ORIGINAL ARTICLE

Longer symptom onset to aspiration time predicts success of needle aspiration in primary spontaneous pneumothorax

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Received 1 February 2019
Revised 22 May 2019
Accepted 26 May 2019
Published Online First
12 June 2019

ABSTRACT

Background Needle aspiration (NA) is recommended as first-line treatment of primary spontaneous pneumothorax (PSP). We aimed to assess NA success and the effect of a longer symptom onset to NA time.

Methods A discovery phase was retrospectively conducted in the intensive care unit of Louis Mourier Hospital (January 2000 to December 2011) followed by a prospective validation cohort (January 2012 to August 2015). The primary outcome was immediate NA success defined by the absence of need for chest tube insertion within 24 hours of the procedure.

Results In the discovery phase, 130 patients were admitted for PSP and 98 had NA as first-line treatment (75%). The immediate success rate of NA was 34.7% and was higher when it was performed ≥48 hours after symptom onset (57.7% vs 25%; p=0.004). In the prospective cohort, 87 patients were admitted for PSP; 71 (82%) had NA as first-step treatment. The immediate success rate was 40.8%. NA was more successful when it was performed after 48 hours of symptoms' onset (34.5% vs 7.1%; p=0.005). A delay between the first symptom and NA procedure ≥48 hours was associated with a higher success of NA (OR=13.54; 95% CI 1.37 to 133). A smaller pneumothorax estimated by Light's index was associated with NA success (OR=0.95; 95% CI 0.92 to 0.98). To what extent some of these pneumothoraces would have had a spontaneous resolution remains unknown.

Conclusion When managing PSP with NA, a longer symptom onset to NA time was associated with NA success.

Trial registration number NCT02528734.

Key messages

What is the key question?

- Does a delay in needle aspiration (NA) treatment of primary spontaneous pneumothorax (PSP) increases its efficacy?

What is the bottom line?

- A longer symptom onset to NA time was found associated with its success in both the discovery and validation phases of our cohort study. Pneumothorax size was also associated with NA success.

Why read on?

- Our data suggest that a delayed NA strategy for the management of PSP could be tested. In this case, a 48 hours delay before performing the NA might increase success rates.

INTRODUCTION

Management of primary spontaneous pneumothorax (PSP) remains debated.[1 2] In British guidelines, needle aspiration (NA) is the recommended first-step[1] in all PSP requiring a therapeutic intervention. A large pneumothorax (defined by an interpleural distance >2 cm at the level of pulmonary hilum) or a small one but occurring in a symptomatic patient are the two main indications for NA,[1 3] while asymptomatic patients with a small PSP may be simply looked upon.

NA has undisputable advantages: fewer hospitalisations, decreased length of hospital stay[4] and less pain.[5] Adverse events, such as subcutaneous emphysema, vasovagal reaction, pneumonia and hemothorax, are rare.[6] Success rates range between 32% and 83%; and the risk of a recurrence is similar to the one of chest tube drainage.[4 7 8] Factors associated with its success have, however, been scarcely investigated. NA failure has been found to be significantly associated with an increased age[9] and the size of the pneumothorax.[6 10–12] The timing of NA to pneumothorax diagnosis has been assessed in a single study, and delaying NA for 3 days had not been significantly associated with its success.[13] Nevertheless, mean delay of hospital admission after symptoms was already 2 days in patients treated with immediate NA.

We therefore thought to investigate the potential relationship between pneumothorax duration prior to NA and the success of NA.

METHODS

Patients

A two-phase cohort study was conducted in our 5-bed intermediate and 12-bed intensive care units (ICUs). The retrospective phase (from January 2000 to December 2011) served as a discovery cohort and the prospective one (from January 2012 to August 2015) as a validation cohort.

To cite: Vuillard C, Dib F, Achamlal J, *et al*. *Thorax* 2019;**74**:780–786.

