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Epidemiology and management of primary spontaneous pneumothorax: a systematic review

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Summary

Primary spontaneous pneumothorax (PSP) is one of the most common thoracic diseases affecting adolescents and young adults. Despite the high incidence of PSP and the availability of several international guidelines for its diagnosis and treatment, a significant behavioural heterogeneity can be found among those management recommendations. A working group of the Italian Society of Thoracic Surgery summarized the best evidence available on PSP management with the methodological tool of a systematic review assessing the quality of previously published guidelines with the Appraisal of Guidelines for Research and Evaluation (AGREE) II. Concerning PSP physiopathology, the literature seems to be equally divided between those who support the hypothesis of a direct correlation between changes in atmospheric pressure and temperature and the incidence of PSP, so it is not currently possible to confirm or reject this theory with reasonable certainty. Regarding the choice between conservative treatment and chest drainage in the first episode, there is no evidence on whether one option is superior to the other. Video-assisted thoracic surgery represents the most common and preferred surgical approach. A primary surgical approach to patients with their first PSP seems to guarantee a lower recurrence rate than that of a primary approach consisting of a chest drainage positioning; conversely, the percentage of futile surgical interventions that would entail this aggressive attitude must be carefully evaluated. Surgical pleurodesis is recommended and frequently performed to limit recurrences; talc poudrage offers efficient pleurodesis, but a considerable number of surgeons are concerned about administering this inert material to young patients.

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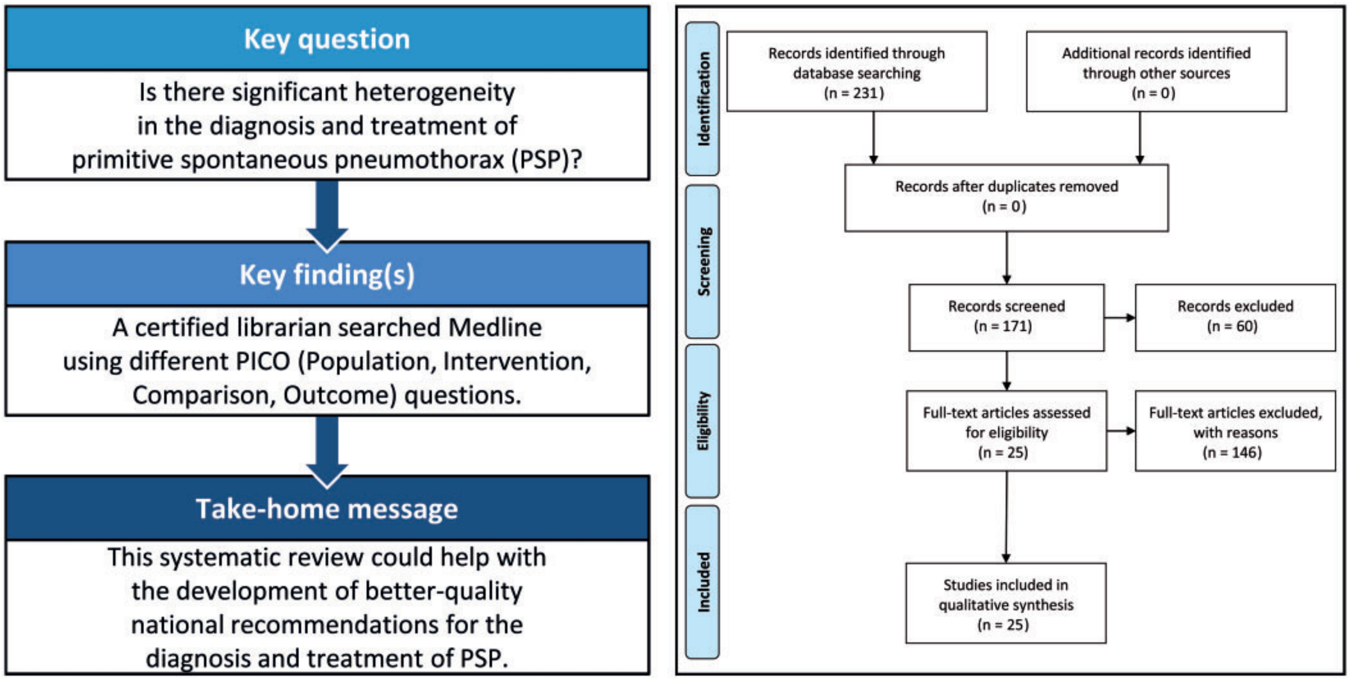

