Review Article

Contemporary interventions for secondary spontaneous pneumothoraces

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Abstract: Secondary spontaneous pneumothoraces continues to be a common problem faced by thoracic surgeons. There are multiple etiologies that result in the development of a secondary spontaneous pneumothoraces. Some of these are congenital in origin and others are acquired. However, emphysema from chronic obstructive pulmonary disease remains the leading cause and as such this paper will primarily focus on pneumothorax resulting from this entity. The past decade has seen several advances in thoracic surgery. These advances include the introduction of endobronchial interventions, new pleurodesis agents and surgical approaches. With the multitude of options available, it can be challenging to decide what the ideal management strategy should be. The purpose of this paper is to provide a summary of the various management strategies and when best to employ them. This paper will also provide a review of the literature around the newer technologies that are being employed and the success rates of each of them. Specifically, the paper will review endobronchial therapies, different chemical pleurodesis agents and the role of video assisted thoracic surgery. The latest guidelines regarding the management of secondary spontaneous pneumothoraces will also be reviewed. Lastly, key points and take-home messages will be provided. This paper hopes to provide a quick and informative read for cardiothoracic trainees and early career surgeons in the management of secondary spontaneous pneumothorax (SSP).

Keywords: Video-assisted thoracoscopic surgery (VATS); pneumothorax; pleurodesis

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Introduction

Spontaneous pneumothorax (SP) is defined by the presence of air in the pleural cavity without any trauma or injury. As opposed to primary spontaneous pneumothorax (PSP), secondary spontaneous pneumothorax (SSP) occurs in the context of an underlying lung disease (1). Recently, SP has been identified as a complication from coronavirus disease 2019 (COVID-19) (2). Chronic obstructive pulmonary disease (COPD) is by far the most common cause of SSP in developed countries, being responsible for 50–70% of reported cases (3-6). The annual incidence of SSP has been reported to be around 6.3 and 2 per 100,000 individuals for men and women, respectively (7-10). Secondary SP occurs at a peak incidence at 60- to 65-year-old (11). As SSP presents in older and more comorbid patients, its management can be quite challenging. Indeed, it is associated with a higher mortality, morbidity, prolonged

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air leak and recurrence rates than PSP (9,12,13). Age, pulmonary fibrosis and emphysema have been identified as risk factors for SSP recurrence. Recurrent rates are as high as 40–56% after the first episode (12,14,15). Therefore, this serious condition needs to be addressed properly and in a timely fashion to achieve optimal outcomes.

However, there exists significant variability in the way SSP is approached and treated (16). In an effort to standardise patients' care, various organizations such as the American College of Chest Physicians (ACCP, 2001) and the British Thoracic Society (BTS, 2010) have published guidelines to assist physicians in management (17,18). As it has been more than a decade since the last publication of these international guidelines, we performed a literature review to reassess and discuss contemporary management of SSP, including those secondary to COVID-19 infection.

Initial management

Initial management of a SSP depends on its size and on the patient's clinical condition. BTS defines a small pneumothorax as measuring less than 2 cm from the hilum while ACCP defines it as presenting with an apex-to cupola distance (distance from the 1st costovertebral joint to the tip of the lung apex) of less than 3 cm. A more voluminous pneumothorax would be defined as a large one by these organisations (17,18).

Small sized pneumothoraces

The ACCP states that observation is a possible approach in stable patients with small SSP. The BTS recommends observation for asymptomatic patients with pneumothoraces less than 1 cm in size (from the hilum) (18). While there is good evidence supporting conservative management in PSP, the same cannot be said about SSP. Indeed, there is no prospective data assessing conservative management in patients with SSP. There is only one retrospective cohort study by Gerhardy *et al.* describing success with this approach (19). They reported safe management without pleural intervention of 25 patients with SSP ≥1 cm at the hilum. Before conservative management for larger SSP can be recommended, prospective trials should be undertaken.