Discovery cohort

The patients from this retrospective cohort were identified over a 12-year period, through our intermediate care and ICU electronic databases. All subjects aged 18 years or more with a discharge diagnosis containing the 'spontaneous pneumothorax' label (J93.0 International Classification of Diseases (ICD)-10 label) were considered eligible and their records assessed. Only those treated with NA were retained for the study.

Validation cohort

Patients from this prospective cohort were eligible if they were aged 18 years or more and admitted for a spontaneous pneumothorax in the intermediate care or the ICU. Those that subsequently underwent a first-line NA were included, unless they refused to participate. In case of multiple episodes, only the first one was collected. The patients were followed-up after hospital discharge during the following year.

Ethics

Data were collected anonymously, and the electronic files were used according to French law ('Informatique et Libertés'). The Ethics Committee of the French National Society of Intensive Care (SRLF, CE 12-364 and 14-08) waived informed consent since the use of NA as first-line treatment of PSP is part of our routine practice. However, subjects and/or families were informed of the study, its purpose and objectives.

Outcomes

The primary outcome of interest was immediate NA success defined in this study by the absence of need for chest tube insertion within the 24 hours following NA.

Secondary endpoints were (i) late success, defined as the absence of chest tube insertion within 7 days; (ii) length of ICU stay; (iii) need for surgical pleurodesis because of persistent or worsening pneumothorax and (iv) occurrence of any short-term complications, that is, hemothorax (defined as haematic pleural effusion requiring thoracic drainage), *a vacuo* pulmonary oedema (defined as occurrence of localised alveolar interstitial opacities on post-procedure chest X-ray) or chest tube insertion site infection (presence of purulent secretions outpouring from chest tube insertion site).

Additionally, the following endpoints were also recorded in the validation cohort: (i) recurrences after 1 month; (ii) length of ICU stay; (iii) length of hospital stay and (iv) maximal patient self-reported pain during procedure (NA or chest tube insertion) with the use of a numeric scale from 0 (no pain) to 10 (worst possible pain).

NA procedure

A first-line NA was performed, as soon as possible after ICU admission, in patients with a large pneumothorax defined by an interpleural distance of more than 2 cm and/or when patients were symptomatic, according to published guidelines.[1]

As usually performed in our units, and previously described,[13] NA procedure used a 20–22 G catheter (Microdard Prodimed, Le Plessis-Bouchard, France). The whole procedure was performed under continuous cardiac and oxygen pulse saturation monitoring. After skin disinfection and local anaesthesia, the catheter was inserted approximately 3–5 cm into the third intercostal space, in the midclavicular line, with patients placed in a semi-recumbent position; the catheter was then connected to a bottle water-seal vacuum system, filled with a Dakin solution to visualise the bubbling, allowing the generation of a −20 cm H_2O pressure. Aspiration was performed until the cessation of bubbling, for a maximum of 15 min; in case of cough, the catheter was gently retrieved until its complete removal. A chest X-ray was performed immediately after aspiration. If lung re-expansion was complete, or if the interpleural distance decreased to less than 2 cm, the patient remained hospitalised for at least 12 hours. A chest X-ray was then performed to allow for discharge or not. Patients were informed of the therapeutic strategy in case of recurrence. They were invited to have their chest X-ray checked after 48 hours. In case of NA failure (defined as an interpleural distance >2 cm), patients underwent a 16–20 French chest tube placement (Trocar catheter, Redax, Poggio Rusco, Italy), left under a −20 cm H_2O depression for a minimum of 24 hours after the last bubbles were seen. The chest tube was withdrawn if the chest X-ray showed no pneumothorax recurrence after being clamped for a 2-hour period. Surgical pleurodesis was considered if bubbling persisted for more than 72 hours.