Keywords: Primary spontaneous pneumothorax • Diagnostic imaging • Conservative treatment • Thoracic surgery • Video-assisted • Systematic review • Guidelines

ABBREVIATIONS

CT	Computed tomography
PSP	Primary spontaneous pneumothorax
VATS	Video-assisted thoracic surgery

INTRODUCTION

A primary spontaneous pneumothorax (PSP) is one of the most common thoracic diseases affecting adolescents and young adults, having an annual incidence ranging from 15.5 to 22.7 per 100 000 people and with a women/men ratio ranging from 1:3.3 to 1:5 [1, 2]. The clinical course of PSP is variable with a recurrence rate ranging from 25% to 54%. The presence of underlying chronic lung disease (e.g. chronic obstructive pulmonary disease) seems to be a significant determinant of recurrence [3]. Although PSP arises in patients without clinically evident lung disease, most PSP patients have emphysema-like changes in the lung parenchyma [4].

Nevertheless, the role of bullae and blebs as the only cause of PSP is questionable, as it is only demonstrated in about 20% of patients [5]. Pleural porosity diagnosed at the periphery of both lungs during fluorescein-enhanced autofluorescence thoracoscopy was proposed as another cause of PSP [6]. Peripheral airway obstruction with air trapping is also supposed to play a role in the pathogenesis of PSP [7].

Despite the high incidence of PSP and the availability of several international guidelines regarding its diagnosis and treatment, a significant behavioural heterogeneity can be found among those management recommendations. Nowadays, in clinical practice, treatment of PSP is carried out by a broad spectrum of physicians: general practitioners, emergency room and intensive care physicians, general surgeons, thoracic surgeons and pulmonologists. Moreover, several studies determined the level of adherence to the current guidelines in clinical practice and found significant heterogeneity in indications and modalities of pleural drainage positioning. Therefore, the management of PSP deviates from the current guidelines in potentially important aspects [8, 9]. On the other hand, patients' preferences, surgeons' perspectives and local resources available could determine significant variations in the management of PSP. Clinical guidelines with clear structure and presentation might help reducing discrepancies in the management of this pathology and improve its quality of care.

Since 2017, the Italian Ministry of Health has tried to delineate good medical conduct through recommendations, guidelines and good clinical practices [10]. The Italian Society of Thoracic Surgery, endorsed by the Italian Ministry of Health, created a working group with the ultimate aim of establishing the national recommendations for the diagnosis and treatment of PSP.

The first accomplished step of the group was the use of the Appraisal of Guidelines for Research and Evaluation (AGREE) II tool to assess the quality of the previously published guidelines, finding the best methodological quality conveyed in the British Thoracic Society (BTS) and the European Respiratory Society guidelines [11]. The second step of the working group was to summarize the best evidence available on PSP through the methodological tool of the systematic review. This systematic review was also propaedeutically carried out to help the development of better-quality national recommendations for the diagnosis and treatment of spontaneous pneumothorax. The Italian Society of Thoracic Surgery working group, in association with the Italian Polyspecialistic Society of Young Surgeons, designed the review under the supervision of senior thoracic surgeons.

MATERIALS AND METHODS

The authors performed the systematic review according to the Preferred Reporting Items for the Systematic Review and Meta-Analyses (PRISMA) statement [12]. A completed PRISMA checklist is available in the Supplementary Material. The protocol has been registered (CRD42018084247) in the International Prospective Register of Systematic Reviews (PROSPERO) (https://www.crd.york.ac.uk/prospero/).