If the size of the SSP is 1–2 cm (from the hilum), the BTS guidelines favor needle aspiration (NA) as initial management while ACCP does not recommend needle aspiration in any situation (17,18). There is some evidence showing a lower success rate of NA in SSP compared to PSP and may explain its limited recommendation in published guidelines (20,21). A subgroup analysis of a recent meta-analysis of 9 randomized controlled trials (RCT) published by Tan *et al.* seem to confirm the inferiority of NA compared with chest tube insertion in SSP in terms of initial success rate, although indicating a lower complication rate (22). A successful NA definition varied from one study to another. Depending on the study, the patient had to be free of symptoms and the residual pneumothorax had to measure less than 10–25% after a follow up of 4–12 h. On the other hand, a successful chest tube management was mostly defined as air leak cessation for 24 h, allowing chest tube removal. One study described outpatient management with chest tube and Heimlich valve. Listed complications included infection, bleeding, tension pneumothorax, subcutaneous emphysema, pneumonia, empyema, and tube blockage. Unfortunately, the number of SSP patients in this study remained limited and they were not well defined, limiting the applicability of these results. More data is needed to better select subgroups of patients with SSP that may benefit from this approach.

Large or symptomatic pneumothoraces

The ACCP suggests a chest tube insertion if the patient experience significant symptoms, becomes unstable or if they have a large SSP. According to ACCP, unstable patients and those at risk of a large air leak should be treated with a large-bore chest tube (24–28 Fr). On the other hand, in a stable patient at low risk of having a large air leak, a smaller chest catheter (<14 Fr) may be acceptable (17). According to BTS, if the patient has a SSP of >2 cm or develops dyspnea, a small-bore (<14 Fr) chest tube should be inserted. They do not routinely recommend larger chest tubes (18). This statement was based on retrospective data published in 2006 by Tsai *et al.* showing no difference in length of hospital stay, extubation time, recurrence rate, and complication in pigtail catheter (10–14 Fr) compared to large-bore chest tube (20–28 Fr) (23). More recently, a RCT including 22 patients also concluded that the use of smaller sized chest tubes (14 Fr) in SSP was as safe and efficient as bigger ones (30 Fr) (24).

Use of suction

Both the ACCP and BTS do not recommend the routine use of suction after insertion of a chest tube. The ACCP recommends suction only if the lung has failed to re-expand

after chest tube insertion (17). The BTS recommends suction in cases where the lung fails to re-expand after chest tube insertion or if there is a persisting air leak after 48 h (20). A RCT including 30 cases of SSP showed equivalent outcomes in patient treated with suction (up to –20 cmH_2O) or without suction (25).

Admission vs. outpatient management

In comparison with PSP, SSP patients present with more severe symptoms and their air leaks have a lower tendency to resolve on its own (13,26). Therefore, most experts, including the ACCP and the BTS, recommend admitting every SSP patients for a minimum of 24 hours for observation and oxygen administration (17,18). Caution should be exercised in patients at risk of CO_2 retention (27). Retrospective studies have shown success rates of up to 78%) for outpatient management of SSP using ambulatory drainage devices in selected patients (28). In 2021, Walker *et al.* performed a multicenter RCT to evaluate the feasibility and length of stay of SSP patients managed as outpatients with flutter valves in SSP patients (29). The study showed no difference in total hospitalization length or readmission at 30 days. However, the subgroup of patients managed with an 8 Fr catheter and the Rocket Pleural vent™ showed a high rate of failure and readmission, while the patients with a 12 Fr chest tube and an Atrium Pneumostat™ device showed more promising results [6/13 (46%) *vs.* 0/8 (0%)]. As appealing as ambulatory management of SSP may seem, more robust data to guide clinicians with patients' selection is required before it can be routinely recommended.

Indications for further interventions

The two main goals of additional intervention in SSP are treatment of a persistent air leak (PAL) and/or reducing recurrence risk. No strong evidence exists to identify the optimal timing for intervention in case of a PAL. A limit of 5 days has been arbitrarily set in the past and seems to have been accepted by most (30). The ACCP uses this definition to guide management, while BTS recommends involvement of a thoracic surgeon if the leak lasts more than 48 hours and/or if the lung does not fully re-expand. The ACCP recommends recurrence prophylaxis after the first episode, while BTS recommends the use of secondary prevention strategies after the second episode, even if the second episode occurs on the contralateral side to the first (17,18). The rationale behind an aggressive approach to recurrence risk reduction is due to the high rate of recurrence with conservative management alone. Furthermore, there is significant morbidity and mortality associated with each episode in this population. In a retrospective and nationwide analysis of SSP admissions in the US, the authors reported that secondary preventative strategies performed during the index admission was beneficial in terms of recurrence, readmission, and mortality rates (31). Of the patients undergoing same-admission recurrence prophylaxis, 80.78% had video-assisted thoracoscopic surgery (VATS), 15.93% had open surgery, and 12.23% had medical pleurodesis.