Data collection

Anamnestic and clinical data were retrieved from patient's records for the retrospective phase, and otherwise collected prospectively. The demographic and clinical factors explored were age, sex, smoking status, body mass index, the presence of a known underlying lung disease at pneumothorax diagnosis, previous history of pneumothorax and interval from symptom onset to aspiration. Symptom onset to aspiration time was defined as the onset of symptoms suggestive of pneumothorax (such as chest pain, dyspnoea or cough) to the time of NA. Time and type of symptoms were recorded. The abundance of the pneumothorax was defined by its complete or incomplete status, and Light's index was measured.[14] During ICU stay, the need for surgical pleurodesis because of persistent or worsening pneumothorax and the occurrence of any short-term complication previously described were collected. All the patients were followed up until ICU discharge and for the following 7 days as part of our routine care. Prospective cohort patients were followed-up after hospital discharge during the following year.

Statistical analysis

Median and IQR to summarise continuous variables and the Mann-Whitney test for comparison between groups were used. Numbers of patients and percentages to summarise qualitative variables, and the χ^2 and Fisher's exact tests as appropriate for univariate comparisons of dichotomous data were used. CI for the differences of medians were computed using the PROC QUANTREG procedure of SAS V.9.3.

Time from symptoms onset to NA was considered as a binary variable (<48 vs ≥48 hours). Univariate logistic regression predicting NA aspiration immediate success was fit to determine the statistical significance of the association between time from symptoms onset to NA and immediate success of NA. The effect of the demographic and clinical variables on the success of NA was considered in a univariate analysis. Because the univariate analysis indicated that Light's index was associated with NA success, a multivariable logistic regression was used to model the effect of the delay between first symptom and NA procedure, adjusting for the effect of Light's index. All p values were two-sided and the significance was set at $p<0.05$. Analyses were performed with SAS V.9.3.

RESULTS

Discovery cohort

A total of 253 cases of pneumothorax were retrieved from the ICU database, of which 130 were PSP and 98 had NA as first-line

Table 1 Patients characteristics and outcomes of the discovery cohort (2000–2011)

	Whole cohort n=98	Immediate NA success n=33	Immediate NA failure n=65	P value
Sex (M/F), n (%)	83/15 (85/15)	27/6 (82/18)	56/9 (86/14)	0.57
Age (years)	30 (26–34)	28 (25–35)	30 (26–35)	0.26
Smoking status, n (%)	72 (73)	20 (61)	52 (80)	
*Active smokers, n (%)	69 (70.4)	19 (57.6)	50 (76.9)	0.06
*Previous smokers, n (%)	3 (3)	1 (3)	2 (30.8)	1.0
Personal history of pneumothorax, n (%)	8 (8.2)	3 (9.1)	5 (7.7)	1.0
Pneumothorax				
*Right, n (%)	56 (57.1)	18 (57.6)	38 (58.5)	0.67
*Complete, n (%)	88 (89.8)	24 (72.7)	64 (98.5)	0.002
Duration of pneumothorax prior to NA, hours	12 (6.5–48)	36 (12–76)	12 (6–32)*	0.007
Duration of pneumothorax prior to NA, days	0 (0–2)	1.5 (0–3)	0 (0–1)*	0.054
>48 hours of pneumothorax evolution prior to NA	28 (28.6)	15 (45.5)	11 (17.5)*	0.007
Late success, n (%)	31 (31.6)	31 (93.9)	–	
Need for surgical pleurodesis, n (%)	28 (28.6)	2 (6.1)	26 (40)	0.0003
Length of ICU stay (days)	3.5 (2–5)	2 (1–3)	4 (3–5)	<0.0001

Data are presented in n (%) or median (IQR) as appropriate. Late success was defined as the absence of chest tube insertion within 7 days; hemothorax was defined as haematic pleural effusion requiring thoracic drainage and *a vacuo* pulmonary oedema was defined as occurrence of localised alveolar interstitial opacities on post-procedure chest X-ray. Patient self-reported maximal pain during the NA and/or chest tube insertion procedure was evaluated with the use of a numeric scale from 0 (no pain) to 10 (worst possible pain).
*The time to NA was missing for two patients.
F, female; ICU, intensive care unit; M, male; NA, needle aspiration.

treatment. Patients' main characteristics are summarised in table 1.