Search strategy

In May 2019, a certified librarian performed certified research on published articles. The main search terms were chosen from Mesh Terms combined by appropriate Boolean logical operators in the electronic database Medline (PubMed). The search was limited to adolescent or adult human patients, English language and availability of full-text manuscripts. A manual search of the reference lists of retrieved studies was also performed to identify any other possible studies meeting the requirements (Supplementary Material). The electronic searches were performed according to the following PICO (Population, Intervention, Comparison and Outcome) questions:

1. Should cannabis or hashish smoking habits be related to PSP epidemiology?
2. Should weather or pollution factors be related to PSP epidemiology?
3. Should the chest X-ray or chest ultrasound be used to diagnose the presence of air in suspected PSP?
4. Should the chest computed tomography (CT) scan or Magnetic Resonance be used to diagnose blebs or bullae in PSP?
5. Should observation/conservative treatment or chest drainage be an accurate treatment of PSP?
6. Should chest aspiration or drainage be an accurate treatment of PSP?
7. Should video-assisted thoracic surgery (VATS) or thoracotomy be used as surgical access to PSP?
8. Should talc pleurodesis or surgical pleurodesis be used for surgical treatment of PSP?
9. Should bullectomy/blebectomy or no lung resection be used for surgical treatment of PSP?

The working group was subdivided into 4 subgroups: 2 investigators for every subgroup manually screened the articles resulting from the search. The disagreements between the reviewers were resolved by discussion with a third senior investigator.

RESULTS

Cannabis

The correlation between marijuana smoking and the PSP onset was first reported in 1984 [13]. Beshay *et al.* [14] concluded that pulmonary emphysema was more frequent and worse in marijuana smokers than in tobacco smokers. Histology showed severe lung emphysema, inflammation and heavily pigmented macrophages in marijuana smokers. No reduction in respiratory function was highlighted in the 2 groups. Hii *et al.* [15] found a bullous alteration of the middle and upper lung fields with earlier onset of symptoms in chronic marijuana smokers and only a slight reduction in pulmonary function. However, an increase in particle deposition and consequent immunoreactive response with barotrauma was recorded. Fiorelli *et al.* [16] investigated the correlation between cannabis and bullae formation. The age of PSP onset was minor in the marijuana-smoking group with a higher incidence of paraseptal bubbles, more likely in the upper lobes, with the absence of emphysema. The pathological findings showed a more significant presence of inflammatory cells. Hedevang Olesen *et al.* [17] noted a significantly increased risk of PSP occurrence in marijuana daily smokers compared with non-smokers. Smoking cannabis and tobacco increased the risk of PSP significantly in men, suggesting a direct correlation and a potentiating effect. Ruppert *et al.* [18], comparing the CT scan findings in PSP depending on cannabis consumption, detected emphysema in 71.9% of tobacco/cannabis smokers and in only 7.7% of non-smokers. Emphysema was significantly present in younger people, suggesting a detrimental role of cannabis use.

The limitations of these studies are related to the small number of patients recruited and the relatively small population evaluated; there is no clear distinction between cannabis smokers and tobacco plus cannabis smokers. Furthermore, data reported could suffer from an underestimation bias since it is common not to declare marijuana use, either for fear of prejudice or because it is illegal in some countries. Moreover, none of the studies evaluated takes the method of cannabinoid intake into account, which often involves the drug being rolled into paper sheets burned and smoked without using a proper filter; only one paper investigated the problem of bong smokers [19].

Pollutants and meteorological parameters

No statistically significant differences were found in the evidence-based literature when relating different meteorological parameters and PSP incidence [1, 20–26] (Table 1).

In 1989, Scott *et al.* [27] found that PSP more often occurred when a fall in atmospheric pressure happened 4 days prior to the onset of symptoms. Noppen *et al.* [28] first reported the relationship between exposure to loud music and PSP, reporting that being too close to sources of loud sounds can be considered as a miniature variant of 'repetitive blasts' causing a lung blast injury.