Special consideration should be given to patients with SSP who are candidates for a lung transplant. A single-centre retrospective study including 554 lung-transplant patients recorded a 1.8-fold increase in postoperative mortality in patients with previous pleurodesis (32). Although previous pleural procedure is not a contraindication for lung transplantation (18), consultation with a transplant center should be done if possible.

Operative management has been identified as the most successful modality in preventing SSP recurrence, decreasing incidence of subsequent pneumothoraces to 0–15.8% (33-40). VATS has progressively replaced open surgery in SSP management over the years. A systematic review from 2007 that also included PSP described a higher recurrence rate with VATS (5.4%) compared with open surgery (1.1%) (41). However, a more recent systematic review and meta-analysis, including 12 studies (4 RCTs and 8 retrospective studies) and a total of 744 patients, did not come to this conclusion (42). When compared with open surgery, patients who underwent VATS procedures had lower recurrence rates [odds ratio (OR) =0.36; 95% confidence interval (CI): 0.20–0.63; P=0.0003]. These patients also had a shorter median (MD) hospital stay than their counterpart (MD =–7.29; 95% CI: –8.76 to –5.82; P<0.01). The lower morbidity, operative time and postoperative opioids requirements must be balanced against the possible higher recurrence rate recorded with this technique (43). This is especially true in the more comorbid SSP patients. Recent reports indicated that despite being effective, surgical treatment has a mortality rate of 2–4% (44-46). Retrospective data has indicated that patients with interstitial lung disease (ILD) have a significantly higher postoperative mortality rate than patients with COPD (15% *vs.* 2% & 21.4% *vs.* 1.4%) (46,47). A poor performance status has also been identified

as a risk factor for postoperative complications in SSP (45,48).

Surgical techniques and approaches

Surgical management of SSP has two main objectives. The first is to stop the active air leak. This is often accomplished by the resection of the visible bullae thought responsible for the air leak. This is commonly performed by using an endoscopic stapler. Other techniques have been described less frequently, such as bulla suturing, endoloop ligation and electrocoagulation (49). There is a lack of data comparing the success rates of these different techniques. The second objective of surgery is to create pleural symphysis to further decrease the recurrence rate. Many techniques have been described to achieve this goal. The most used techniques include pleurectomy, pleural abrasion or chemical pleurodesis (talc or other agents) (50). Unfortunately, there is a paucity of relevant data comparing surgical treatments in SSP. However, a meta-analysis of 51 studies included 6,907 patients with PSP and reported that patients who underwent only a bullectomy had the highest recurrence rate (9.7%). Those who underwent a bullectomy and a chemical pleurodesis had the lower recurrence rate (1.7%) (50). These results hint at the importance of combining the interventions, especially in the VATS cases. Concerns about the ability of the more fragile SSP patients to tolerate the invasiveness of surgery under general anesthesia, authors have described VATS with epidural or local anesthesia with good outcome (51). An important point that needs to be explored is whether the benefits of non-intubated VATS compared with bedside medical pleurodesis in high-risk patients are worth the technical and anesthetic challenges that come with awake surgery. Noda *et al.* published a retrospective cohort study, with 60 patients, in 2016 comparing awake VATS and chemical pleurodesis for management of high-risk SSP patients (52). Their results indicated that the length of prolonged air leak and chest tube drainage was shorter in the VATS group. However, more robust prospective data is needed before definitive conclusions can be made regarding the utility of non-intubated VATS in this population.

Non-operative secondary prevention

Chemical pleurodesis

Medical pleurodesis refers to bedside administration of a sclerosing agent through a chest tube to induce pleural symphysis. For this technique to be successful, it is necessary that the lung is fully expanded so the visceral and parietal pleura remain in contact during the inflammatory phase. As per ACCP and BTS, SSP patients who are not appropriate surgical candidates or are unwilling to undergo surgery, medical pleurodesis is an alternative therapeutic option (17,18). The reported SSP recurrence rates after medical pleurodesis are between 10–25% (53,54). Multiple agents have been used and described in past literature., These include tetracycline and its derivatives, talc slurry, D50 dextrose and autologous blood patch (18,55,56). There is a lack of prospective data indicating superiority of one agent compared to another in treatment of SSP. There is certainly variability between centers in the choice of sclerosing agent. The choice of agent is guided by the patients' status, the clinician's experience, and the product's local availability (56). Talc is reportedly the most frequently used pleurodesis agent, as it is most efficient and least expensive of all the agents (57,58). Initial concerns about this product were the risks of acute respiratory distress syndrome (ARDS). This was found to be directly related to the total administered dose and the particles' size. Indeed, in a prospective multicenter study, Bridevaux *et al.* enrolled 418 patients to receive thoracoscopic pleurodesis with large-particle talc. After a 30-day observation period, the authors recorded no ARDS, intensive care unit admission or death, and only 1.7% of minor complications (59). As the complication rate is rare with appropriate dosage and particle size, BTS recommends using 5 g of graded talc (18). ACCP states that for medical pleurodesis, both talc (very good consensus) and doxycycline (good consensus) are the agents of choice (17). A recent retrospective cohort study described a success rate of 83% (5/6 patients) in treating persisting air leak in SSP patients (59).