The immediate success rate was 33.7% (33/98), and the late success rate of 31.6% (31/98). The median (IQR) time from symptom onset to aspiration was 12 hours (6.5–48) and was longer in patients with NA success compared with those with NA failure (36 hours (12–76) vs 12 hours (6–32), respectively; difference between medians 24; 95% CI −1.2 to 49.2). Success rate of NA was higher when it was performed 48 hours or more after symptom onset (57.7% vs 25.7%; p=0.007). The median length of ICU stay of the patients with immediate NA success (2 days) was shorter than that of the patients with immediate NA failure (4 days) (difference between medians 2; 95% CI 1.3 to 2.7).

Surgical pleurodesis was more frequently required when NA failed (40% vs 6.1%; p=0.0003).

Validation cohort

During the prospective study period, 133 patients were admitted in our units for a pneumothorax, 87 of whom had a PSP and 71 had a NA (figure 1). Median (IQR) age was 30 years (23–36) with a male predominance (82%). Pneumothorax was complete in 97% cases (n=69) with a median (IQR) Light's index of 58% (37–93) (table 2).

The immediate and late success rates of NA were 29/71 (41%) and 26/71 (37%), respectively. Three patients underwent chest tube insertion in the following week (delayed failure), all of whom required surgical pleurodesis (figure 1).

The median duration of time from symptom onset to NA in patients with NA success (29 hours) was longer than that of the patients with NA failure (10 hours) (difference between medians 19; 95% CI 0.2 to 37.5) (figure 2).

NA success rate was higher in patients who underwent the NA 48 hours or more after symptoms' onset compared with those who underwent the aspiration within the first 48 hours of symptoms' onset (34.5% vs 7.1%; p=0.005).

Patients with NA success had a smaller pneumothorax with a median Light's index of 33% vs 84% in patients with NA failure (difference between medians 47; 95% CI 24.8 to 69.5).

In patients with immediate success, Light's index did not differ according to the delay to NA (ie, 38% when NA was performed in the 48 hours, and 33% for patients in whom NA was performed after 48 hours of PSP evolution; p=0.4).

In multivariable analysis, factors associated with success of NA were a delay between the first symptom and NA procedure of 48 hours or more (OR=13.54; 95% CI 1.37 to 133) and a smaller pneumothorax size estimated by Light's index (OR=0.95; 95% CI 0.92 to 0.98).

Of the 42 patients with immediate NA failure, one was directly referred for surgery. A total of 34 (81%) underwent pleural drainage, and surgery was necessary for 17 of them. In the seven in whom a second NA was attempted, six underwent pleural drainage (five of whom underwent surgery) and one was directly referred to surgery. Thus, 23 patients with NA failure (55%) underwent a surgical pleurodesis.

ICU and hospital lengths of stay of the patients with NA success were shorter than those of the patients with NA failure (difference between medians 2, for both the lengths; 95% CI 1.2 to 2.7 for ICU length of stay and 1.1 to 2.9 for hospital length of stay) (figure 2).

There was no significant difference in recurrence rate at 1 month and 1 year between the two groups. None of the prespecified complications occurred during hospital stay.

Median maximal patient self-reported pain in patients treated with pleural drainage was 4 vs 3.6 in those with NA (p=0.09) .

DISCUSSION

In our two-phase cohort study, where NA was performed as first-line treatment for all PSP without indication for immediate drainage, main results can be summarised as follows: (i) immediate success rate of NA was 36.7%; (ii) longer symptom onset to NA time was associated with NA success in both the phases, with an increased success rate when NA was performed after 48 hours of PSP evolution and (iii) pneumothorax size was also associated with NA success.