Bulajich *et al.* [29] in a retrospective study found a significant influence of an anticyclone with hot and dry weather on PSP incidence, the presence of a cold air front and the passing of the cold front. A Turkish group found a higher incidence of PSP on rainy days when the atmospheric pressure 1 and 2 days before the diagnosis was significantly lower. It was also found that the maximum temperature level was significantly lower on the day of admission for PSP [30].

Chen *et al.* [31] found that the relative humidity was positively associated with the monthly incidence of PSP in men, while in women ambient temperature and rainfall were significantly associated with PSP events.

The study of Spasic *et al.* [32] in Serbia, although unclear, showed a certain degree of relationship between climate and PSP.

Table 1: Should cannabis or hashish smoking habits be related to PSP epidemiology?

First author	Number of patients	Mean age (years)	Results
Beshay	177	25 (16–46)	• In marijuana smokers, there was higher evidence of pulmonary emphysema than in tobacco smokers • Histology of severe emphysema, with inflammation and pigmented macrophages • The time frame smoking of marijuana in the worsening of emphysema seems relevant
Hill	10	40 (37–51)	• Prevalent bullous alteration of medium and upper lung fields compared to COPD with earlier onset of symptoms • Higher inspiratory volume (+70%) with an increased particle deposition and a consequent immunoreactive response (macrophage dysfunction and immune system depression) as well as barotrauma
Fiorelli	153	26 (19–45)	• Lower average age of first episode in marijuana smokers than non-smokers • Paraseptal bullae, mostly in the upper lobes with absence of emphysema and alpha-1 antitrypsin values in range in smokers • Histiocytic accumulation (predominant inflammatory reaction) and haemorrhagic accumulation in marijuana and cocaine users
Kepka	915	Not reported	• There are no statistically significant factors that increase the risk of PSP
Hedevang Olesen	416	28 (13–40)	• Indifferent involvement of right, left or both lungs • No differences in BMI between males and females • Confirmation of the increased risk of pneumothorax associated with tobacco smoke but also increased risk of pneumothorax in tobacco and cannabis smokers • No difference in non-smokers compared to cannabis smokers in the last month alone (reduced consumption)
Ruppert	83	33 (27–44)	• Lower age in marijuana smokers compared to tobacco-only smokers (30 vs 36.5) • In the cannabis smoking group earlier blebs and bullae formation with prevalent upper lobes distribution

COPD: chronic obstructive pulmonary disease; PSP: primary spontaneous pneumothorax.

Obuchi *et al.* [33] found that a decrease in hours of sunshine, an increase in average temperatures 2 days before the occurrence and the days following a thunderstorm with lightning all significantly correlated with PSP occurrence. Zhang *et al.* [34] found that the occurrence of PSP was associated with the solar terms 'Spring Equinox' (early April) and 'End of Heat' (early September). The term with the lowest incidence was 'Great Snow' (end of December). Haga *et al.* [35] observed a decrease in the average atmospheric pressure when comparing the previous days and the day of onset of PSP and an average increase in atmospheric pressure in days without PSP. Díaz *et al.* [36] found that on the days when pneumothorax occurred the mean atmospheric pressure was higher than the average monthly pressure. Bertolaccini *et al.* [37] found that the variables that had the most considerable influence on the onset of PSP were temperature anomaly, the mean wind, the minimum air-concentration of ozone and the maximum air-concentration of nitrogen dioxide. Lastly, Araz *et al.* [38] found no correlations between the effects of the lunar cycle and daily weather changes on PSP development. In 2018, Motono *et al.* [39] found a statistically significant association between atmospheric temperature >25°C and the occurrence of PSP but no correlation between atmospheric pressure and occurrence of PSP.

Some limitations emerged: most papers do not consider the smoking history of patients, nor their body mass index or physical shape, and this could have led to a strong bias in the population selection. In a significant part of the articles, authors included only PSP patients who were treated in surgical departments, thus leaving out all those episodes that require only medical observation or minor interventions, therefore underestimating the extent of the problem. Lastly, articles dealing with relationships between weather and PSP occurrence in specific regions or even cities suffer, inevitably, from a geographical limitation.

