospital stay was found with the intraoperative use of sealants. The authors of this review conclude that surgical sealants reduce postoperative air leaks and time to chest drain removal but this reduction is not always associated with a reduction in length of postoperative hospital stay. Therefore, systematic use of surgical sealants with the objective of reducing hospital stay cannot be recommended at the moment.

Buttressing of staple lines

Staple lines are the obvious sources of air leaks after pulmonary resections, hence buttressing of staple lines might help to prevent PAL. In one prospective randomized multicentre trial by Miller *et al.* (72), 80 patients undergoing lobectomy or segmentectomy were assigned either to receive buttressing with bovine pericardial strips or standard treatment. No advantage of this technique could be noted concerning length of ICU stay, time to chest tube removal or hospital stay. Only a trend towards shorter air leak time was found. Since there were only a small number of patients included in this trial, further studies are needed to clarify whether buttressing might be an effective method for preventing PAL in selected patients.

The STS guidelines on the intraoperative and postoperative management of alveolar air leaks, published 2010 by Singhal S *et al.* (11) recommend buttressing staple lines in performing non-anatomic pulmonary resections in patients with moderate to severe pulmonary emphysema (FEV1 <60% predicted) to prevent postoperative air leaks. For anatomical resection in the same group of patients buttressing is reasonable, particularly in patients undergoing segmentectomies and those with incomplete fissures. In patients with emphysema less than moderate the use of buttressed staples is not well established and should be avoided given the increased costs of treatment.

Special considerations for infectious conditions

Pneumothorax and infection

SSP associated with an underlying infectious disease has been

found to be a more complicated situation than SSP due to a non-infectious condition. Chen *et al.* (73) retrospectively studied the outcome of SSP due to different conditions managed by pigtail catheter. Of the 168 cases included, 38 were associated with infectious diseases. Only 50% of these were successfully treated with a pigtail catheter, compared to 75-81% due to COPD or malignancy. Furthermore, length of hospital stay was significantly longer in patients with underlying infectious diseases than in the other conditions.

Rare cases such as one published by Chaudhry *et al.* (74) involving bullous disease with bilateral pneumothorax due to tuberculosis might even call for sophisticated surgical intervention in addition to medical treatment in order to lead to re-expansion of the lungs and clinical improvement.

Capitonnage after resection of hydatid cysts (Invited comment)

The surgical treatment of pulmonary echinococcosis might necessitate extensive resections of destroyed lung parenchyma such as lobectomy. Although there is no consensus yet, surgery of pulmonary hydatidosis should be as lung sparing as possible and include capitonnage to avoid postoperative complications like air leakage at an excellent long-term outcome regarding freedom of recurrence (75,76). Size and even bacterial superinfection of a cyst does not seem to be a contraindication to lung sparing surgical treatment including capitonnage and only one percent of patients of this series underwent lobectomy for completely destroyed lobes. Capitonnage may not be necessary in cysts facing the diaphragmatic pleura.

Residual spaces after lung resection for infectious disease

Solak *et al.* (41) studied the long-term outcome of residual postoperative pleural spaces (RPPS), which occurred in 58 cases of a study cohort of 140 patients after partial lung resections. Chest X-ray was routinely performed on days 1 and 7, as well as in weeks 4 and 12 to document duration of RPPS and possible complications. In week 12, RPPS still persisted in 10.4% of patients. Major complications included PAL and infection and occurred in 13.7% of cases, half of which had to undergo re-operation, while the other half was managed by re-drainage. Complications were associated with prolonged additional hospitalization (13 days in re-operated compared to 58.5 days for re-drained patients). Infection of pleural spaces occurred after weeks 3 to 4, while pleural spaces that were uncomplicated after one month remained so. The authors conclude that early re-operation should be performed in complicated pleural spaces, while there is no need to follow-up uncomplicated spaces after

one month.

De Giacomo *et al.* (77) describe the successful treatment of an infected pleural space by an autologous platelet-leukocyte gel administered via a chest tube. These gels have previously been shown to stimulate and accelerate healing of soft tissues and bones and could also be effective for treatment of complicated air spaces after lung resections.

Plastic surgery

Even though surgical repair techniques are rarely indicated, they have been proven to be safe and effective when conventional tube thoracostomy has failed to solve the problem of PAL. A combined latissimus dorsi-serratus anterior transposition flap has been proposed by Woo *et al.* (78) The authors studied this method on five cases with PAL. The latissimus dorsi and the proximal part of the serratus anterior were exposed by a lazy-S incision, and both muscles were mobilized as pedicled flaps. The pleural cavity was filled with the latissimus dorsi through a thoracic window in order to seal the fistula, while the serratus anterior was used to close the rib cage. The method was effective in all five cases studied. The air spaces resolved and the chest tubes could be removed after a mean of five days. In a follow-up period of one year no recurrence of air leaks was noted.