NA is a recognised and effective method of PSP management.[1] Its main advantages over pleural drainage are the limited pain experienced by the patients (mainly because of the presence of the chest tube for a few days) and the very limited occurrence of complications, which are often minor.[1 6 15] Nevertheless, this technique remains underused in favour of pleural drainage, as evidenced by a recent survey.[16] In this international survey of 178 physicians from 27 different countries, 93% of responders declared pleural drainage as first-line

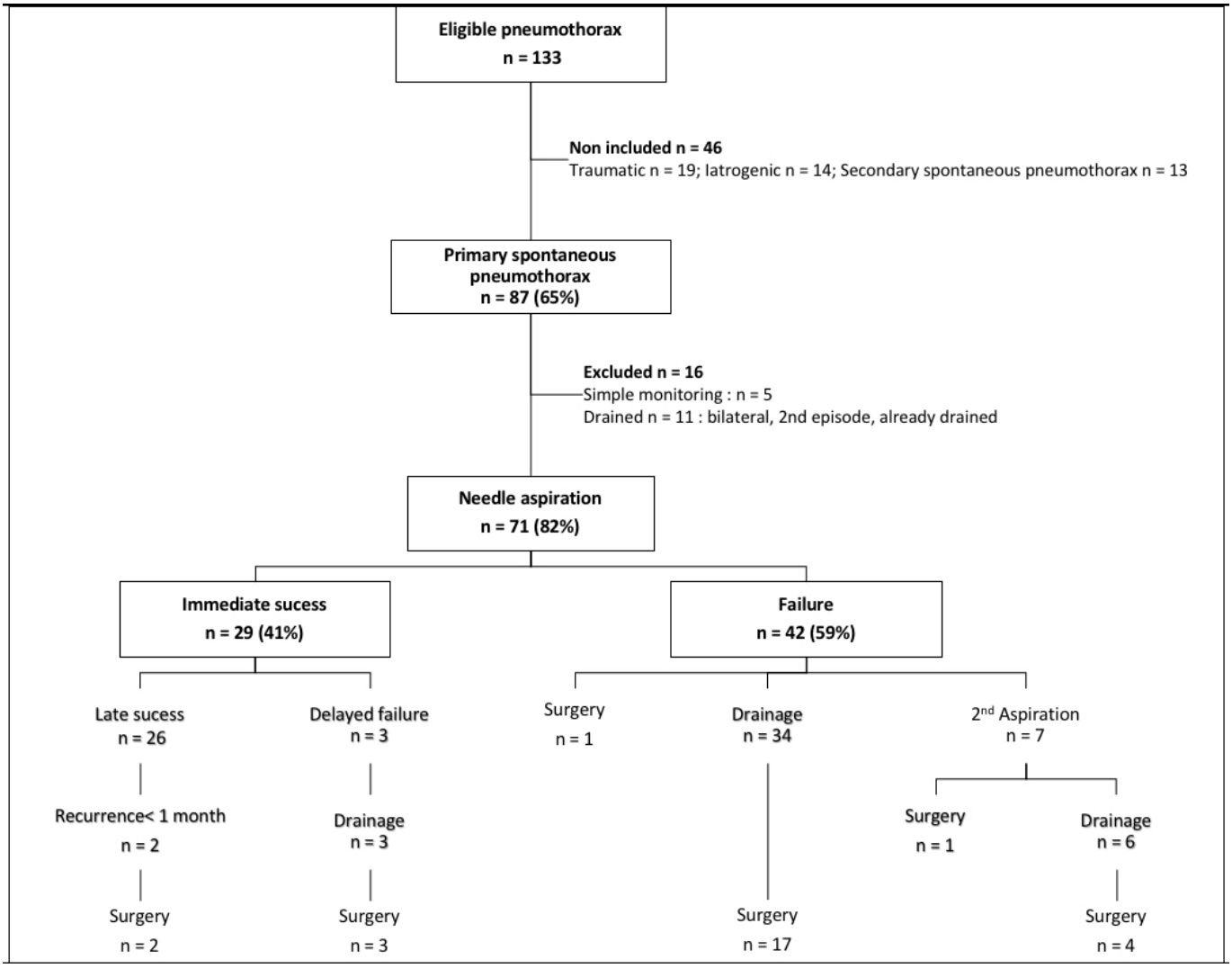

Figure 1 Flowchart of the validation cohort. A total of 133 patients had been admitted for a pneumothorax, 87 of whom had a primary spontaneous pneumothorax. Among those, 71 were treated with a needle aspiration. The immediate and late success rates were 40.8% and 38.0%, respectively.