Imaging

Garofalo *et al.* [40] evaluated the effectiveness of ultrasound by comparing chest radiography with CT scan used for the diagnosis of pneumothorax and reported that ultrasound had a sensitivity and specificity of 95.65% and 100%, respectively, and diagnostic effectiveness of 98.91%. More recently, Jalli *et al.* [41] prospectively compared the accuracy of ultrasound with chest radiography in the detection of pneumothorax, using a CT scan as the reference standard. The sensitivity and specificity in the detection of PSP were 80.4% and 89%, respectively, with an overall accuracy of 85%.

Karagoz *et al.* [42], in a prospective blinded study, stated that bedside chest ultrasound could be safely used in the follow-up of selected patients affected by pneumothorax and treated with tube thoracostomy, with a sensitivity and specificity of 95.6% and 100%, respectively.

Karacabey *et al.* [43] showed a high sensitivity (97.5%) and specificity (100%) of ultrasound in the detection of pleural sliding to differentiate the presence of bullae from a pneumothorax. Urbaneja *et al.* [44] revealed the improvement of sensitivity in the detection of pneumothorax using digital radiography with bone subtraction compared to a standard chest X-Ray.

A retrospective review by Laituri *et al.* [45] concluded that chest CT does not appear to be specific in the identification of pleural blebs, and operative decisions should be based on clinical judgment. Kim [46] observed that the preoperative detection of emphysema-like changes on the axial-coronal combined view was significantly higher than on the conventional axial view alone. Moreover, Lee *et al.* [47] reported better sensitivity of high-resolution CT over routine CT in preoperative detection of blebs and bullae. These results suggest that high-resolution CT may improve the identification of blebs or bullae and may help to treat spontaneous pneumothorax successfully.

Table 2: Should weather or pollution factors be related to PSP epidemiology?