Especially in situations with a combination of PAL with an infected apical space, the use of flaps can be crucial for a successful management. Surgery for pulmonary cavity associated with fungus ball is challenged by chronic lung disease. Rergkhang C *et al.* (79) found tuberculosis (70%) as the most common underlying pulmonary disorder very often complicated by massive hemoptyses. Lobectomy was successfully performed in 55% of patients and 30% had a cavernostomy with transposition of muscle flap. An emergency setting and cavernostomy with transposition of muscle flap increased the risk of a compromised postoperative course. The authors propose elective surgery with formal pulmonary resection as the therapeutic option of choice for low risk patients. Cavernostomy with transposition of muscle flap should be reserved for patients with poor pulmonary reserve.

Apical spaces after operations for tuberculosis

Lung surgery for tuberculosis is indicated in special situations and complications such as failure to respond to chemotherapy in multidrug-resistant disease, destroyed lung, concomitant or subsequent aspergilloma, hemoptysis, persistent cavities and pleural spaces and others. Surgical interventions for pulmonary tuberculosis and its sequelae range from wedge resections to pneumonectomy, with cavernostomy, pleural partition by muscle

flaps and thoracoplasty being special procedures in rarer cases. Complications after lung surgery for tuberculosis including apical spaces and PAL have been reported to be more common than in pulmonary resections for other underlying diseases.

In a study by Mohsen *et al.* (28), of 23 patients being operated on for multidrug-resistant pulmonary tuberculosis, 52% had a lobectomy and 48% a pneumonectomy, followed by chemotherapy. PAL occurred in four patients (17%). In another paper by Olcmen *et al.* (29), who retrospectively studied the outcome of 57 patients with a total of 72 thoracic surgeries for pulmonary tuberculosis, 28 complications in 18 patients are reported. Of these, PAL (21%) and residual spaces (12%) were the most common. In line with these studies are the data by Lang-Lazdunski *et al.* (30), who also report a high rate of PAL (28%) after lung resections for *Mycobacterium xenopi* infection.

Though all these reports conclude lung surgery for tuberculosis to be effective and associated with acceptable morbidity and mortality, duration of hospital stay is longer and complication rates are higher than for similar procedures due to other underlying diseases.

A special situation following pulmonary tuberculosis is pulmonary aspergilloma or aspergillosis. Al-Kattan *et al.* (80) compare the outcome of lung surgery for aspergilloma on the basis of tuberculosis (20 patients) to aspergilloma due to acute myeloid or lymphoid leukemia (10 patients). The indication for a surgical intervention in the tuberculosis group was hemoptysis in all cases. Interventions performed ranged from lobectomy to pneumonectomy. In the leukemia group, lobectomy and wedge resections were performed. 10% of patients in the tuberculosis group had PAL, and there was one postoperative death reported due to massive hemoptysis. In comparison, there was no postoperative morbidity and mortality in the leukemia group.

Csekeo *et al.* (32) report on the outcome of 84 patients with 71 undergoing pulmonary resections, 12 cavernostomies and one lung biopsy for aspergillosis. In about half of the cases tuberculosis was the underlying disease leading to aspergillosis. The authors report the post-operative occurrence of PAL or residual spaces in 23 patients (32%), which were more frequently observed in patients with cavernae near the chest wall. Even though lung surgery for aspergilloma due to tuberculosis is followed by a higher complication rate than similar interventions for other conditions, a surgical approach often remains the ultima ratio for aspergilloma.

Special techniques to resolve persistent pleural spaces after lung surgery for infectious diseases such as tuberculosis include pleural partition with intrathoracic muscle tent and thoracoplasty. Rocco (81) describes the method of pleural partition with muscle transposition which has been used to

successfully treat residual spaces after lung resections in three patients in his report. After removing parts of the second or third rib the latissimus dorsi and serratus anterior muscles are transposed into the thoracic cavity and sutured to the pleura or periosteum and intercostal muscles to form a muscle tent covering the lung and resolving the air space.

Thoracoplasty as salvage option for the rare cases of treatment-refractory complicated residual pleural spaces was studied by Hopkins *et al.* (82). They report 30 cases in a 14-year period, where 23 patients had tuberculosis as the underlying disease for their complications. Persistent air space associated with PAL after lung resection was the most common indication for thoracoplasty. Destroyed lung due to tuberculosis was the main reason for persistent pleural spaces in four patients, and local infection of long-term pleural spaces after therapeutic pneumothorax for tuberculosis was the indication for the procedure in another four cases. Thoracoplasty was successful in 73%. A total of four deaths and six failures of the procedure were reported. The authors conclude that thoracoplasty as the final strategy can be an effective tool for resolving complicated pleural spaces in carefully selected patients.

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