therapy for a large PSP in a stable patient while only 7% cases suggested an NA.[16]

However, as underlined by international guidelines,[1] pleural drainage holds frequent and serious complications, ranging from subcutaneous emphysema to hemothorax,[17] expansion pulmonary oedema[18 19] and abdominal organ or diaphragm perforation.[20]

Several factors associated with NA failure have been described.[9 11 12] An age above 50 years is associated with a significant increase in failure rates. Nevertheless, one can speculate on the fact that a pneumothorax occurring in patients over 50 years is not likely to be 'primary' nor 'spontaneous', and a certain degree of underlying respiratory disease may exist.[9] The pneumothorax abundance evaluated by the volume of the evacuated air seems of paramount importance in NA success. Harvey and Prescott showed that the volume of aspirated air was significantly lower when NA was successful than when it failed (1.5±0.7 L vs 2.5±0.9 L; p<0.01).[11] This figure of 2.5 L was also the one found in a retrospective study, which showed that a volume of aspirated air exceeding 2.5 L was associated with NA failure.[12] Accordingly, 2.5 L is the threshold used by the British Thoracic Society (BTS) in 2003 as an indication of drainage.[12] The volume aspirated during NA was not measured in our study, because we used a closed circuit that does not allow for an additional syringe. A very controversial question is whether the initial radiographic size of pneumothorax is a predictor of NA failure. Harvey and Prescott showed no influence of the radiographic size of the pneumothorax on success (although the amount of air aspirated was greater in NA failure), and others showed that a large pneumothorax was associated with aspiration failure.[6 10–12]

In our study, a small pneumothorax size estimated by Light's index was associated with a success of NA. One can only hypothesised on pathophysiological mechanisms of such findings: smaller pneumothorax might be associated with less leakage, or smaller pleural breach, allowing for a better physiological pleural symphysis, and better aspiration efficiency. Finally, one cannot exclude the possibility that some of these pneumothoraces may have evolved towards spontaneous resolution.

In the discovery cohort, the median time from symptom onset to aspiration was 12 hours (6.5–48) and was significantly longer in patients with NA success (p=0.007), a finding confirmed in the validation cohort. The success rate of NA is higher when performed 48 hours or more after symptom onset in both the discovery and validation cohorts. In the

Table 2 Patients characteristics and outcomes of the validation cohort (2012–2015)

	Whole cohort n=71	Immediate NA success n=29	Immediate NA failure n=42	P value
Sex (M/F), n (%)	58/13 (82/18)	24/5 (83/17)	34/8 (81/19)	0.85
Age (years)	30 (23–36)	28 (21–32)	31 (24–38)	0.09
Body mass index (kg/m^2)	20.4 (20–23)	20 (19–22)	21 (20–23)	0.08
Smoking status, n (%)	56 (79)	21 (72)	35 (83)	
*Active smokers, n (%)	50 (70)	19 (65)	31 (73)	0.45
*Previous smokers, n (%)	6 (8)	2 (7)	4 (10)	1
Personal history of pneumothorax, n (%)	11 (15.5)	5 (17)	6 (14)	0.7
Acute respiratory failure, n (%)	3 (4)	0	3 (7)	0.14
Pneumothorax				
*Right, n (%)	38 (54)	14 (48)	24 (57)	0.39
*Complete, n (%)	69 (97)	27 (93)	42 (100)	0.08
*Light's index (%)	58 (37–93)	33 (19–50)	84 (45–95)	<0.0001
Duration of pneumothorax prior to NA, hours	14 (6.5–29)	29 (7–56)	10 (6–16)	0.006
>24 hours of pneumothorax evolution prior to NA	21 (30)	16 (55)	5 (12)	0.001
>48 hours of pneumothorax evolution prior to NA	13 (18)	10 (34.5)	3 (7.1)	0.005
Occurrence of at least a short-term complication, n (%)	0	0	0	0
Patient self-reported maximal pain* during ► Needle aspiration, units ► Chest tube insertion procedure, units	3.6 (0–6) 4 (1–7)	2 (1–5)	5 (0–7)	0.09
Need for surgical pleurodesis, n (%)	28 (39)	5 (17)	23 (55)	<0.0001
Length of ICU stay (days)	2 (1–3)	1 (1–2)	3 (3–5)	<0.0001
Length of hospital stay (days)	2 (1–3)	1 (1–2)	3 (3–5)	<0.0001
One-month recurrence rate, n (%)	3 (7)	2 (7)	1 (2)	0.7