First author	Number of patients	Mean age (years)	Results
Primrose	148	NA	• Fewer admissions during May, June and July • Higher incidence in males • Smoking is highly associated with PSP
Scott	192	39.2 ± 1.8	• A fall in atmospheric pressure below the fifth, or a rise above the ninety-fifth percentile was marked as 'unusual'. Most of the reported cases had been exposed to at least one 'unusual' episode in the 4 days prior to the onset of PSP • PSP occurrence was significantly more frequent among those with 4 or more 'unusual' exposures suggesting a strong correlation
Smit	115	NA	• No statistically significant result was found relating atmospheric pressure differences to PSP • Increase in average temperature the day before the occurrence of pneumothorax compared with a 0.08°C fall on the days with no onset of PSP • No correlations emerged from the analysis of PSP onset on days with thunderstorms while there were on the following day, and on the 2 days following a thunderstorm • Presence of clusters of incidence of PSP was also noted
Suarez-Varela	62	15–77	• No association between the development of PSP and changes in atmospheric pressure was found
Gupta	22.749	NA	• Weekly incidence of emergency admissions for pneumothorax showed no seasonal pattern (data not fully displayed in the article)
Noppen	4	19–24	• A correlation between loud music exposure and PSP occurrence is suggested
Bulajich	659	NA	• No relation between atmospheric pressure or temperature changes and PSP onset was found • Significant influence on PSP by the presence of an anticyclone with hot and dry weather, the presence of a cold air front and the passing of the cold front
Ayed	254	24.5 ± 5.8	• No significant relationship between PSP and variations in atmospheric pressure, humidity or temperature • Significant increase in incidence of PSP was noted during July. The major risk factors of PSP are smoking, low BMI and male gender.
Mohebbi	2235	26.43 ± 5.85	• The decline in respiratory function (linked to silicosis) could be a PSP predictive factor
Ozpolat	669	34.0 ± 15.5	• Greater incidence of PSP in periods with more rainy days • Average rainfall amount on the day of onset, 1 day before and 2 days before hospitalization for PSP was significantly higher in cluster days • Higher incidence of PSP was detected when the atmospheric pressure was lower in the days before the diagnosis • Maximum temperature was lower on the day of admission for PSP in periods with higher incidence • Lower incidence of PSP in periods with the highest thermal excursion
Celik	175	NA	• No relevant relationship between mean atmospheric pressure, variation of daily atmospheric pressure, relative humidity and PSP occurrence was found • Mean temperature differences showed significant relation with PSP onset • No PSP incidence difference was observed among seasons and months • No statistically significant differences between first and second episode of PSP were noted regarding atmospheric pressure and average temperature
Schieman	149	29	• No significant differences in the rate of PSP on chinook days versus non-chinook days • No significant differences in the rate of PSP among seasons • No influence of mean temperature or mean relative humidity on PSP • Higher average wind speed and lower mean atmospheric pressure on days with PSP occurrence
Chen	8575	15–44	• The incidence of PSP was not significantly associated with either seasons or months • No association with average atmospheric pressure, relative humidity, average temperature, sun hours per day, precipitation or monthly trend • Relative humidity was positively associated with the monthly incidence of PSP while ambient temperature and rainfall were significantly associated with PSP events in women
Spasić	159	NA	• Most cases occurred in March and December compared to the remaining months • Biometeorological phase 2 (Cyclone, Warm, Wet), 3 (Cyclone, Warm Front) and 9 (Anticyclone, Hot, Dry) • The lowest number of cases occurred in September and in phase 8 (Anticyclone, Cold, Wet) • A certain degree of relationship between climate and PSP
Obuchi	317	31.3 (14–86)	• No significant differences between days with and without occurrence of PSP in terms of atmospheric pressure, rain amount, average temperature, maximum and minimum or average and minimum humidity • Multivariate analysis instead revealed that a decrease in hours of sunshine, an increase in average temperatures 2 days before occurrence and the days following a thunderstorm with lightning were all significantly correlated with the occurrence of pneumothorax
Zhang	337	30.53 ± 2.41	• PSP was associated with days of higher temperature and lower atmospheric pressure • The occurrence of PSP was associated with the solar terms Spring Equinox (early April) and End of Heat (early September); the term with the lowest incidence was 'Great Snow' (end of December) • No significant influence of average humidity and wind speed on PSP was found
Haga	1051	29.3 ± 12.8	• Decrease of average atmospheric pressure was found in the days just before PSP onset • An increase of atmospheric pressure was observed in days without PSP • The difference in mean air pressure between the previous days and the day of onset of PSP was lower than that on the days when no PSP occurred

Continued

Table 2: Continued

First author	Number of patients	Mean age (years)	Results
			• No statistical differences were found in terms of temperature, hours of sunshine, amount of precipitation and humidity between days with and without PSP • No association was found between the presence of lightning and the occurrence of PSP
Díaz	288	30.7 ± 13	• The mean atmospheric pressure on the days when pneumothorax occurred was higher than the average monthly pressure • More than expected cases were observed in a normal distribution in January, February and September and smaller numbers in April • The risk increases by 1.15 times for each hPa (hectopascal) of increasing atmospheric pressure, regardless of gender, age and mean monthly pressure
Bertolaccini	451	32 ± 12	• PSP was not correlated with annual, seasonal or monthly cycles • Max temperature, temperature anomalies, atmospheric ozone concentration and anomalies are the most correlated to PSP • The variables that had the greatest influence on the onset of PSP were the temperature anomaly, the mean wind, the minimum concentration of O_3 and the maximum concentration of NO_2
Bobbio	42 595	39 ± 20	• No significant monthly or seasonal variation in distribution • Mean age was significantly higher in women than in men
Heyndrickx	106	24.8 ± 4.86	• Different incidence of PSP not statistically significant among seasons • No significant differences based on the different climatic parameters tested • No threshold value in atmospheric variation can be used to determine the onset of PSP • Changes in relative humidity, rain, wind speed and mean temperature did not show statistical significance
Araz	131	32.4 ± 12.2	• Highest rate at the end of the summer and during the autumn peak in September • The incidence was statistically related to mean atmospheric pressure, relative humidity and external temperature • No correlation with the lunar phases

BMI: body mass index; NA: not reported; PSP: primary spontaneous pneumothorax.