Endoscopic interventions

An endobronchial valve (EBV) is a device installed by flexible bronchoscopy in a lobar, segmental or subsegmental bronchus. Its purpose is to allow the air to go out of the lung without re-entering it. Its use has been described in prolonged air leak in the context of a lung resection surgery or a SP (60). In theory, by occluding the air leak, the EBV allows the lung to re-expand and the leak site to heal. Decreasing the length of the air leak might have the potential benefit of reducing the risk of complications from delaying chest tube removal as well as decreasing hospital length of stay. For this concept to work, the air leak site must be localized accurately. Collateral ventilation

(e.g., from an incomplete fissure) has been identified as an obstacle to this technique's success (61,62). In 2018, Yu *et al.* published the first retrospective cohort study treating solely on PAL in SPs (63). They included 37 patients with SPs and PALs treated with EBV because they refused surgery or were deemed not a surgical candidate. EBV could not be implanted in 18 patients, as one patient did not tolerate the procedure and the air leak could not be localised in the other 17. In total, 8 out of 37 patients (22%) had a successful EBV installation that resulted in air leak cessation. These results suggest that despite a high failure rate, EBV could represent an alternative solution to chemical pleurodesis in well selected SSP patients. However, prospective trials are needed to evaluate this further.

Conclusions

SSP is a clinical entity that can have serious consequences on the frail and heterogenous population it tends to affect.

Small and asymptomatic SSP can be observed, while more significant ones need to be drained. While needle aspiration appears to be safe for pneumothoraces measuring 1–2 cm from the hilum, its effectiveness remains limited. In most cases, a smaller size chest tube is adequate and initial suction is not required. In selected cases, outpatient management could be conceivable.

Aggressive recurrence prophylaxis should play a pivotal role in management. If the patient is deemed an acceptable surgical candidate, operative management should be offered. Bullectomy, when appropriate, combined with pleurodesis is the intervention associated with the higher success rate. A VATS approach has mostly supplanted open surgery in management of SSP. In patients with prohibitive surgical risk, bedside chemical pleurodesis should be proposed. Invasiveness and effectiveness vary among the available procedures and care should be taken to make sure the therapeutic choice is consistent with the patients' comorbidities and wishes. Stronger, prospective data is needed to help clinicians target which groups of patients with SSP would benefit more from each therapeutic approach.

The data surrounding COVID-19 patients with SSP is evolving and helping understand its implications in this complex disease in terms of clinical course and prognosis.

Key points/take-home messages

(I) Secondary spontaneous pneumothoraces occur in older, more comorbid, and heterogenous population. They are associated with higher morbidity and mortality than primary spontaneous pneumothoraces. The two main goals of management in SSP are treatment of a PAL and/or reducing recurrence risk.

(II) Small and asymptomatic SSP can be considered for observation only or needle aspiration. However, most patient will require drainage of pleural cavity. A small-bore chest tube (14-Fr) should be used in majority of cases and suction is not required routinely. More data is needed to guide SSP patient selection for potential outpatient management.

(III) Recurrent rates are as high as 40–56% after the first episode (15-17). Whenever possible, aggressive recurrence prophylaxis should play a central role in SSP management.

(IV) Surgical approach represents the most efficient way to prevent SSP recurrence when patients' comorbidities allow it. Intervention should be aimed towards controlling the air leak and creating a pleural symphysis. It usually combines bullectomy with either talc pleurodesis, pleurectomy or pleural abrasion. When patients are deemed poor surgical candidates, bedside chemical pleurodesis is a reasonable alternative to surgical treatment. Multiple agents are available for use, but talc slurry appears to be the most popular one, with reported efficiency and safety profile.

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