Data are presented in n (%) or median (IQR) as appropriate. Late success was defined as the absence of chest tube insertion within 7 days; hemothorax was defined as haematic pleural effusion requiring thoracic drainage and *a vacuo* pulmonary oedema was defined as occurrence of localised alveolar interstitial opacities on post-procedure chest X-ray. Patient self-reported maximal pain during the NA and/or chest tube insertion procedure was evaluated with the use of a numeric scale from 0 (no pain) to 10 (worst possible pain).

*Patients self-reported pain was available for the 58/71 NA and 27/39 chest tube insertion procedures.

F, female; ICU, intensive care unit; M, male; NA, needle aspiration.

multivariable analysis, in spite of a wide CI, we showed that NA performed after 48 hours of PSP evolution was associated with success. Two hypotheses can be drawn to explain these results. First, the delay to NA might allow for the local inflammatory reaction to participate in the closure of the pleural breach, and thus contribute to the success of NA. Next, one can suspect that NA might be more successful if the air leak is of limited importance. In the same line of reasoning, PSP with small leaks may be better tolerated, and referred later to the hospital than PSP with larger leaks. Regarding the latter,

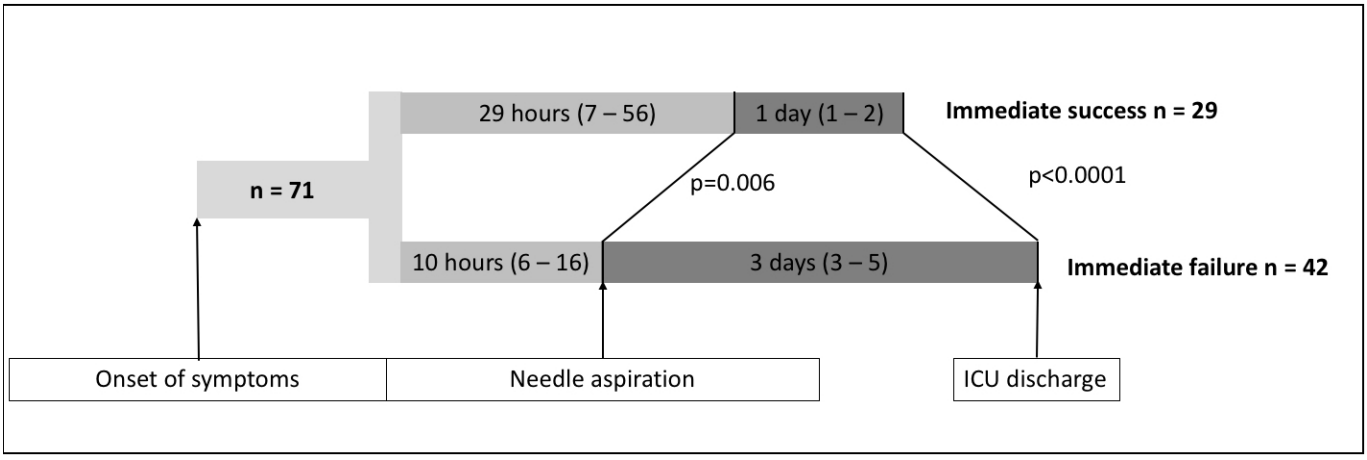

Figure 2 Time chart of needle aspiration and length of stay according to immediate success of the procedure in the validation cohort. A significant difference in duration of pneumothorax was evidence according to the success of NA. Likewise, patients with an NA success had a significant shorter length of intermediate care or ICU stay. ICU, intensive care unit.

however, we did not evidence any significant difference in Light's index according to the delay of PSP evolution. As the third hypothesis, one could speculate that some of these pneumothoraces could have had a spontaneous resolution. Obviously, only a randomised trial of an immediate versus delayed NA would answer this question.