Although CT scanning is the best method to measure the size of the pneumothorax, a precise measurement could have a relative clinical value. The estimation of the size of the PSP is traditionally based on the Light index calculated on the chest roentgenogram. The light index is based on the proportional relationship between the diameters of a collapsed lung and its hemithorax:

$$\text{Estimated pneumothorax percentage} = 100 \times \left(1 - \frac{L^3}{H^3}\right)$$

where H = hemithorax diameter and L = diameter of the collapsed lung [48]. The BTS guidelines acknowledged that the plain radiograph is a poor method of quantifying the size of pneumothorax, yet then went on to use 1 radiographic method of assessment to estimate the degree of lung collapse [49]. The size of a pneumothorax is classified into 'small' or 'large' depending on the presence of a visible rim of <2 cm or ≥2 cm between the lung margin and the chest wall. There is considerable variability in previous international guidelines concerning the treatment of pneumothorax. There is general agreement on the idea that treatment is always required for clinically compromised patients. For clinically stable patients, treatment recommendations have been based, at least partially, on the size of the pneumothorax ('small' or 'large'), although the definition of a large pneumothorax differs among guidelines. A study comparing the size classifications used by the different guidelines demonstrated poor agreement between them, and there is no current evidence to support the approach of treatment decisions based on the size of pneumothorax alone. Most physicians adopt a symptom-driven approach, with close follow-up to ensure resolution, rather than basing initial management on the PSP's size alone [50].

Conservative treatment

The possibility to submit pneumothorax to observation or intervention is a matter of choice, currently related to personal inclination and local policy.

Ashby *et al.* [51] found that there is no possibility to conclude whether conservative treatment is superior to interventional treatment. Besides, analysis of the risk of bias is misplaced eventually. Regarding the interventional treatment, the indication to evacuate the air volume from the pleural space can be conducted using aspiration or chest tube. A permanent catheter is more often suggested rather than simple aspiration. To evaluate which option is to be favoured over the other, 7 papers have been analysed. Aspiration was found to be less probably successful by Andrivet *et al.* [52], although similar hospital stays and recurrence rate after 3 months were described alongside. Parlak *et al.* [53] randomly submitted patients with the first episode of pneumothorax, symptomatic or asymptomatic, to aspiration or chest tube and found an immediate success rate of 68.0% and 80.6%, respectively. Reduced hospital stays and recurrence rates were also described but it has to be noted that the study was underpowered because recruitment fell short of expectation. Another randomized trial added pain evaluation as an objective of the study; aspiration seemed to be less painful than drainage positioning. Overall, effectiveness, recurrence and immediate resolution of the pneumothorax were similar between the 2 techniques [54]. Thelle and Bakke [55] designed a randomized trial on PSP to be treated through aspiration or chest tube placement, excluding complicated settings (tension pneumothorax, bilateral pneumothorax, recurrence and need for ventilator assistance). Therapeutic success was significantly higher after aspiration in the immediate setting, it was similar for both techniques after a

1-week evaluation with a two-fold longer hospital stay after chest tube placement. Complications did not arise in patients treated with aspiration while they were described for those treated with a chest tube placement. However, a significant limitation to this result was the presence of a volume discrepancy of pneumothorax entity between the 2 groups of patients. Moreover, the use of a certain tube calibre may have influenced the complication rate. In a 2010 systematic review and meta-analysis, drainage appeared superior to aspiration when treating the first episode of PSP and the time-lapse to a second event did not vary between the 2 differently treated groups of patients [56]. In a retrospective monocentric study, Hofmann *et al.* [57] conclude that the recurrence rate of PSP is significantly lower after VATS compared with a primary conservative approach. Besides, a Danish multicentre randomized trial identified the presence of large bullae as an independent risk factor for the recurrence of PSP [58].