Limitations

Our results must be interpreted in light of the following limitations. First of all, the study was underpowered, which may explain the lack of differences observed in this report. One consequence of the small sample size was the wide CI for the measure of association between the delay in performing NA procedure and its outcome. Another consequence of the small sample size is the limited support to the generalisability and reproducibility of the findings. Next, in the discovery cohort, necessary parameters to calculate Light's index were not always recorded, so we were unable to provide the Light's index for this cohort. This is the reason why we were not able to merge both cohorts in the multivariable analysis, which would have noticeably increased the power of our analysis. During both study periods, the first chest X-ray, necessary to calculate Light's index, was frequently performed outside the hospital. Some of those were, therefore, lacking in the patients' files. Furthermore, some pneumothoraces were localised, therefore preventing Light's index calculation. In the prospective phase, Light's index was calculated in the vast majority of patients (73% (52/71)).

It has to be underlined that the median Light's index was 33% in PSP with NA success. BTS guidelines advocates that NA is recommended in case of interpleural distance of more than 2 cm at level of the hilum (equivalent to a Light's index of 50%) or in the case of symptomatic PSP.[1] We do acknowledge the fact that some NA were performed in patients who could have perhaps benefited from a simple ambulatory monitoring, according to British guidelines, and a wait full strategy could have been sufficient. However, most of these pneumothoraces were complete and because NA is a minimally invasive technique, physicians in charge believed it was reasonable to perform the NA in order to hasten patient's discharge. Of note, most of these patients were referred to in our centre for drainage, which may have influenced our physicians to act rather than to wait and see. Interestingly, physicians faced with complete but asymptomatic PSP may have very different therapeutic attitudes. In a survey of 178 intensivists asked how to manage a complete and asymptomatic PSP, with an interpleural distance of 1 cm at level of the hilum, 60% of responders would have performed a thoracic drainage, while 22% would have chosen a conservative strategy[16] and only 17% a NA. Last, it should be stressed that it is our routine policy to admit patients with PSP for a minimal 12 hours monitoring. Therefore, our strategy could have no impact on admission rates but only on length of stay. As in a great number of French hospitals, we are prone to admit in our intensive or intermediate care unit patients with pneumothorax, even though they do not exhibit acute respiratory failure signs.

Clinical implications

Our findings may help clinicians to identify patients most likely to respond to a treatment by NA. Our data suggest that a strategy of delayed NA for the management of PSP could be tested. In this case, a 48 hours ambulatory treatment before performing NA might increase success rates.

CONCLUSION

In the treatment of PSP, longer duration of time from symptom onset to NA and pneumothorax size predicts the success of NA. Further prospective studies are needed to confirm these results and to optimise the best management of PSP.

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Contributors CV, J-DR and JM contributed to the manuscript's conception, design, drafting and critical revision, and agreed to be accountable for all aspects of the work. FD, JA and DD made substantial contributions to analysis and interpretation of data, were involved in drafting the manuscript, gave approval of the present version of the manuscript and agreed to be accountable for all aspects of the work. SG, DR, MC and NJ made substantial contributions to interpretation of data, revised the manuscript for important intellectual content, gave approval of the present version of the manuscript and agreed to be accountable for all aspects of the work.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests J-DR and JM received reimbursement of congress fees from Fisher & Paykel.

Patient consent for publication Not required.

Ethics approval The Ethics Committee of the French National Society of Intensive Care (SRLF, CE 12-364 and 14-08) approved the study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

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