Surgery

When looking for the best surgical approach to PSP and comparing VATS and thoracotomy, the answer seems simple and predictable. Almost all groups perform surgical procedures for PSP using VATS, with excellent results in terms of the low rate of recurrence after surgery, length of hospitalization, functional recovery and cosmetic results [59–62]. However, in a study reporting data from the Epithor (French database), the incidence of recurrence after surgery was lower in the thoracotomy group compared to the VATS group [63]. A Randomized Controlled Trial concludes that uniportal VATS approach is less painful besides being as efficient as 2- or 3-portal VATS approaches PSP [64].

In a young population, performing talc pleurodesis instead of surgical pleurodesis (several types: pleural abrasion, pleurectomy, pleural tent) showed several complications in the short-term (Acute Respiratory Distress Syndrome) and consequences in the long term (respiratory function, oncological issues, difficulties in successively needed thoracic surgical interventions). In terms of results (prevention of recurrences), the 2 procedures were equivalent. Talc pleurodesis is reported to offer excellent results (even if a comparative study has not been carried out yet), but it should not be preferred in a young population [65, 66]. Regarding the possibility to cover the staple line in blebs/bullae resection, there are no evident differences in using 2 different materials such as polyglycolic acid and regenerated cellulose mesh in terms of PSP recurrence [64]. When blebs or bullae are detected on a CT scan or surgical view, their resection is always required because of increased risk of recurrences [67]. Furthermore, a recent Japanese cohort study showed that the neo-formation of neo-genetic bullae after bullae resection for PSP is not prevented by adding coverage of the staple line to the resection itself [68].

DISCUSSION

The purpose of this review was to summarize the best evidence available on PSP. The main finding was the paucity of high-quality, prospective, randomized trials. Current literature mainly comprised single-institution case series. To the best of our knowledge, this is the first systematic review assessing several PICO questions about epidemiology, diagnosis and management of PSP. Over the past years, only a few papers on randomized trials of surgical techniques in the management of PSP were available for inclusion in this analysis. The need for high-quality, multicentre, prospective randomized trials assessing the efficacy of different interventions is still needed. The ideal prospective randomized trial would include interventional arms that are safe, commonly performed and effective at reducing future risk of recurrence [69].

Our paper presents several limitations. First, it is a systematic review of mainly case series, with a consequent increased risk of selection bias. Likely, there is a certain amount of heterogeneity within patient populations and intervention groups, and this has implications for the external validity of the study. Some treatment groups comprised a small number of published studies and were therefore subject to reporting bias.

CONCLUSIONS

Cannabis smoking is associated with an increased risk of developing bullae and subsequent PSP due to the smoking method, which can lead to increased intrabronchial pressure and the accumulation of pigments inside macrophages. Concerning PSP physiopathology, it is not currently possible to confirm or reject the hypothesis of a direct correlation between changes in atmospheric pressure and temperature and incidence of PSP.

The high-resolution ultrasound scan is significantly more sensitive to pneumothorax detection (especially for minimal pneumothoraces) when compared to standard chest radiography. A chest roentgenogram seems to have a higher specificity than the ultrasound scan for PSP entity estimation. A high-resolution ultrasound scan performed by a trained physician can be helpful for a quick diagnosis of PSP in the emergency department.

Regarding the choice between conservative treatment and chest drainage in the first episode, there is no evidence on whether 1 option is superior to the other. When a decision towards an intervention is taken, aspiration is an agile approach and it is associated with good results, but a permanent chest tube would give a more reliable outcome with no reported effects on the risk of recurrence. VATS represents the most common and preferred surgical approach to treat the PSP. In case of the presence of blebs or bullae, their removal is strongly suggested to reduce the incidence of recurrence; in Vanderschueren's stage I (no endoscopic abnormalities), pulmonary resection may not be required [70]. Surgical pleurodesis (pleural abrasion, pleurectomy, pleural tent) is recommended to limit recurrences.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *ICVTS* online.

Conflict of interest: none declared.

Author contributions

Paolo Mendogni: Conceptualization; Data curation; Formal analysis; Investigation; Supervision; Validation; Visualization; Writing—original draft; Writing—review & editing. **Jacopo Vannucci:** Data curation; Writing—original draft; Writing—review & editing. **Marco Ghisalberti:** Data curation; Writing–

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